PEOPLE'S DEMOCRATIC REPUBLIC OF ALGERIA
MINISTRY OF HIGHER EDUCATION AND SCIENTIFIC RESEARCH
UNIVERSITY OF CHAHID HAMMA LAKHDAR, EL OUED, ALGERIA

FACULTY OF EXACT SCIENCES
DEPARTMENT OF CHEMISTRY

Chemistry of natural products

A lecture series dedicated to third-year organic chemistry students

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Contents

Introduction

Introduction

It was not easy to prepare a publication on the chemistry of natural products, and this is due to the lack of availability of foreign references dedicated to teaching this course to chemists. However, I was able to prepare this publication that addresses the topics of the natural products course, and I prepared most of its topics in the academic year 2023-2024 in the form of lectures and modified it more than once. In line with the Natural Products Chemistry course curriculum, we began our topic with a brief introduction to natural products in general, and then we touched on the study of the following topics:

- **Terpenes**
- **Steroids**
- **Alkaloids**
- **Phenols**
- **Saponins**

I place this humble effort in the hands of dear students, and I hope that it will be useful to them in their studies. In conclusion, I say that achieving perfection is impossible, and it is human nature that his work is always marred by imperfection.

I greatly hope that no one will hesitate to make any comments or corrections.

The first axis
General concepts about natural product chemistry

I. General concepts about natural products chemistry :

Natural product chemistry is a science that studies organic compounds of natural origin. Natural products are substances produced by living organisms; the most important of these ingredients are those that play a role in metabolic interactions and are separated from plants and microorganisms, Natural products can be divided into two large parts:

- Primary metabolites: They often refer to the basic metabolic processes that result in simple carboxylic acids and amino acids, sugars, lipids, and proteins.

- Secondary metabolites: Primary metabolites are the primary substances of secondary metabolites. There are three main primary substances: chequic acid, acetate, and amino acids. Construction units are considered secondary metabolites.

The products of secondary metabolism themselves are divided into different types, but the method used to divide them varies from one source to another. They may sometimes be classified according to the natural sources from which they are produced, and other times they may be classified according to their physiological effects (some of them are used as antibiotics, some are antivirals, and some are pain relievers). They may also be classified, which are the most common cases, according to their structural composition, or at least be studied in groups. Where it is classified into:

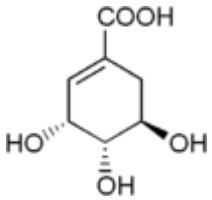
- Terpenes
- Phenolic compounds
- Alkaloids
- Vitamins
- Steroids
- Saponins

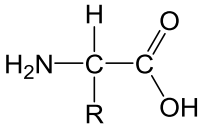
Although many compounds derived from their natural sources offer great benefits to humans, their role in plants has not been defined before, In recent years, it has been shown that one of their functions is to secure the survival of a particular organism in harsh living conditions.

Secondary metabolic products are also considered to have a variety of therapeutic characteristics, as they play a major role in the field of medicine and pharmacy, because of their functional physiological effects on the organism, particularly human beings, and their presence in plants earns

them a special classification as medicinal plants. Perhaps the most practical steps the student is exposed to in the field of natural products can be limited to:

- How to get these products and extract them from their natural sources.
- How to separate these natural ingredients from each other, in order to obtain pure compounds.
- How to identify the structural composition of pure compounds using physical and chemical methods (melting point, boiling point, measuring optical activity, and performing some reactions to determine the identity of the active groups contained in the natural compound) as well as spectroscopic analysis methods.

Shikimic acid: 

acetate: CH_3COO^- Amino acid : 

I.1. Metabolism in living organisms:

Metabolism is the sum of the chemical and physical transitions that a substance passes through in a living cell. It provides the living organism with the energy and matter it needs. These reactions catalyzed by enzymes allow living organisms to grow and reproduce, maintain their structures, and respond to their environments in order to achieve three goals: converting food into energy to run cellular processes, converting food into building blocks for proteins, fats, nucleic acids, and some sugars, and removing metabolic waste. Most of the structures that make up animals, plants, and microbes are made up of three basic categories of molecules: amino acids, carbohydrates, and fat. The metabolic function is concentrated in the use of these molecules to build cells and tissues, divide them, and use them as an energy source. These chemicals can combine to form polymers such as DNA and proteins, thus classifying metabolic reactions into two categories:

I.1.1. Catabolism: the breakdown of complex substances with the release of energy.

I.1.2. Anabolism: the formation of complex materials with energy storage.

Construction in self-fed organisms begins with the process of photosynthesis, which leads to the construction of carbohydrates, fats, proteins, acids, and vitamins. The construction process includes:

1. Photosynthesis: the formation of simple sugars (carbohydrates) in the form of glucose from water and carbon dioxide in the presence of sunlight and chlorophyll dyes.

2. Fat formation: Like the provision of glycerin and fatty acids, the cell creates all the fats and lipids it needs.
3. Protein formation: It is composed of amino acids in the cell through aminotransferase with ketoacid (carbohydrate or fat).

I.2. Antibiotics

I.2.1. Definition of antibiotics

They are effective substances or medications used to eliminate bacteria. They are produced by extracting them from plants, or producing them fully industrially. They work either by eliminating the bacteria directly, stopping their growth, or weakening them to be overcome by the immune system of the human body.

I.2.2. Mechanism of action of antibiotics:

Antibiotics work through different mechanisms, including:

- Destroy bacterial cell walls and prevent their formation, which is the most common mechanism in antibiotics.
- Destroy proteins found in bacterial cells and inhibit their functioning.
- Inhibit DNA division within bacteria.

I.2.3. Types of treatment :

Antibiotics treat several diseases caused by bacteria:

- Sore throats are caused by streptococcal bacteria.
- Serious and acute bacterial infection.
- People who suffer from chronic health problems such as asthma, diabetes, and lung disease.
- Older people or those with weak immunity generally suffer as a result of some illness.
- Middle otitis.
- Conjunctivitis (eye ashes).
- People with a high susceptibility to gastrointestinal diseases and complications.
- Dermatitis, tissue, or urinary tract.

I.3. Antivirals:

I.3.1. Definition of antivirals

It is a drug (pills, liquids, or powder for inhalation) used to treat viral infections (colds, influenza, etc.).

I.3.2. Viruses and their discovery and antidotes:

Viruses cause familiar infectious diseases such as: the common cold, influenza, and warts. They also cause severe diseases such as: HIV, smallpox, and Ebola. The discovery of antivirals has been delayed compared to antibiotics, because the virus is a genetic material with some enzymes surrounded by a protective layer of protein.

I.3.3. Virus reproduction cycle

Viruses are one of the smallest parasitic organisms in our world and are characterized by their inability to reproduce without relying on other organisms' cells, whether they are plants, animals, humans, or bacteria.

Viruses are transmitted to organisms in many ways, and they exist around us everywhere in huge numbers. Although there are different types of viruses, there are basic steps similar to the life cycle of viruses. The virus's reproduction cycle includes:

1. Binding to and penetrating the host cell surface: all cells in organisms have a wall surrounding their components, which contains receptors located on its surface. Viruses use appendages on the surface of their outer shell to bind to receptors on the surface of the host cell wall and act as a gateway to enter it. The different components of these receptors determine which types of viruses have the potential to enter and reproduce in certain cell and organism types.
2. Getting rid of the virus from its outer layer: After the virus succeeds in attaching to the cell surface, the process of getting rid of the outer shell of the virus begins in a way that allows it to penetrate the cell to reach the cytoplasm. either through enzymes excreted by the virus or by host cell enzymes, spreading the virus's DNA into the host cell in preparation for its reproduction.
3. Reproduction of virus genetic material: viruses can only replicate by using ribosomes found in the host cell, the genetic material of the virus is produced by the host cell instead of reproducing the genetic material of the organism. which leads to a defect in the functions of the host cell, and the production of virus-specific proteins. The step of cloning the genetic material is the most important step in the virus reproduction cycle, and the main difference in

this process is between the different types of viruses that contain deoxyribonucleic acid (DNA) and ribonucleic acid (RNA).

4. Production of a group of viral particles: After the virus successfully uses the host cell to clone its genetic material and create viral proteins, the process of combining these ingredients with each other begins to produce new viral particles in order to sustain the virus' reproduction cycle.
5. Release of viral particles: After producing new viral particles, the process of releasing these viruses into neighboring host cells begins. Before releasing the virus, an outer shell is formed that allows the new viruses to leave the current host cell. This process, which differs between different types of viruses, takes place

in one of the following two ways:

- Budding outside the cell without destroying it.
- Decomposition of the host cell wall, leading to its destruction and death.
- What happens to the virus after it reproduces in the body?

After the virus enters the body and the virus reproduction cycle begins, the immune system begins its work to eliminate the virus and infected host cells. If there are antibodies to the virus, either as a result of a previous infection or vaccination, the immune system quickly recognizes and eliminates it.

In the event of infection with the virus for the first time, the immune system usually needs 3–4 days to produce immune cells against the virus, and during this period, symptoms may appear as a result of the virus destroying some infected body cells, in addition to the body's attempt to resist the infection through methods including high temperature, sneezing, and diarrhea. Until the full immune response occurs and the virus is eliminated,.

The body's ability to resist viruses depends on the type of infectious virus, and the ability of the immune system to eliminate the virus, which makes the response to certain types of viruses vary from person to person and from virus to virus.

- Where is the risk of viruses?

The danger of viruses lies in their ability to manipulate the genetic material of the host cell, which may sometimes cause the following: The occurrence of cancers, such as: human papillomavirus (HPV),.

Chronic viral infection, such as: hepatitis C virus and the acquired immunodeficiency virus (HIV).

In addition, viruses have the ability to mutate and develop their own viral proteins to attack cells in other living organisms and increase the speed of their transmission.

These characteristics of viruses are among the most dangerous factors that lead to the emergence of epidemics, especially viruses that are transmitted from animals to humans, such as: swine flu, bird flu, and coronavirus.

In general, the antivirals that have been discovered are less effective than expected. This is because viruses have the ability to reproduce quickly and in a very frightening manner, and they have the ability to cause mutations that make them resistant to drugs.

I.3.4. Antiviral medications:

One of the categories of antimicrobial drugs is a large group that also includes antibiotics, antifungal drugs, and anti-parasitic medicines. These drugs are relatively harmful and can therefore be used in the treatment of infections. In this regard, a distinction should be made between an antiviral drug and an antiviral killer who does not fall under the category of medicines, but destroys virus particles outside the body.

Antivirals are divided into the following types:

- Antivirals recommended for treating influenza: The Centers for Disease Control and Prevention have recommended antivirals approved by the Food and Drug Administration to treat and prevent influenza, and they include the following:
- Oseltamivir: Side effects include vomiting and nausea.
- Baloxavir marboxil: This medicine cannot be used by pregnant or breastfeeding women.
- Zanamivir: Using this medication may cause bronchospasm.
- Peramivir: One of its most prominent side effects is diarrhea.
- Antivirals to treat HIV:

Efavirenz: Its most prominent symptoms are depression, nervousness, dizziness, insomnia, and fatigue.

- Antivirals recommended for the treatment of hepatitis C:

Adefovir: Its use may cause headaches, diarrhea, gas, indigestion, and general weakness.

I.3.5. Antiviral resistance:

All antimicrobials, including antivirals, may be subject to what is known in medicine as drug resistance because pathogens mutate over time, which reduces their response to treatment.

I.4. Painkillers

I.4.1. Definition: Those drugs or drugs that specifically and selectively relieve pain without obstructing the connections of nerve impulses or affecting sensory cognition, this selectivity is what distinguishes between analgesics and psychedelics.

I.4.2. Types of Painkillers

Painkillers are classified into two types:

1. Anti-inflammatory drugs: They relieve pain by reducing local inflammatory responses, and are used to relieve short-term pain and localized or mobile pain such as headaches, muscle strain, arthritis, and bruises.

Most of these painkillers are drawn from three compounds:

- Salicylic acid (perazolone or perozolate): Organic compounds are an unsaturated five-ring consisting of three adjacent carbon and two nitrogen atoms and have important applications in medicine and pharmacy due to their anti-inflammatory and anti-heat palliative properties.
- Vitacitin, or acetophenetidin, is a compound derived from ampedophenol and exists in the form of colorless crystals that are poorly soluble in water. It is used to reduce fever and remove headaches, nerve pain, and rheumatism. Although these drugs are not of chemical origin, It has the ability to relieve mild to moderate pain through procedures that reduce inflammation at its source.
- Acetylsalicylic acid, or aspirin, is the most widely used mild analgesic and is considered the prototype of anti-inflammatory treatments.

I.4.3. Narcotic painkillers

They affect the brain and are called narcotics because they cause drowsiness and induce sleep. Opioid painkillers are used to treat moderate and severe pain or chronic pain. These painkillers work by binding to opioid painkiller receptors, which are abundant in the brain and spinal cord, and work to relieve severe pain in the short and long term.

- ✓ Opium: is a dried powder of poppy juice or liquid. When taken orally, opium helps sleep and stimulates a state of happiness and relaxation. It was also found that opium extract contains

more than 20 alkaloids, the most important of which are morphine, codeine, and papaverine. These pure alkaloids were used as an alternative to crude opium extracts in treatments.

- ✓ Codeine: It is a natural opioid alkaloid that can be manufactured and is a useful oral analgesic. The mechanism of action of codeine depends on changing the way the brain and nervous system respond to pain, which leads to reducing the feeling of pain for specific periods.
- ✓ Morphine: It is a powerful pain reliever from the opioid class that works directly on the central nervous system to reduce the feeling of pain. It can be used for both acute and chronic pain. It is extracted from the opium plant.
- ✓ Papaverine: It is an opioid alkaloid, an antispasmodic and analgesic drug, and is considered a vasodilator drug. There are also synthetic analogues of morphine, such as: meperidine, Demol, methadone, and taloxone.

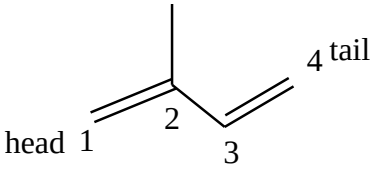
Just as painkillers have benefits in treating some infections, relieving spinal pain and toothache, relieving the pain of cramps, and reducing fever, they also have negatives, as they are capable of causing digestive and kidney problems, nausea, facial redness, itching, etc., so it is not recommended to use them frequently. Except for necessity.

The second axis

(Terpenes)

II. Terpenes:

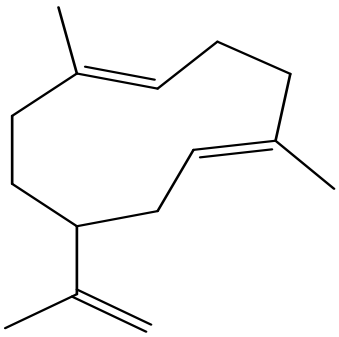
II. 1-Definition: Terpenes constitute the largest group of products in the plant kingdom. They are compounds with chemical formulas whose structures include multiples of five carbon atoms (C_5H_8). In the early twentieth century, Ruzicka was able to identify the common structural unit in terpenes. The arrangement of the groups that each consists of these, there are five carbon atoms within each compound that can be attributed to the 2-methyl buta-1,3-diène (isoprène) molecule, i.e., multiples of the isoprène .



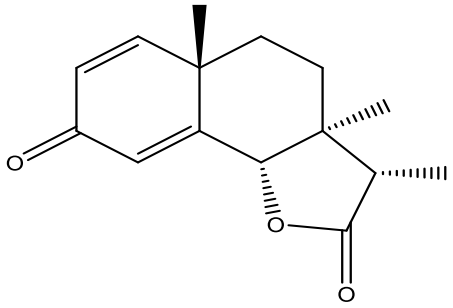
Unit Isoprene units are mostly linked to each other via a C1 (head) unit with a C4 (tail) of another isoprene unit. According to this rule, terpenes are divided into:

- ✓ monoterpenes (two units of isoprene) ..... C_{10}.
- ✓ Sesquiterpenes (three isoprene units) ……C_{15}.
- ✓ Diterpenes (four isoprene units) ..... C_{20}.
- ✓ Sesterterpenes (five isoprene units) ……C_{25}.
- ✓ Triterpenes (six isoprene units) .....C_{30} .

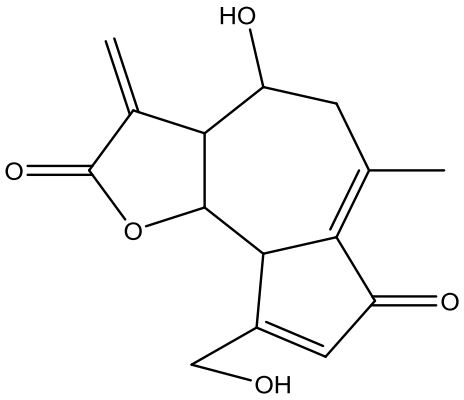
The volatile (essential) oils in aromatic plants are nothing but monoterpenes and sesquiterpenes (half-triplets), and the latter constitute that part of the volatile oil that has a higher boiling point. Fifteen carbon atoms are included in the structure of the sesquiterpenes (C_{15}), and they have different structures. They may be open or cyclic, monocyclic, bicyclic, or tricyclic. Monocyclic ones are more widespread in nature than their noncyclic counterparts. The germacrene structure is more famous in nature in the form of lactone sesquiterpenes. The latter is generally considered the most widespread type of these terpenes. It comprises more than 3,000 known structures. The history of terpenes is very ancient. A compound such as santonine or lactucine has been known for more than a century.



germacrene



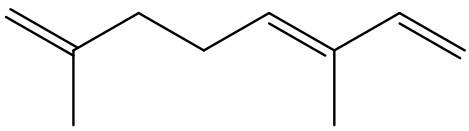
Santonine



lactucine

II.2. Category:

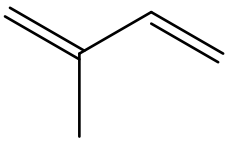
What most terpenes have in common is the presence of a central isoprène unit in the structure, which can be present more than once, resulting in multiple isoprène formulas.



3,7-Dimethylocta-1,3,7-triène

Ocimène

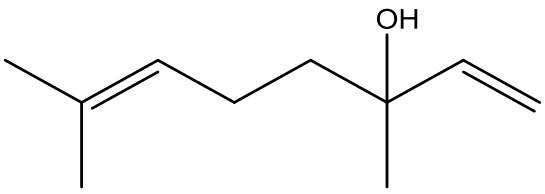
($C_{10}H_{16}$)



isoprène

2-méthyl buta-1,3-diène

(C_5H_8)



3,7-dimethylocta-1,6-dièn-3-ol

linalol

($C_{10}H_{18}O$)

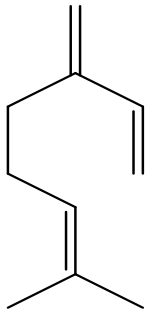
These terpenes may appear at first to be the result of the condensation of isoprène molecules with each other, but in reality the primary basic material for building terpenes within their natural sources is not isoprène, but rather there is another mechanism that takes place called biosynthesis (La biosynthése) starting from a carboxylic acid, and the terpenes are divided. to me:

II.1.2. Mono tenpène:

II.1.1.2. Chemical structure:

In the case of hydrocarbons, the monoterpene compounds often have the general formula $C_{10}H_{16}$, whose structure in three basic states is as follows:

- ✓ **A structure with three double bonds**: in the case of acyclic monoterpenes.

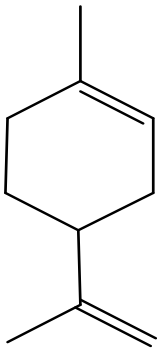


7-Methyl-3-methylene octa-1,6-diène

Myrcène

(Laurier)

- ✓ **Structure with two double bonds and a carbonic cycle :** a monoterpene cyclic state.



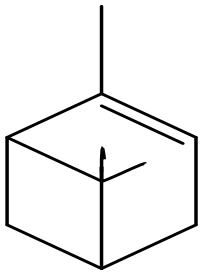
(1,1-Dimethyl 4-vinyl cyclo hexene)

limonène

(Citron)

- ✓ **Structure with a double bond and two carbonic cycles :** this is the case of a monoterpene dicyclique.

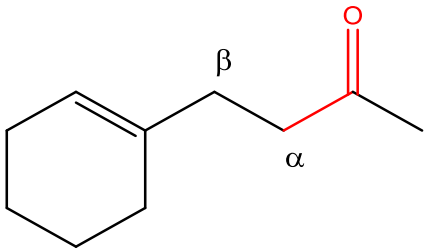
Example:



α_pinène (Pin)

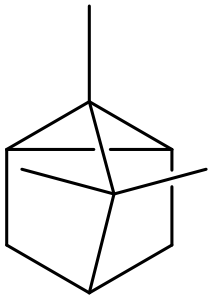
(The difference between α and β) is that the first carbon atom attached to the active group of the terpene is called α , and the next atom is called β .

Example:



- ✓ **Three carbonic cycles structure**: This is a very rare case and comes from the isomers found in essential oils (les huiles esentielles).

Example:

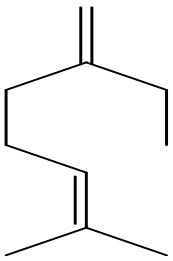


Tricyclène

Notes:

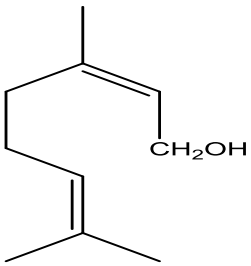
- ✓ Non-cyclic terpenes are represented in a semicyclic form, which enables them to bond more easily than their isomers or cyclic counterparts due to the large number of unsaturated bonds.

  Example: Myrcene



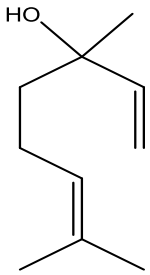
(Myrcène)

- ✓ compound Oxygenated monoterpenes: They are either alcohols, ketones, or aldehydes. In the case of alcohols, the general formula is $C_{10}H_{18}O$, which relates to the addition of water to monoterpene hydrocarbons or the oxidation of allyl sites. Example:



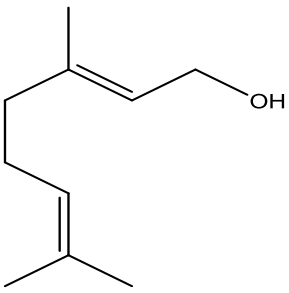
nèrol

(cyclamen)



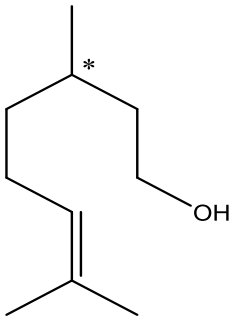
linalol

(La vande)



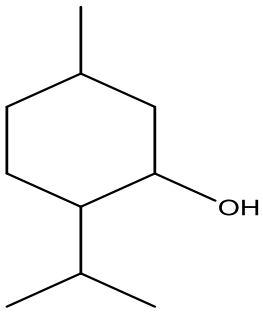
géraniol

(rose)



citronellol

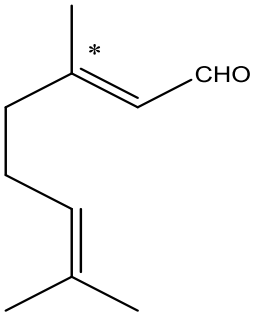
(citron)



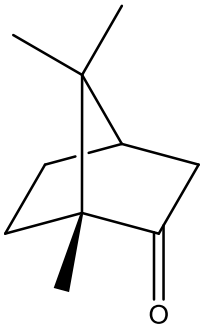
mentol

(menthe)

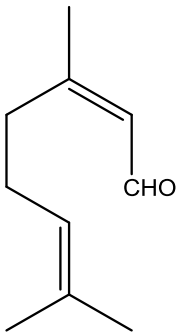
- ✓ Carbonyl derivatives come from the oxidation of alcohols and generally have the general formula $C_{10}H_{16}O$.



géranial



Camphre



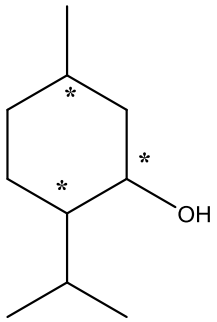
néral ✓

- ✓ Terpenes are usually in the form of an oil mixture (essence), such as rose oil (essence de roe), containing (40 to 60%) geraniol and (20 to 40%) citronellol and hydrocarbons.

2.1.2. Physical properties and isomers:

Physical properties and isomers Monoterpenes are usually in liquid form, with the exception of camphor, which, in its solid state, has a melting point of 180°C.

The above-mentioned formulas for monoterpenes contain structures that are often chiral. We can find a dextrogyre (right-rotated R), lévogyre (left-rotated S), or racemique (S,R) compound. Example: If we take (menthol) .



Menthol contains three asymmetrical carbon atoms. Asymetiqu, it is possible to find eight stereoisomers ($2^n=2^3=8$) in the form of dextogyre or levogyre, and Figure 1 shows the various isomers of menthol:

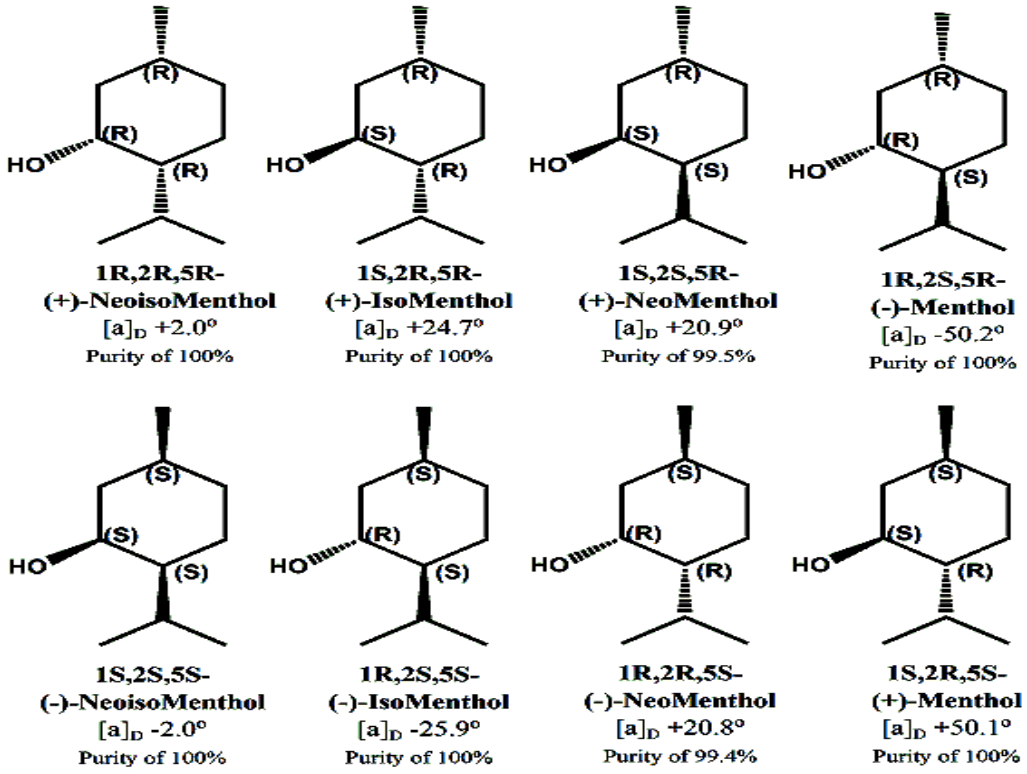
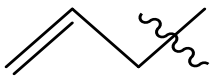


Fig. 1: isomers of menthol

II.2.1.3. Chemical properties:

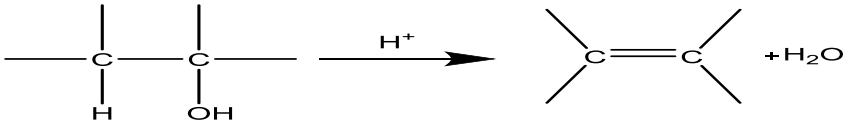
Moterpenes are considered very active due to the presence of T-bonds, either isolated or conjugated within the structure. Therefore, we find several typical reactions among their types (addition, isomerization, cyclization, re-position, etc.).

- ☒ The oxidation reaction may be related to the allyl positions. In the terpene compound, this is a very common reaction, which explains the sensitivity of perfumes to air.



allyl

- ☒ Concerning alcohols, they can be subjected to a dehydration reaction when the temperature rises, as follows:



A. The case of terpene hydrocarbon compounds: Pinéne compounds are among the most widespread monomers and the most easily obtained compounds, and the presence of the cyclobutane ring in them gives the compound high effectiveness.

☒ **Air oxidation:** In the case of a pinéne, we obtain a mixture of verbenol and myrtenol, accompanied by verbenone and myrténol, as in **Figure 2.**

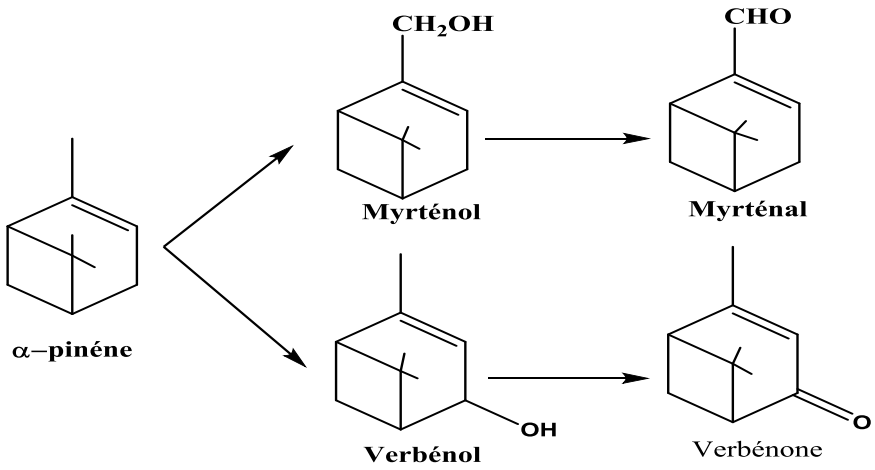


Fig. 2: Oxidation of α -pinéne by air

We notice in this case that the alcoholic functions enter the allelic positions, and this explains why the reaction is radical, as the hydrogen is removed, leading to a stable allelic radical, and this allelic radical then stabilizes the oxygen present in the air to obtain the required alcohols and then carbonyl derivatives.

$$R^{\cdot} \xrightarrow[h\nu]{O_2} R\text{-}O\text{-}O^{\cdot} \xrightarrow[-R^{\cdot}]{RH} R\text{-}O\text{-}OH \xrightarrow[h\nu]{} RO^{\cdot} + {}^{\cdot}OH \xrightarrow[-R^{\cdot}]{RH} ROH + H_2O$$

- **Thermal dehydrogenation reaction (thermal hydrogenation):** This reaction leads to obtaining aromatic hydrocarbons (hydrocarbons aromatique). This reaction can be used in the analysis of terpenes, as shown in **Figure 3**.

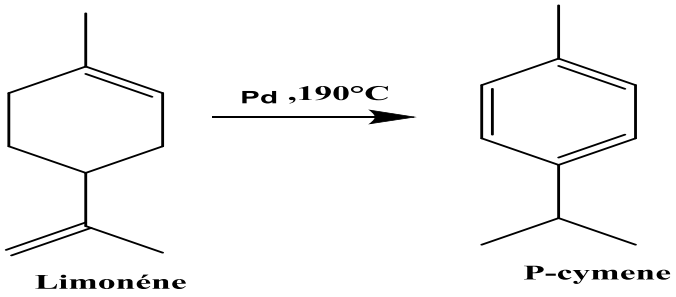


Fig. 3: Thermal dehydrogenation reaction

In the first stage, H_2 is removed. From the cycle structure, the hydrogen is fixed to the double bond of the alkyl radical due to the presence of palladium, Pd, and is not fixed to the ring because the cycle structure is stabilized by the mesomeric action inside the ring, making it stable.

- **Addition of chlorine acid (HCl) in the gaseous state to pinénes:** This interaction is temperature-dependent, as the cyclobutanes ring does not react at temperatures below 17°C. In this case, a-pinene and B-pinene produce chloropinane. The mechanism involves electrophilic addition following the Markovnikov rule, as depicted in **Figure 4**.

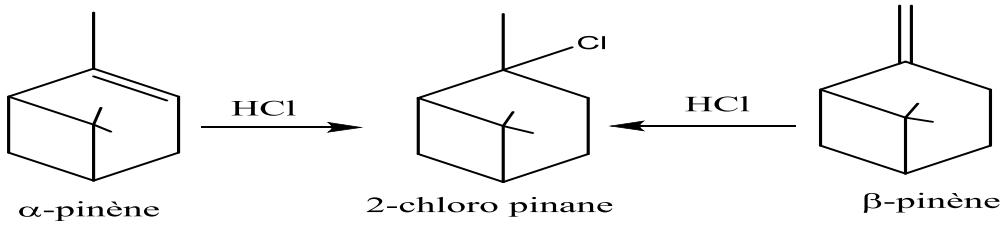


Fig. 4: Reaction of adding HCl in the gaseous state to pinénes

Upon heating the previous mixture or initiating the reaction from the outset at elevated temperatures (°C), a less stable ring opening occurs, accompanied by a rearrangement facilitated by the Wagner-Meerwein shift. The initial step always involves protonation, yielding the pinyl cation. However, in this scenario, there is a possibility of obtaining more stable carbocations through rearrangement. Consequently, the appearance of the carbocations (fenchyl and bornyl) results in a nucleophilic attack on carbon (C), yielding two primary products: fenchyl chloride and bornyl chloride. Bornyl chloride predominates, indicative of the higher substituent group's reactivity, as depicted in **Figure 5.**

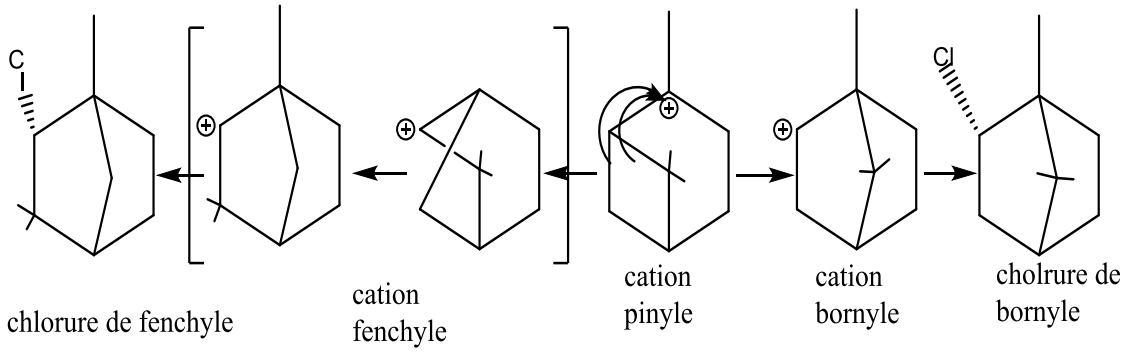


Fig. 5: Nucleophilic attack of (Cl^-) on the carbocation (bronyle, fenchyle)

- **Adding liquid HCl to pinenes :**

regardless of their initial structure (primary or otherwise), results in the opening of the cyclobutane ring of the pinyl cation. This produces the menthenyl cation, which is then attacked by the chloride ion (Cl) to form chloromenthene. Subsequently, chloromenthene can undergo further addition with another molecule of HCl, resulting in the final product of the reaction, dichloromenthane, as depicted in **Figure 6**.

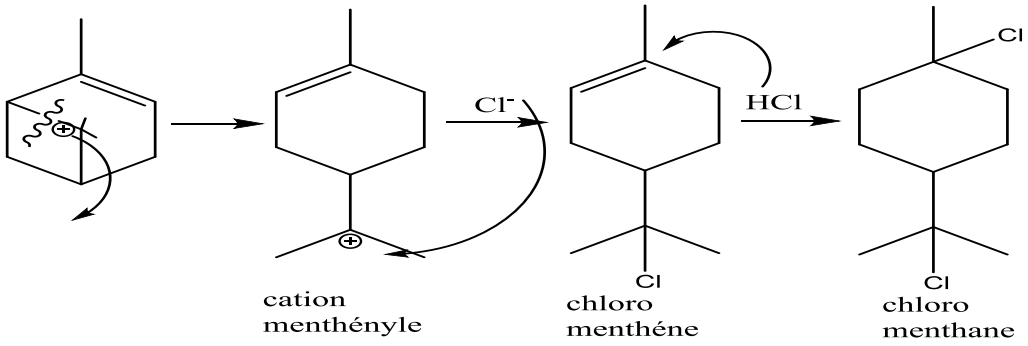


Fig. 6: Reaction of Adding Liquid HCl to Pinénes

- **Adding dilute H_2SO_4 to pinenes :**

follows a mechanism similar to the previous one, yielding unstable terpene sulfonic acid, which readily hydrolyzes to produce terpinole. The second attack leads to the final product, terpinene, in the cis form, which is the most stable. Dehydration of the product yields eucalyptol, utilized pharmaceutically as a respiratory antiseptic, as shown in **Figure 7.**

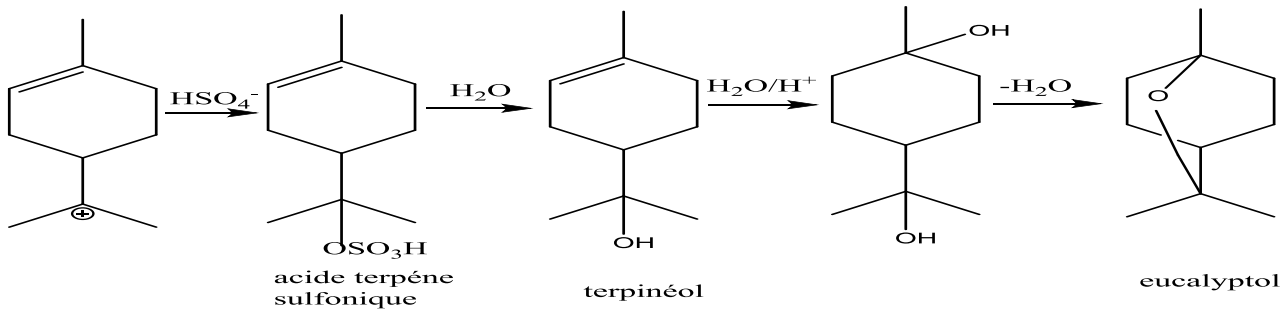


Fig. 7: Reaction of adding diluted H_2SO_4 to pinénes

- **Adding water in an acidic medium**, **for example (myrcene) :**

The first step involves protonation to produce the linalyl carbocation, which undergoes resonance to generate the freely rotating neryl carbocation. This allows for the conversion of the linalyl carbocation to the geranyl carbocation. Each carbocation yields alcohol by water addition, where water attacks the carbocationic position, as depicted **in Figure 8.**

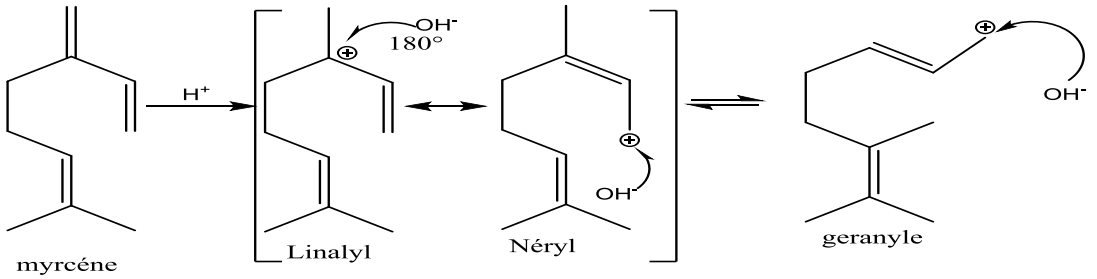


Fig. 8: Water addition reaction in an acidic medium, example of myrcéne

A-alcohol case: Cyclization in an acidic medium This reaction generally produces six-membered rings; for example, nerol readily cyclizes to form terpineol, as shown in Figure 9.

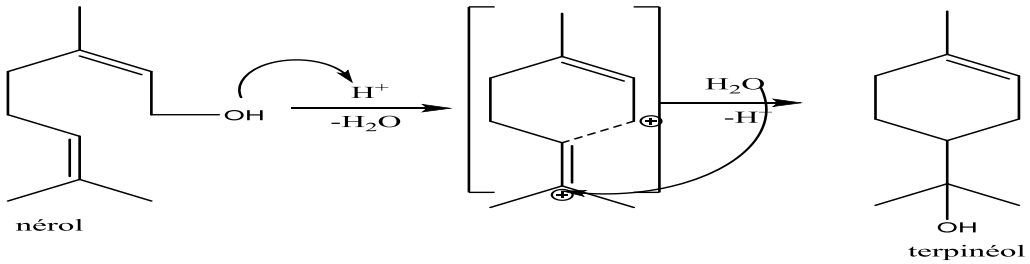


Fig. 9: Water addition reaction in an acidic medium, an example of myrcéne

B- In the case of aldehydes and ketones: One of the most studied compounds is camphor (OXO-bornane Campire-2) due to its widespread occurrence. In the case of the bromination reaction with camphor, proton substitution occurs with bromine at the 1 position, as depicted in **Figure 10.**

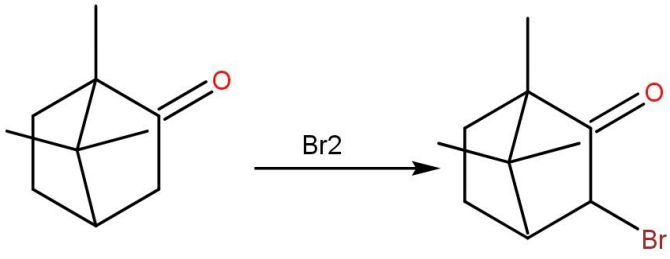


Fig. 10: Bromation reaction in camphor.

In the presence of sodium amide (NaNH2) and carbon dioxide, a carbonylation reaction occurs. Additionally, proton substitution takes place at the same site, as depicted in **Figure 11.**

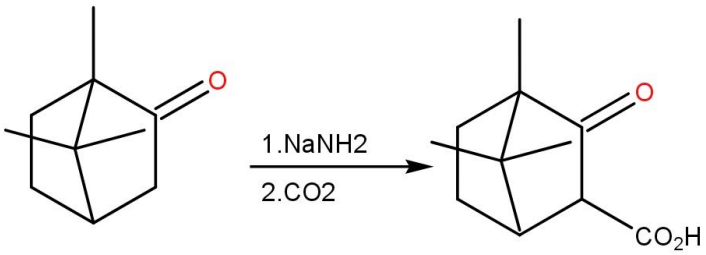
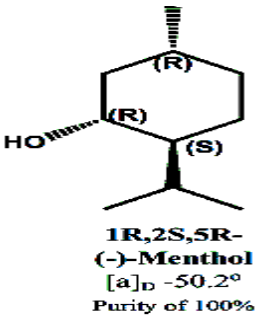


Fig. 11: Substitution reaction in camphor.

II.2.1.4. Organic preparation of monoterpenes:

Preparing menthol: Verbéneol is obtained by the air oxidation of α-pinene, which undergoes thermal decomposition at 200°C under pressure, leading to the opening of the cyclobutane ring and the formation of pipériténol. Catalytic hydrogenation of pipériténol yields a mixture of alcohols, from which menthol (-) can be isolated.

The interaction occurs as shown in **Figure 12.**



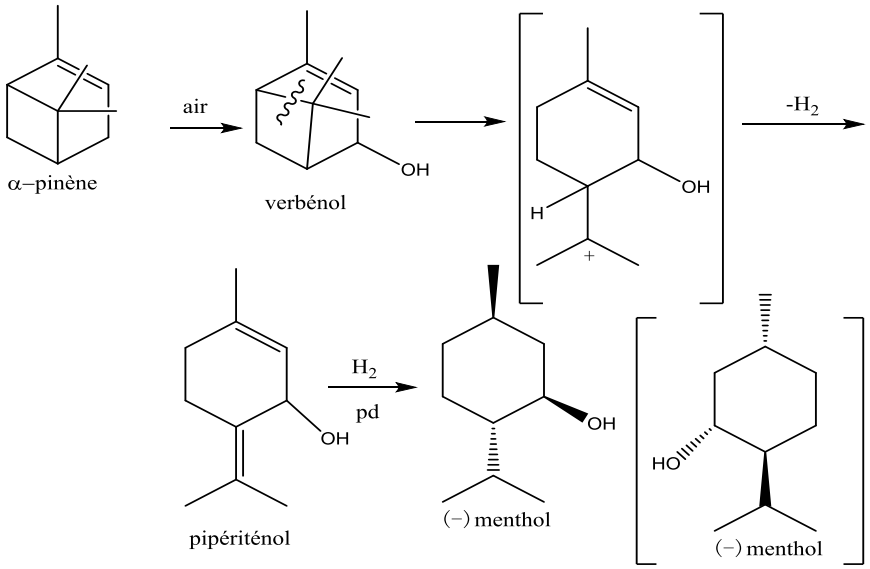
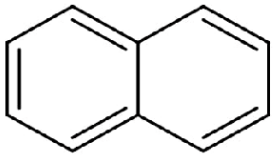


Fig. 12: Menthol preparation reaction Menthol

is naturally extracted from peppermint oil and is a well-known pharmaceutical product as a cough suppressant.

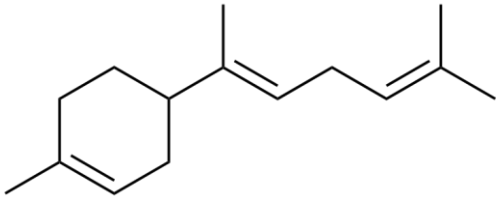
II. 2.2. Les Sesquiterpenes:

Sesquiterpenes, also known as sesquiterpenoids, consist of three isoprene units and exhibit a wide variety of chemical structures. The large number of possible structures presents challenges in elucidating their chemical makeup, particularly for compounds that are not readily transformed into naphthalene-like derivatives Naphtalénique structure



Naphtalénique structure

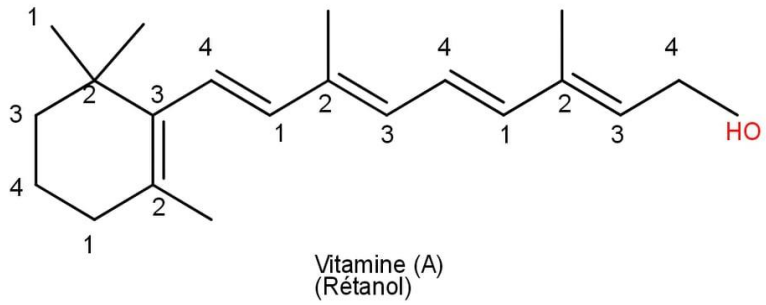
One of the well-known non-cyclic sesquiterpenes is farnesol, extracted from the lily tree (Lys). It is represented as an E isomer at the level of the double bond. Farnesol can undergo dehydration in an acidic medium to produce bisabolene, an oil found in bergamot oil, which can be extracted from bergamot fruit, a citrus fruit resembling a pear.



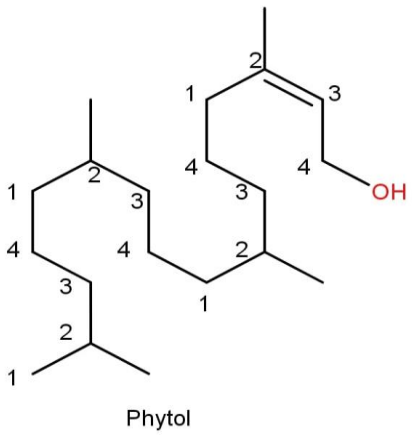
Bisabolène

II.2.3 Diterpenes: Diterpenes consist of 4 units of isoprene (C_5H_8), with most being polycyclic.

Example:



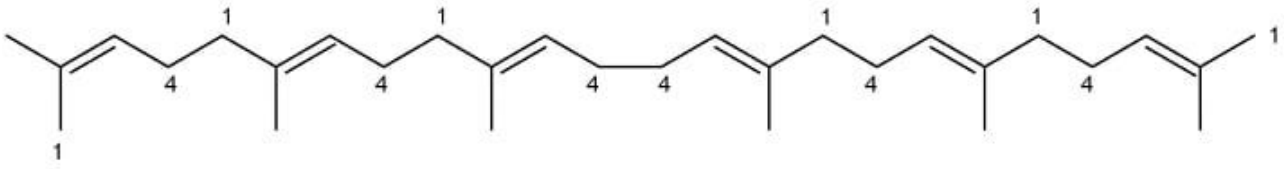
Vitamine (A)
(Rétanol)



Phytol

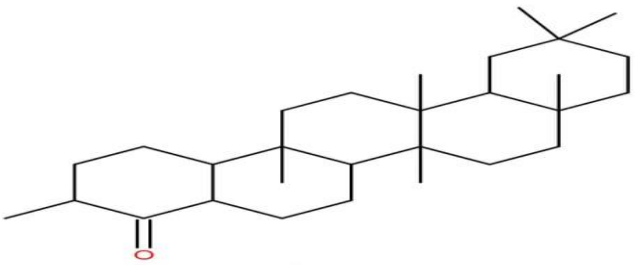
We find particularly phytol, which is in the form of an ester in chlorophyll, while retinol A vitamin oxidizes to obtain the aldehyde (retininal), which plays an important role in vision. Moreover, diterpenic acids, found in pine roots, are of great importance in their industrial aspect due to their low extraction cost. - Stereoelectronic chemistry plays a crucial role in these compounds, such as the effectiveness of vitamins associated with the presence of the trans bond.

II.2.4. Triterpenes: Tricyclic terpenes are predominantly in cyclic form and are highly significant, as we will see later, as they are the source of steroids. The most famous compound is squalene, which is the precursor of cholesterol. It is characterized by an open structure and a molecular structure consisting of adjacent tail-tail units containing two farnesyl units.

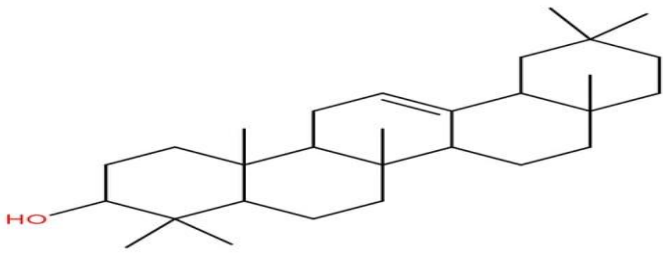


Squaléne

Among the tricyclic terpenes, there are cyclic ones such as β-amyrin and friedelin, found in plant resins and cork. They have a pentacyclic structure.



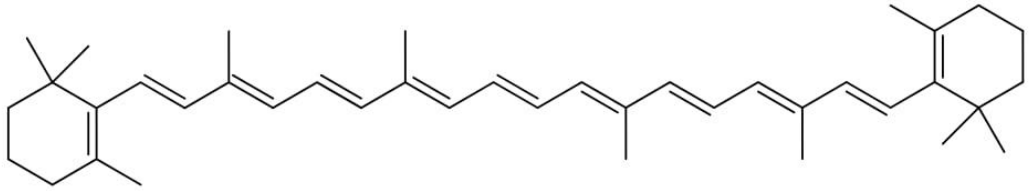
Frideline



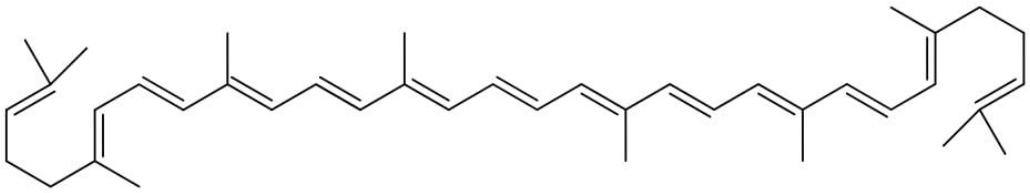
- amyrine

II.2.5. Quaternary terpene (Tetraterpene):

It is a family with an isoprene structure of the formula $C_{40}H_{56}$. The high degree of unsaturation results from the presence of branched double bonds in the trans form, and these components form a colored dye, whose name is carotenoids. As an example, consider carotene, found in carrots, and lycopene, found in tomatoes.

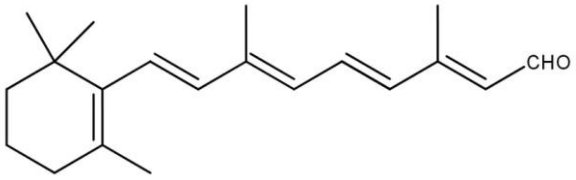


-Caroténe

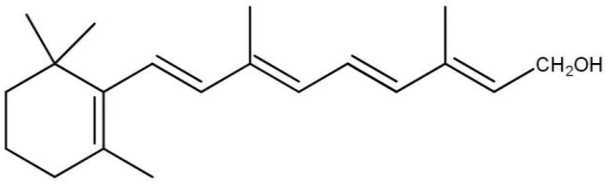


Lycopéne

β-Carotene can be subjected to chain breaking by oxidation in humans and in vertebrates in general, which produces retinal, which plays an important role in the process of color vision, and the latter results in Vitamin A,which we have seen.When studying binary terpenes.



Rétinal



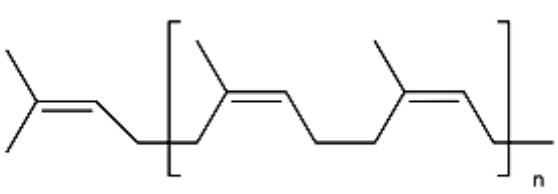
Vitamine A

II.2.25.Multi-terpenes (Polyterpenes) :

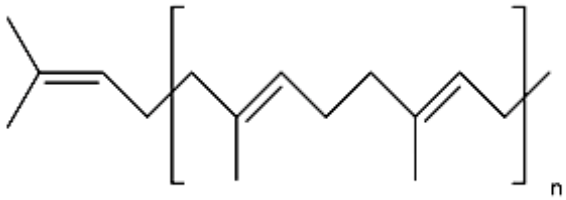
Rubber multi-domain terpenes (Caoutchoues), which are found in the sap of some trees, Retinal Lycopene β-Carotene.

- **Caoutchouc naturel (natural rubber):** It is a very large molecule (Macromolecule), which weighs 400,000, of connected isoprene chains of the type Head-tail, and the stereostructure of the double bond is in the form of Cis.
- **gutta percha**: It is a stereoisomer of rubber found in tropical trees with a polyisopréne structure in the trans form.

  Note: Only Cis rubber is known to be used in industry, due to its high elasticity.



Gaouthouc naturel



gutta percha

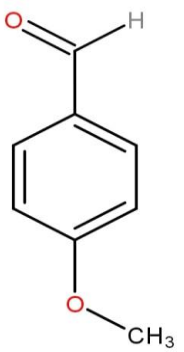
II.2.6.Chemical study (detection and extraction) of some types of terpenes:

II.2.6.1. Chemical study (detection and extraction) of lactone sesquiterpenes:

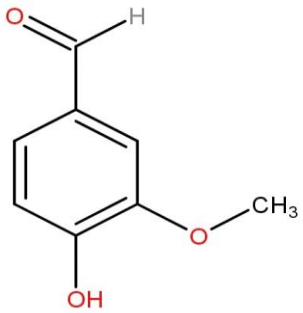
A - Extraction:

20 g of the crushed aerial plant part is treated with 100 ml of chloroform ($CHCl_3$). The filtrate is concentrated under low pressure, and the remainder is dissolved in 25 ml of ethanol (C_2H_5OH (95%), either cold or heated, and in a steam bath for a short time, after which the solution is treated. With 25 ml of aqueous lead acetate $Pb(CH_3COO)_2,3H_2O$ (4%), the solution is filtered and the filtrate is concentrated to a smaller volume until water remains or oily spots appear, then extraction is made with $CHCl_3$, and the extract is concentrated and dried.

B: Initial detection: The extract is directly analyzed by TLC and IR spectroscopy, as for TLC. The chromatogram containing lactic sesquiterpene compounds will show brown spots when exposed to iodine vapors in a closed container. Green, brown, yellow, or red spots may appear when the chromatogram is sprayed with concentrated H_2SO_4 acid and when heated for 5 minutes at 100–110 °C. The color can be determined. Highlighted are features of the structures of certain lactones. There are also other reagents that are constantly used to demonstrate sesquiterpene lactones, such as anizaldehyde and vaniline.



Anizalddhyde



Vaniline

II.2.6.1. Chemical study of tri terpenes:

A. Extraction:

First, extraction is carried out with petroleum ether, where the crushed plant tissues are soaked in petroleum ether (60–80 °C) in order to rid them of fats and chlorophyll. Then, alcoholic extraction is carried out using warm or cold methanol (or ethanol) for a prolonged period (a week), after which it is concentrated. The alcoholic extract is under low pressure, and part of it is subjected to acid or enzymatic hydrolysis to release the aglycones (when glycosides are present), followed by extraction with chloroform. The final extract is concentrated and ready for separation. Immediately after the alcoholic extraction, a process of distribution between water and solvent and not mixing with them through liquid extraction may be used. A liquid using a medium-polar solvent, usually chloroform; triterpenoids may also be extracted using a soxlet device using solvents such as AcOEt, $CHCl_3$, and n-C_6H_{14}.

B Initial detection:

The Liebremann-Buchard reaction is widely used to detect triterpenes and steroids, where a change in the color of the compound to blue-green indicates the presence of steroids, and if a red ring forms, this indicates the presence of triterpenes.

C. Separation and technique:

Separating the triterpenes is a delicate process because if these components are present in significant quantities, they are in the form of complex mixtures due to their high polarity, relative ease of breakdown, and minor structural differences between components with significant molecular masses. All of this makes obtaining completely pure molecules neither easy nor quick. usually. The methods for separating this type of compound from each other are based on chromatographic separation techniques. “Open” or medium-pressure columns, or HPLC, as well as preparatory TLC using the usual stationary phases (silis, aluminum). As for CPs, they have become rarely used, even though they were very important for the separation of steroids. It is considered Separation on paper is sometimes valuable for distinguishing several glycosidic triterpenes. Lists of many reagents used to indicate triterpenes have been prepared, the most famous of which is the Carr Price reagent (20% trichlorure antimoine in chloroform), and adapting the Liebermann-Buchard reaction as a reagent on TLC has also become commonly used by spraying the chromatogram with a mixture of: 50 ml CHCl3, 20 ml acetic anhydride, and 1 ml H2SO4. Then heat it for 10-15 minutes at 85–90 °C, as a range of colors is formed for the different triple terpenes, especially the red color. This mixture is

considered to have a high sensitivity (µg 5 -2), in addition to the use of other reagents applied to all terpenes, such as H2SO4. Concentrated or diluted with water, alcohol, anizaldehyde, or vaniline.

II.2.7. Physical properties of terpenes in general:

Terpenes are colorless, although impure samples are often yellow. Boiling point scale by molecular size: monoterpenes, sesquiterpenes, and diterpenes, respectively, at 110, 160, and 220 degrees Celsius. Being highly non-polar, it is highly flammable and has a low density (it floats on water).

For volatile oils: In general, exposure of volatile oils to heat, humidity, light, and air leads to physical and chemical changes, including:

1. Color: Volatile oils vary greatly in color depending on their source and method of obtaining them. Most oils are transparent in color, whitish-yellow to greenish, and rarely blue, as in the case of chamomile oil. Some oils may take on a red color as a result of the period of collecting the plant sample. Or due to a defect in the distillation process, and in general, the color becomes dark as a result of the long period of distillation and storage.

2. Smell: Volatile oils have a beautiful aromatic smell, and their smell is rarely undesirable. Specialists can distinguish between different volatile aromatic oils through their smell, as each essential oil has its own distinctive smell.

3. Volatility: Essential oils are characterized by their volatilization or evaporation at normal temperature, except for a few that do not volatilize, as in the case of lemon oil, because it contains some non-volatile compounds, and this is what distinguishes them from fixed oils. Volatile oils are exposed to heat, humidity, light, and air, which leads to physical changes in their properties, manifested in an increase in their viscosity and a change in color

4. Solubility: Essential oils do not dissolve in water (or are poorly soluble, especially in sugar solutions), but they dissolve in organic solvents such as 95% alcohol and ether, and they dissolve slightly in aqueous alcoholic solutions, especially when they contain a high percentage of terpenes. The water is separated from the oil while withdrawing it from the distillation device by adding anhydrous sodium sulfate, as water causes cloudiness in the oil. It is worth mentioning the use of the property of solubility in alcohol as a means of detecting falsification in essential oils by adding other vegetable oils, as these added oils cause a reduction in the solubility of essential oils in alcohol.

5. Density: Volatile oils float on the surface of water due to their low specific density compared to the density of water, except for cinnamon and clove oils, which settle under the surface of water due to their high density compared to the density of water. The density range for all volatile oils ranges from 0.8 to 1.17.

The third axis
Steroids

III. Steroids:

III. 1. Definition:

We call steroids every compound that has a structure with four rings (A.B.C.D.). The compound is in the form of alcohols called sterols, and we find them in the non-saponifiable parts of plants or animals. The most widespread are of animal origin, and the most commonly known compound is cholesterol, which has been isolated since the nineteenth century in human bile sacs, where there is an amount of 200 grams constantly present in the brain and spinal cord, the four rings referred to as A.B.C.D. The agreed-upon numbering of positions in steroids is shown in the following figures **13** and Figure **14**.

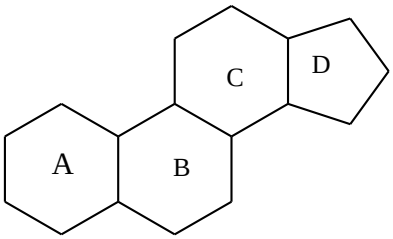


Fig. 13: General structure of the steroid

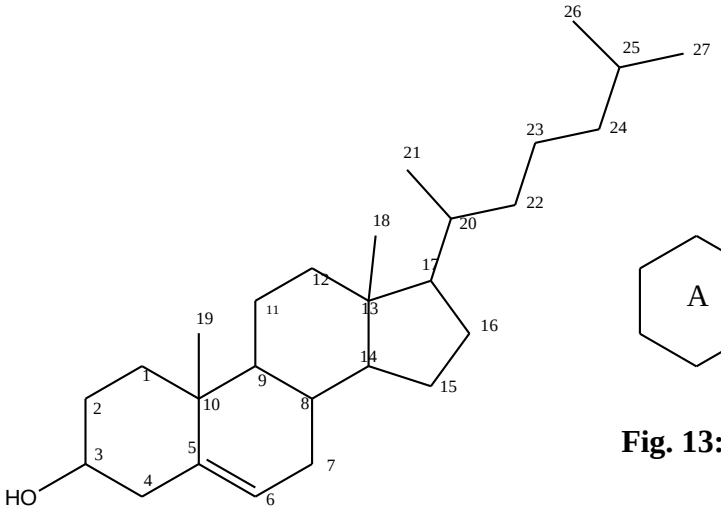


Fig. 14: Steroid numbering

III.2. Stereoisomerism and nomenclature:

Through cholesterol, we can notice the presence of a large number of asymmetric carbon atoms (carbones asymetriques), which necessitates the presence of a large number of stereoisomers, but there are only some compounds present in the natural state, and this results from a method of selection between the two rings (C.B.) as well as between the two rings (D.C.), which is always in the form (trans). The basic difference between steroids comes from the meeting between the two rings (B.A.), which can be in the trans form, as in the case of cholestane, or in the cis form, as in the case of coprostane. These two hydrocarbons are produced by reducing cholesterol and form the basis of the systematic nomenclature of steroids, as shown in **figure 14.**

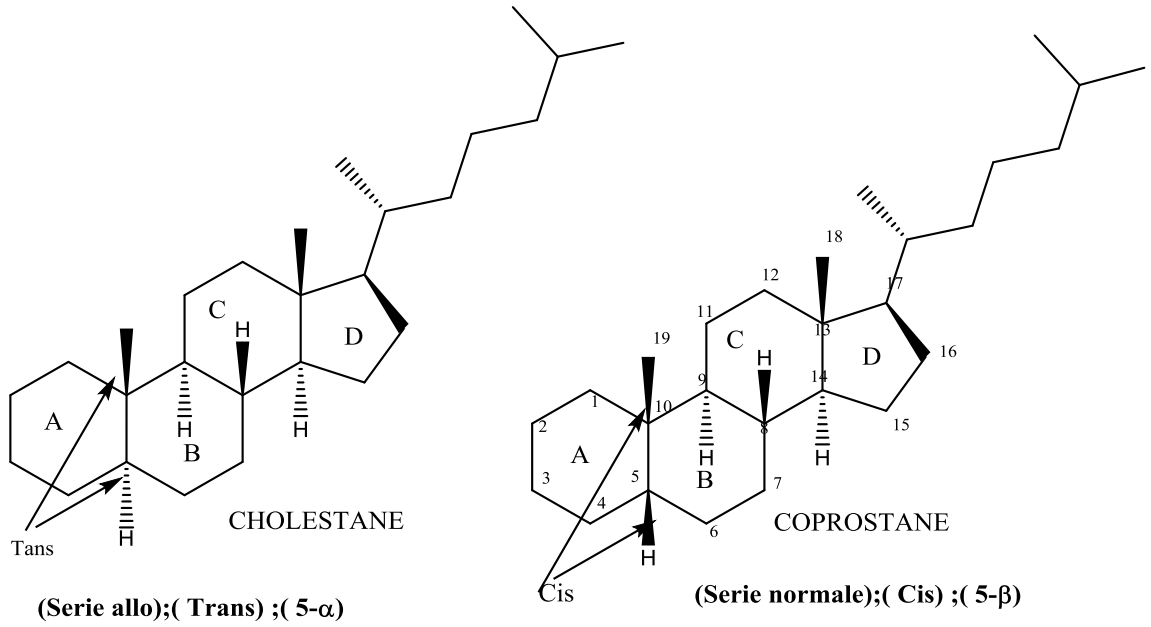


Fig. 14: The difference between steroids in the way they meet the two rings (B.A.)

. In steroid chemistry, all steroidal compounds with ‘’Cis’’ configurations are referred to as the ‘’normal series’’. This series of steroids is particularly common in bile acids under the designation 5-β.

- Which means that the hydrogen in position five (5) is above the reference plane. As for the steroids with the ‘’Trans’’ configurations, such as the cholestane, they are called the ‘’Allo Series’’ and are given the designation 5-α meaning the hydrogen in position five (5) is below the reference plane.

- Stereo-chemical studies of the cholestane molecule reveal that all of its cyclohexane rings are of the chair form, which is characterized by the presence of angular methyl groups in positions [19; 18] in β configurations. This is most steroids default form (Cis-Chair) since its minimal angular strain yields greater stability. **Figure 15.**

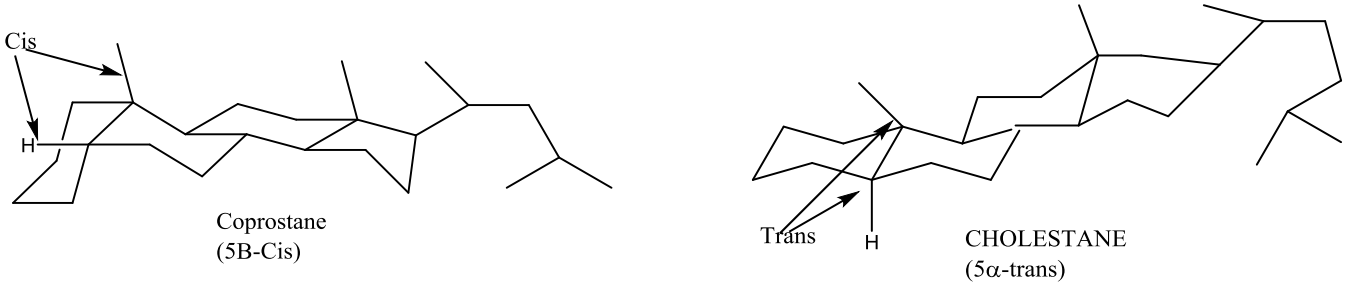


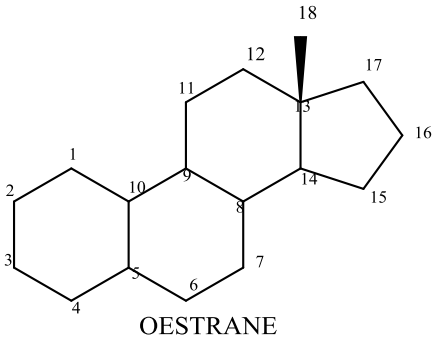
Fig. 15: Difference in the stereoscopic structure of steroids

- Stereo-chemical Differences between the Normal and Allo Series Implementation of such a naming system allows for a much more effective classification of steroids based on their stereochemistry (Cis or Trans), depending on the relative spatial positions of the hydrogen atoms where the rings fuse together, i.e., 5-α or 5-β.

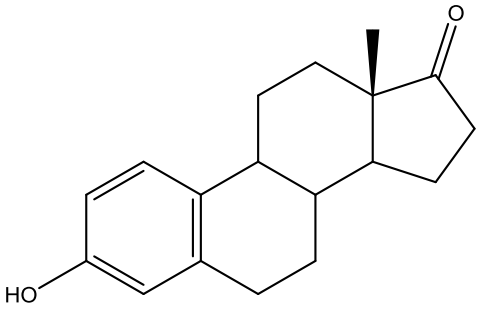
III.3. Classification:

Steroids can be classified based on the patterns that arise from the presence or absence of three distinct types of hydrocarbon substituents in three determined positions [10, 13, 17], and thus we find five unique steroid patterns or series:

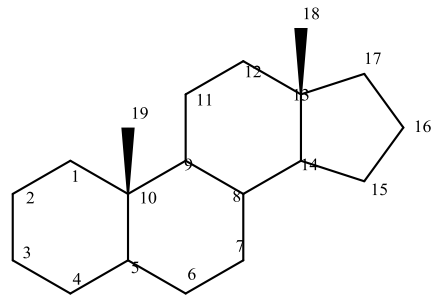
- **Estrane Series :** (or Nroandstrane), which consists of four rings (A, B, C, and D), i.e., the nucleus with a single methyl group in position [13]. Estrone, an estrogen (female sex hormone), belongs to Estranes.
- **Androstane Series :** which, besides consists of two methyl groups in positions [10; 13]. A prime example of this is the well-known androgen (male sex hormone): testosterone.
- **Pregnane Series :** in addition to two methyl groups in postions [10; 13], it has an ethyl group in position [17], for example: cortisone.



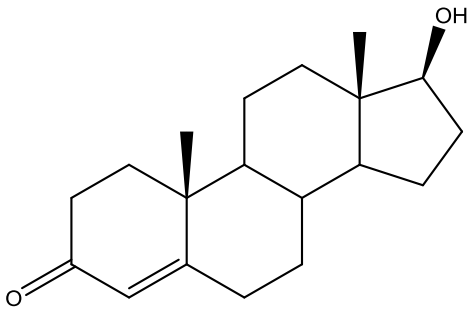
OESTRANE



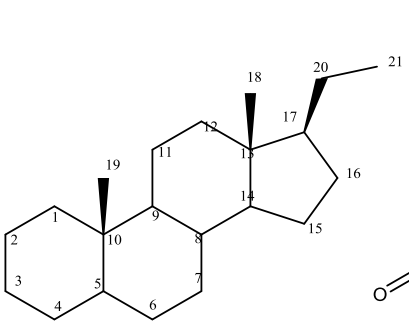
OESTRONE



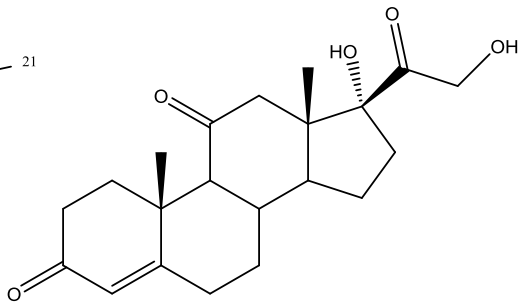
ANDROSTANE



TESTOSTERONE

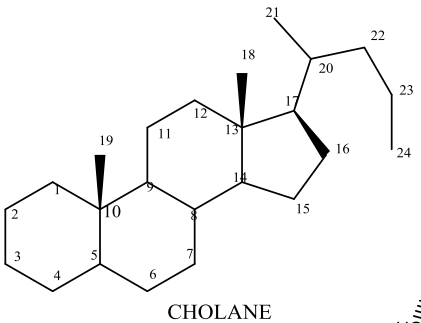


PREGNANE

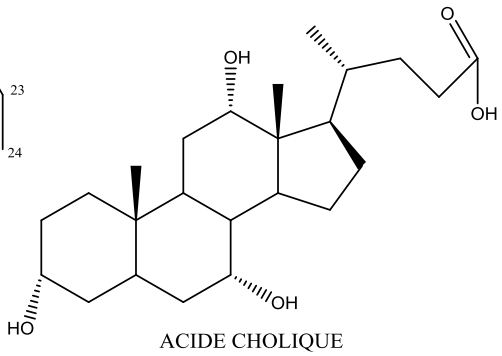


CORTISONE

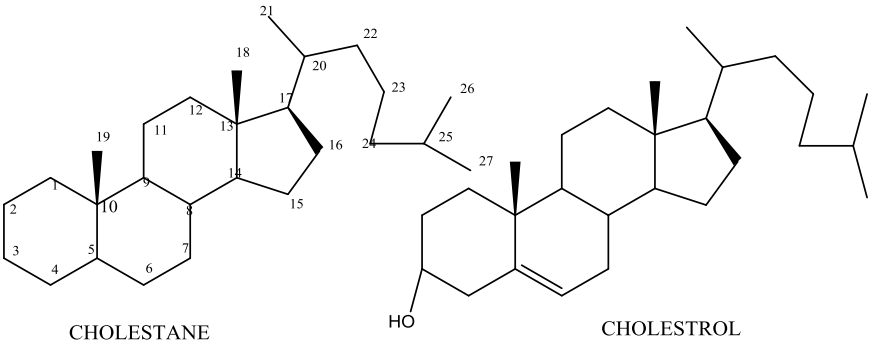
- **Cholane Series :** Consists of 21 carbon atoms; it has two methyl groups in [10; 13] in addition to a sec pentyl group in position [17]. This series includes bile acids such as cholic acid.
- **Cholestane Series :** 27-carbon molecules with two methyl groups and a methyl isoheptyl group in positions [10; 13; 17], respectively. For example, cholesterol .



CHOLANE



ACIDE CHOLIQUE



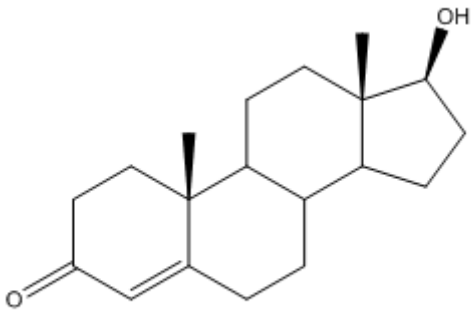
CHOLESTANE CHOLESTROL

III.4. Essential Steroids:

The most important steroid structures in biochemistry are those found primarily in hormones, bile, and some vitamins.

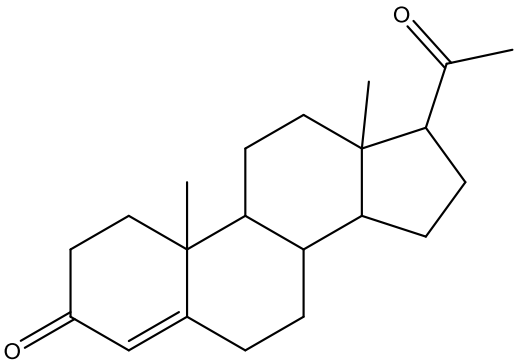
III.4.1. Hormones: Cholesterol serves as a building block for a great number of hormones through a series of metabolic processes. Endocrinology (the discipline of hormone studies) is relatively new, with many of its major breakthroughs made in the last fifty years. This is largely because they are usually present as traces in biological systems. There are three main types:

a) Androgens (male sex hormones): such as testosterone, which is the main factor in the development of male physiology and characteristics, an androstane.



TESTOSTERONE

b) Estrogens (female sex hormones): such as estrogen, the abundance of which in the urine is a sign of pregnancy, and progesterone, which is a pregnane hormone largely responsible for preparing the body for embryo implantation and maintaining its stability throughout this crucial phase.



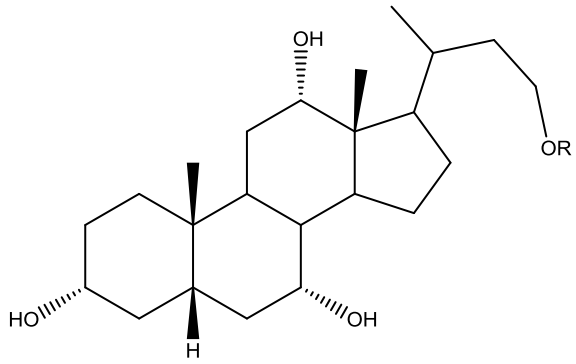
Progesterone

c) Corticosteroids: like cortisone, a synthetic anti-inflammatory agent that reduces inflammation, swelling, pain, and redness in the affected area; and natural cortisol hormone, a product of the adrenal gland situated above the kidney in the human body, it helps:

- reduce stress and anxiety;
- regulate glucose levels in the bloodstream;
- maintain blood pressure;
- stabilize the immune system to prevent overreaction in stressful circumstances.

III.4.2. Bile Acids: (Biliary Juice):

Bile, or biliary juice, is a basic, extremely bitter yellowish-green digestive fluid produced by the liver and stored in the gallbladder, which secretes it into the small intestines during digestion, where it helps in cholesterol catabolism. One of the key components of bile is cholic acid, which, mainly present in the form of glycocholic acid, emulsifies fats and thus facilitates the work of digestive enzymes. This acid and other bile salts, which are amphipathic molecules found in bile, surround fat globules and break them down into smaller droplets. This process increases the surface area of the fat, making it easier for lipases to access and break down the fats into smaller molecules, such as fatty acids and glycerol, that are then absorbed by the intestine.



Acide cholique (R=OH)
Acide glycholique (R=NH-CH_2-COOH)

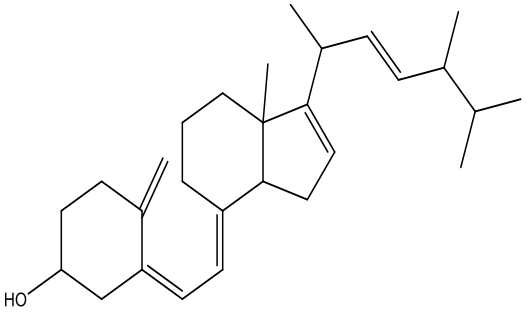
III.4.3. Vitamins and Other Compounds:

Vitamin D2, which plays a major role in the metabolism of calcium electrolytes, is formed because of sun exposure and is responsible for increasing intestinal absorption of calcium, magnesium, and phosphate. The main natural source of the vitamin is the synthesis of cholecalciferol in the lower layers of the epidermis through a chemical reaction dependent on sun exposure. Cholecalciferol and ergocalciferol can be obtained through dietary means,

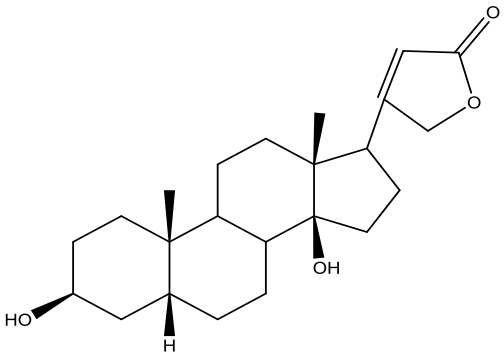
but only a handful of foods, such as fatty fish meat, naturally contain significant amounts of vitamin D2.

Still, synthetic vitamins are a viable alternative; consequently, in the United States and other countries, cow's milk and plant-derived milk substitutes are supplemented with vitamin D2.

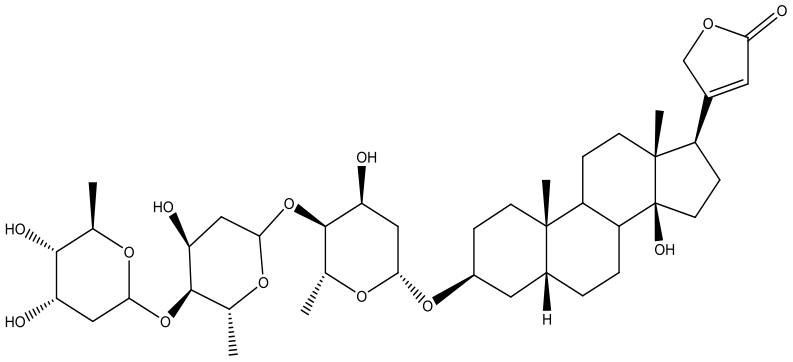
It is also worth mentioning the interesting case of digitoxigenin, a steroid found in some plants as a sugar-bound glycoside that has the tendency to maintain a Cis configuration between the rings [A/B] and [C/D] to form (Digitoxin) Digitaline, a drug used for the treatment of certain heart conditions.



Vitamine D2



Digitoxygenine



Digitaline

III.5. Steroid Reactivity:

The steroid skeleton of four rings grants steroids structural rigidity and stability that are exploited in studying the mechanism of reactions; therefore, they are considered exemplary molecules in the field.

- **Addition on the double bond (ex: cholesterol):** Hydrogenation (reduction), catalyzed by nickel, of the cholesterol π bond affords cholestanol, as shown in **Figure 16.**

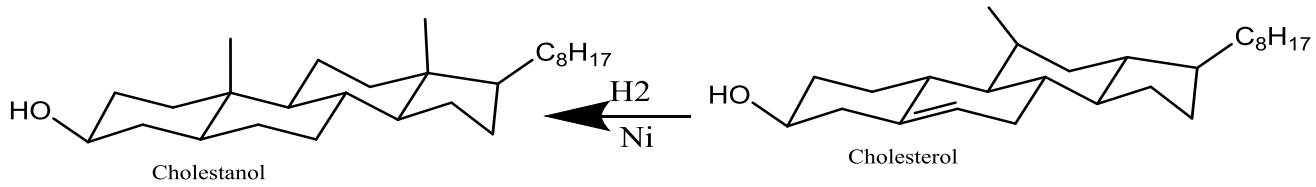


Fig. 16: Cholesterol Hydrogenation (Reduction).

- **Addition of X_2 (Br_2) to Cholesterol:** At ambient temperatures, the addition of Bromine (Br_2) to Cholesterol results in the formation of dibromo cholestanol, where a bromonium bridge is formed, which is then attacked by the Br^- to form 5-dibromo cholestanol, as in **Figure 17 .**

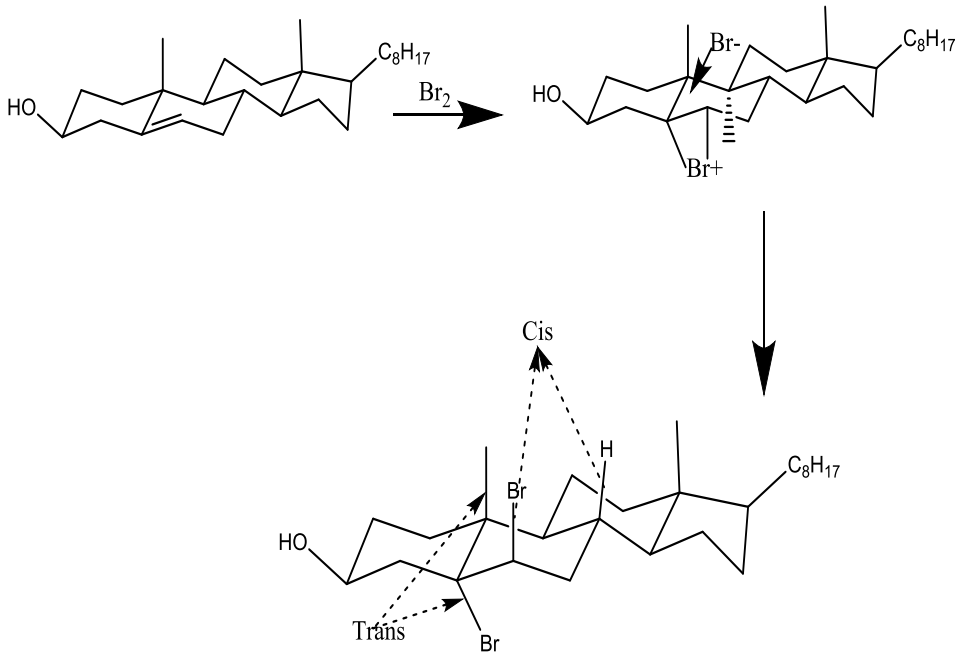


Fig. 17: Cholesterol Brominatinon (Reduction).

III.6. Steroid Synthesis:

Example: Cholecalciferol (Vitamin D3) Synthesis: Cholecalciferol is a vitamin that regulates calcium and phosphorus levels in the body and their absorption. It is also used as a drug to prevent and treat vitamin D deficiency. Its synthesis has the same principle as

natural preparation, where 7-dehydrocholesterol, which is found in the skin of humans, in milk of mammals, or in the wool of animals, is irradiated by solar UV rays.

Its synthesis: initially, 7-dehydrocholesterol is treated with UV radiation, which in turn initiates a retro-diels-Alder reduction reaction resulting in the formation of Vitamin D3 , as in **Figure 18 .**

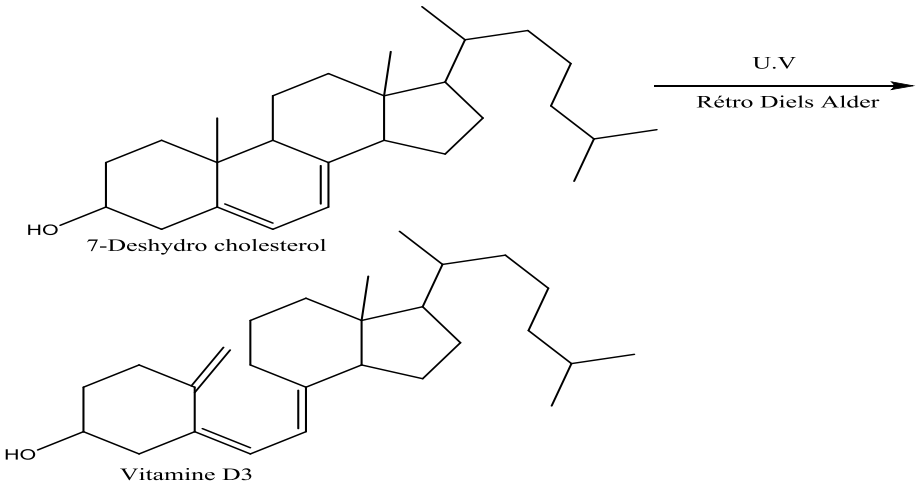
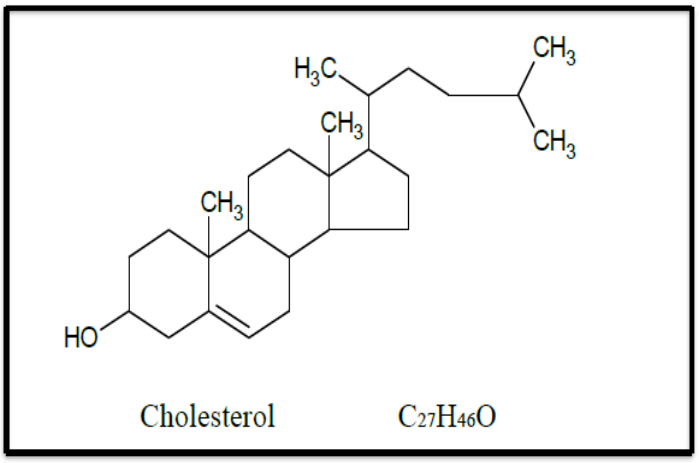


Fig. 18: Retro Diels-Alder Vitamin Synthesis.

III.7. Detection and extraction of steroids:

III.7.1. Detection of steroids (specific tests for cholesterol): Cholesterol is a steroidal fatty substance consisting of 27 carbon atoms distributed over four hydrocarbon rings, containing a hydroxyl group at position 3 and a hydrocarbon side chain at position 17.



When steroids containing unsaturated bonds are treated in anhydrous conditions with strong acids, they react and produce compounds with distinctive colors, depending on the experimental conditions. The resulting colors show significant differences from one compound to another.

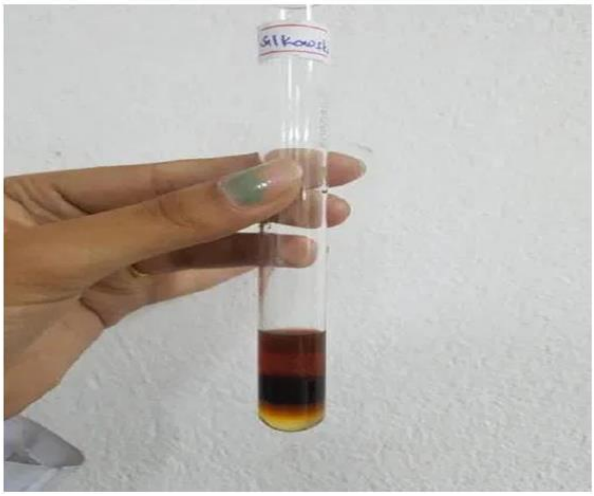
1. Salkowaki test : The Salkowaki test is used to detect cholesterol in a solution. It is an important test used to detect cholesterol levels based on the distinctive and clear colors resulting from the interaction of cholesterol with concentrated sulfuric acid.

Method:

1- Place one milliliter of cholesterol in a test tube, then add the same volume of H_2SO_4 and shake well.

2- Leave the tube until the mixture separates well into two layers: the upper layer is red and the bottom layer is green.

Caution: For this test to be successful, the tubes must be dry and the solutions must be non-aqueous.

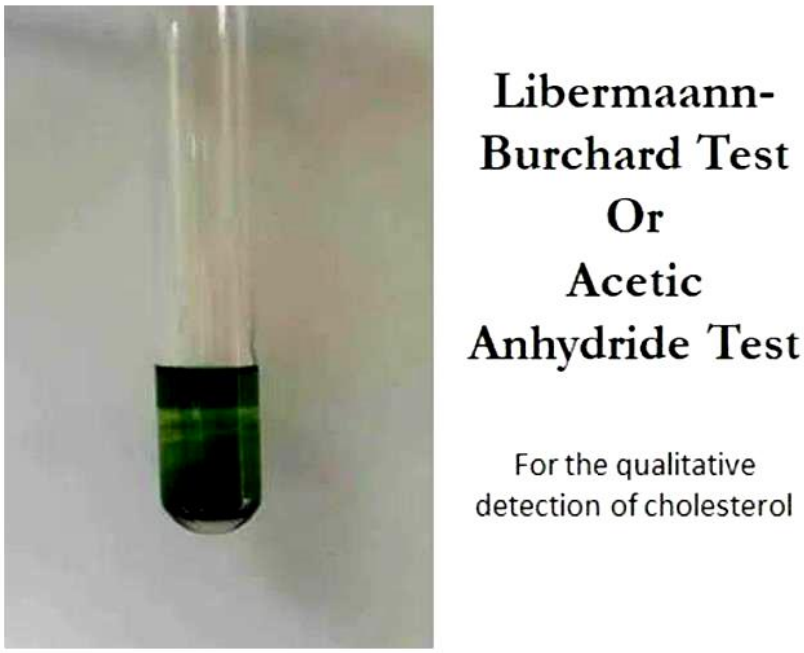


2-Liberman-Burchards test: The Lieberman-Burchard test is a qualitative determination of cholesterol as a typical **alcohol** with strong concentrated **acids** to give colored substances. In this test, **acetic anhydride** is used as a solvent and drying agent. **Sulfuric acid** is used as a drying and **oxidizing** agent. After adding these acids to the cholesterol solution, it is observed that the color of the solution becomes blue-green.

Method:

1- In a clean and dry test tube. Add 1 ml of cholesterol 5 dissolved in chloroform to 1 ml of acetic anhydride, then add two drops of H_2SO_4, add them to the same tube, and shake well.

2- Note the color change ,we notice the appearance of a greenish-blue color.



Lieberman-Burchard reaction mechanism: A test to detect steroids, especially cholesterol, by adding a few drops of sulfuric acid to a solution of cholesterol in acetic anhydride. A blue-green color appears in the solution.This is a chemical reaction that is mainly used as a test for cholesterol, as shown in **Figure 19**.

Reagents: A solution of the substance to be determined in chloroform, concentrated sulfuric acid, and acetic anhydride

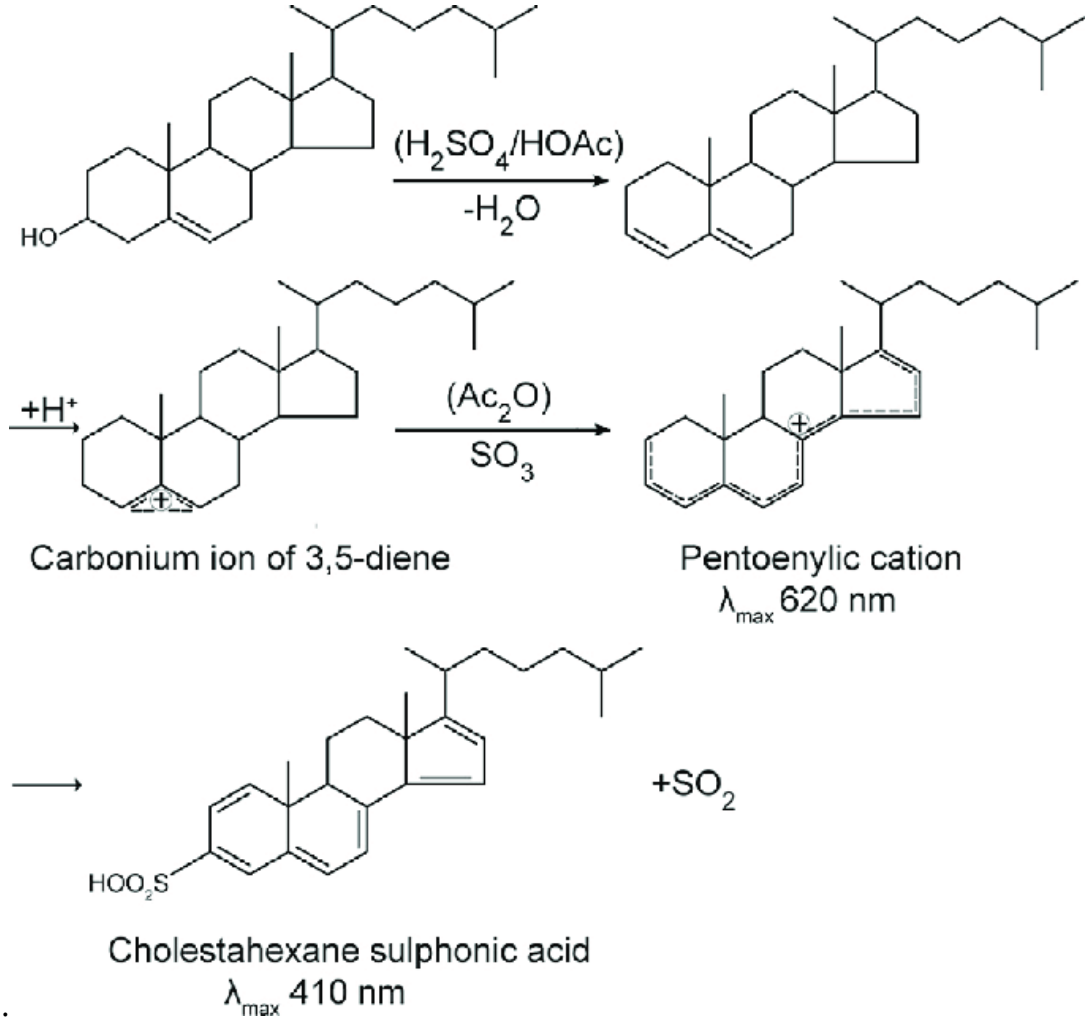


Fig. 19: Lieberman-Burchard reaction mechanism.

III.7.2. Extraction:

The extraction of steroids is done in the same way as the extraction of triterpenes due to their similarity in chemical structures. Column chromatography, or HPLC, is used to separate the triterpenes and steroids from each other due to the slight structural differences between them.

The fourth Axis
Les Alcaloides

IV . Alkaloids:

IV.1. Identification:

They are heterocyclic compounds that contain one or more nitrogen atoms and are found in plants. The word alkaloids (alkaloids) comes from the word alkali, which means alkali. Because they are organic bases that we find in plants linked to acids in the form of salts When an alkaline compound combines with an acid, for example, the following acids (lactique, citrique, oxalique, and acétique), the result is a salt compound.

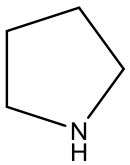
- The name of the alkaloid is often derived from the name of the plant and most often contains the ending (ine). For example Cocaine From coca leaf and quinine From quinquina
- Despite their often complex structure, they are easily found and play an important role due to their physiological, toxicological, and therapeutic effectiveness.

IV.2. Category:

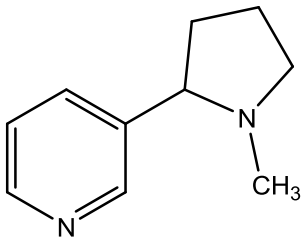
There are many thousands of alkaloid compounds in nature, and it is difficult to classify them, but groups can be found based mainly on heterocyclic rings. Among the most important alkaloids are those that belong to the indole family, and among the most important alkaloid families we find:

IV.2.1 Pyrrolidine family:

Among the known compounds of this family is nicotine from tobacco leaves. It is characterized by containing a pyrrolidine ring.



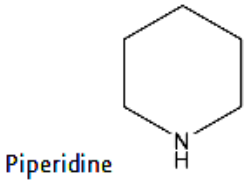
Pyrrolidine



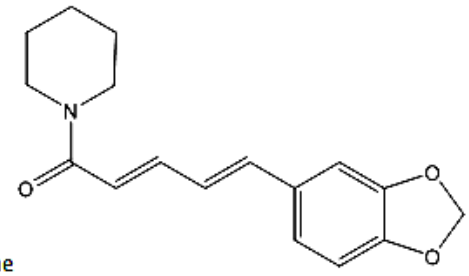
Nicotine

IV.2.2 Piperidine family:

It is a family that mainly contains piperidine. An example of this is piperine from the plant (white pepper).



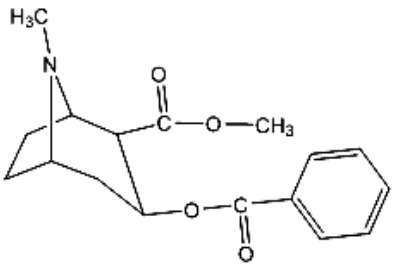
Piperidine



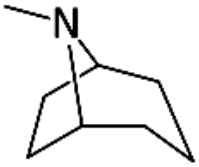
Piperine

IV.2.3. Tropane family:

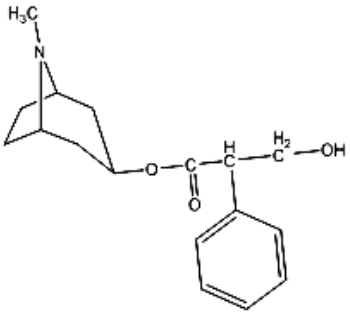
It is a bicyclic organic alkaloid compound that contains nitrogen, which is what forms many drugs and poisons. The basis of its chemical structure is that it mainly contains a tropane, which is a piperidine ring linked at the C1 and C4 positions with a propyl bridge. Examples of this include cocaine from the cacao leaf and atropine from the plant (Atropan belladonna), which is characterized by containing a tropane structure.



Cocaine



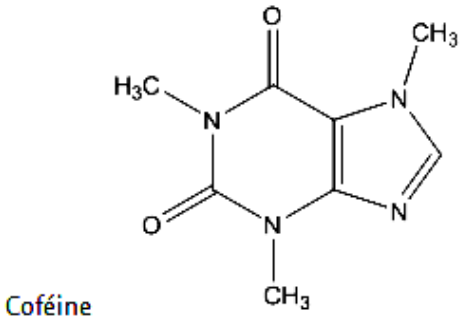
Tropane



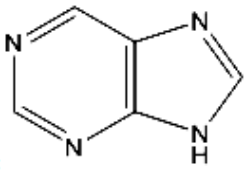
Atropine

IV.2.4 Purine family:

It mainly contains a purine compound, including coféine from coffee beans and tea leaves, which is a well-known stimulant.



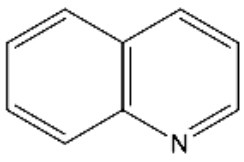
Coféine



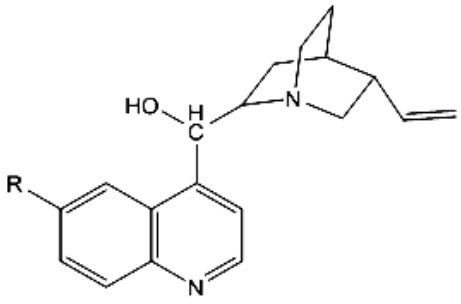
Purine

IV.2.5 Quinoleine:

It consists mainly of a heterocyclic organic compound, which is quinoleine. Examples of this include quinine (a powerful antimalarial) and cinchonine (from the bark of the quinquina plant).



Quinoleine



$R = OCH_3$: Quinine / R = H : Cinchonine

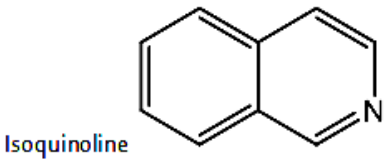
IV.2.6. Isoquinoleine:

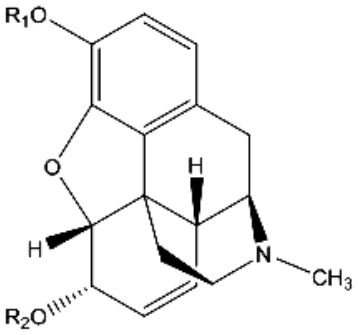
It consists mainly of a heterocyclic compound, which is isoquinoline.

Examples of this include: morphine; heroin; Codeine and these compounds are found in opium, which is the juice we obtain from the green capsules of the poppy plant (pavot), and then we dry it. Morphine is the most abundant alkaloid (10% of opium) and is used as an anesthetic and sleep aid (narcotic), but heroin derived from morphine, which contains (R_1 and R_2) diacetyl, has a stronger effectiveness than morphine and is a very powerful and well-known narcotic. These alkaloids cause

addiction, unlike morphine, which is less sedating, does not cause addiction, and is used as a pain reliever and antitussive. Codeine is an opiate preparation used as a painkiller, cough medicine, and antitussive.

It is present in 3% of opium.





$R_1 = R_2 = H$: Morphine / $R_1 = R_2 = COCH_3$: Heroine

$R_1 = CH_3$ / $R_2 = H$: Codeine

Codeine is considered the main compound of weak and moderate opiates such as tramadol.

IV.2.7. Indole family:

It consists mainly of the indole compound, and this type of alkaloid is found in large and abundant quantities, which necessitated its presence under the classification (sous classification) into:

- **Simple Indolic Alcoloids :** In the group of simple indoles, we find, for example, the compound tryptamine, and we also find serotonin, which is present in the brain and plays an important role in mental balance in humans. It is also called the happiness hormone. In the human body, it is made within the central system and in the internal cells of the digestive system. Its deficiency in the body causes migraines and depression due to its deficiency in the brain. Serotonin is also found in plants, especially walnuts, which contain 300 µg/g, as well as in pineapple, bananas, cocoa, etc.

- **Alcoloids Indole Ergot:** In the group of fungal indoles, we find, for example, lysergique acid, which is derived from the ergot fungus. If the latter contains diethylamide (diethylamide), it gives a drug known under the name LSD (lysergique diethylamide), and its consumption leads to a state of hallucination, which is the result. Due to a decrease in serotonin in the brain, it also causes

disturbances in vision and mood. It has been banned since 1971 in most countries in the world, with it only being allowed for use in the field of scientific research.

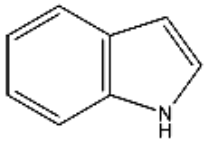
♦ **The most important differences between them are:**

- Simple indole alkaloids belong to the non-isoprenoid indole alkaloids, and fungal indole alkaloids belong to the isoprenoid indole alkaloids.

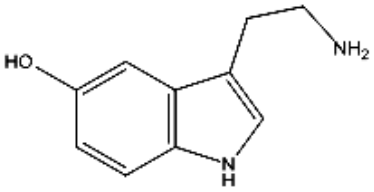
- Simple indole alkaloids are one of the simplest and most widespread indole derivatives. They are the biogenic amines tryptamine and serotonin, both of which are found in plants and animals. For example, serotonin is an important neurotransmitter in mammals.

- As for the fungal indole alkaloids found in fungi, for example, psilocybin mushrooms contain tryptamine derivatives. Argoline, like lysergic acid, includes structural elements of both tryptamine and phenylethylamine, which is a semi-synthetic drug and has a strong effect.

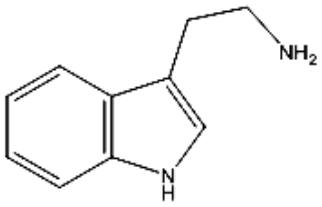
- Ergot alkaloids produce lysergic acid amides that cause muscle contractions, and they have derivatives of toxic alkaloids such as lysergamide, ergotamine, and ergoline. These alkaloids act on the activity of the brain and nervous system, and most of them are used as anesthetic drugs and as anti-tumors. As for simple alkaloids, studies conducted on animals have shown that ibogaine has the potential to treat addiction to heroin, cocaine, and alcohol, as it is banned in many countries as a powerful drug with serious effects on overdose.



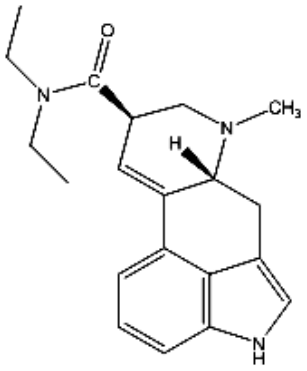
Indole



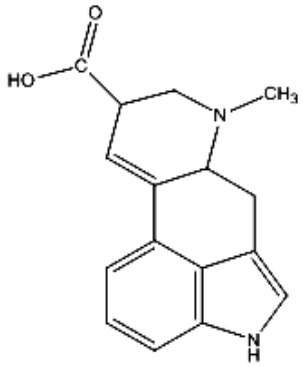
Sèrotonine



Tryptamine



LSD (Lysergique Diethyamide)



Acide Lysergique

IV.3 General properties of alkaloids:

- In addition to the nitrogenous N, alkaloids contain the elements (C, H), and some of them contain the elements (O).

- Most of the non-volatile alkaloids are solid in texture, but the volatile alkaloids are preserved in liquid form (at low temperatures) and do not contain the element O.

- Most of the odorless, non-volatile alkaloids are crystalline, have a bitter taste, and are white in color, except for the following alkaloids, which have a different color:

  - Berberine and colchicine alkaloids are yellow in color.
  - Caradine alkaloids are orange in color.
  - Sanguinarine alkaloids are colorless.

- Colorless alkaloids can be colored salts, such as ;

  - sagunarine salt, which is red in color.

- Hydrastuinine salt is yellow in color.

- Most alkaloids do not dissolve in water and may dissolve, but only partially, with the exception of colchicine alkaloid, which dissolves well in water. Most alkaloids dissolve in alcohol and chloroform.

- Most alkaloids have a physiological effect, some of which are toxic.
- It is possible to precipitate alkaloids using the following reagents: Mayer Reagen, Wagner's reagent, and Dragendorff's reagent.

IV.4 Some therapeutic and general uses of alkaloids:

A blood pressure booster, such as Ephedrine. or a blood pressure lowerer, such as Reserpine. Mydriasis, such as atropine, or mydriasis, such as pilocapic anthelmintics, such as pelletierine. A brain stimulant like caffeine. Diuretics such as xanthines.

IV.5 Chemical study of alkaloids:

A. Detection of alkaloids: To detect these alkaloids, there are several methods, including:

- **The first method (general alkaloids):**

We take 1 gram of dry powder for various plant organs, add 5 ml of chlorine acid (HCI, 1%), filter it, and add to the filtrate an ammonic solution (NH_3) until it reaches a basic degree (PH = 9). We extract the solution with chloroform ($CHCl_3$) 2-3 times, then we evaporate the chloroform ($CHCl_3$) and add 2 ml of chloric acid (HCI, 1%) to the precipitate. We add three drops of Mayer's reagent. We notice the turbidity of the solution or the presence of a white precipitate, indicating the presence of alkaloids.

- **The second method (alkaloid salts):**

We take 1 g of dry powder for various plant organs, add 10 ml of ethanol (C_2H_5OH), shake for an hour, then filter, evaporate 2 ml of ethanol solution (C_2H_5OH), add to the precipitate 5 ml of chloric acid (HCI, 10%), and heat a little. We filter the resulting solution and add drops of ammonium hydroxide (NH4OH) to it until the solution becomes basic (PH = 9). We extract the solution with diethyl ether ($(C_2H_5)_2O$), then evaporate the solvent, add to the precipitate a little chlorine acid (HCI, 2%), then add drops of Mayer's

reagent and Wagner's reagent. The appearance of the precipitate indicates the presence of alkaloids.

Note: Reagents are prepared as follows:

1. **Mayer's reagent** (which consists of two solutions A and B):

Solution A: 13.55 g of mercury chloride ($HgCl_2$) + 20 ml of distilled water.

Solution B: 49.8 g potassium iodide (KI) + 20 ml distilled water. Mix solutions A and B and dilute with distilled water to 1 liter.

2. Wagner's reagent:

We put 2 g of potassium iodide (Kl) and 1.27 g of iodine (l_2) in 75 ml of distilled water. Dilute the mixture with 100 ml of distilled water.

The result of the reaction occurring when adding reagents to alkaloids is:

1. Mayer's test:

A positive result of the Mayer test is confirmed by the appearance of a white precipitate. Consisting of a compound of the alkaloid potassium needed in the formation of Mayer's reagent, where a solution of mercuric (II) chloride was added with potassium iodide and produced a red precipitate of mercuric iodide.(II). The increased addition of potassium iodide leads to the formation of potassium tetraiodomercury II. Alkaloids consist of nitrogen atoms that have lone pairs of electrons. Lone-pair electrons are screened to form a covalent bond with the metal ion. In alkaloid determination with Mayer's reagent, the nitrogen present in the alkaloid was predicted to react with the potassium metal ion (K+) of potassium tetraiodomercury (II), resulting in a compound of precipitated potassium alkaloid.

$$HgCl_2 + 2KI \longrightarrow HgI_2 + KCl$$
$$HgI_2 + 2KI \longrightarrow K_2[HgI_4]$$

$$Alkaloid + K_2[HgI_4] \rightarrow Alkaloid^{+} + K[HgI_4]^{-}$$

A white precipitate of potassium alkaloid

2. Wagner test:

Positive results of the alkaloid test in the Wagner test are confirmed by the presence of brown to yellow precipitates. The precipitate was predicted to be a potassium alkaloid. In the preparation of Wagner's reagent, iodine reacts with an ion of potassium iodide, producing an I3-ion (brown solution). In the Wagner test, the metal ion K will attach by a covalent bond to the alkaloid nitrogen, producing a complex precipitate of potassium alkaloid.

$$I_2 + I^- \rightarrow I_3^-$$

$$Alkaloid + KI + I_2 \rightarrow Alkaloid^+ + I_3^-$$

A brown precipitate of potassium alkaloid

B. Extraction of alkaloids:

✓ **Extraction with a polar organic solvent:** To extract alkalis, we follow the scheme as shown in **Figure 20** below.

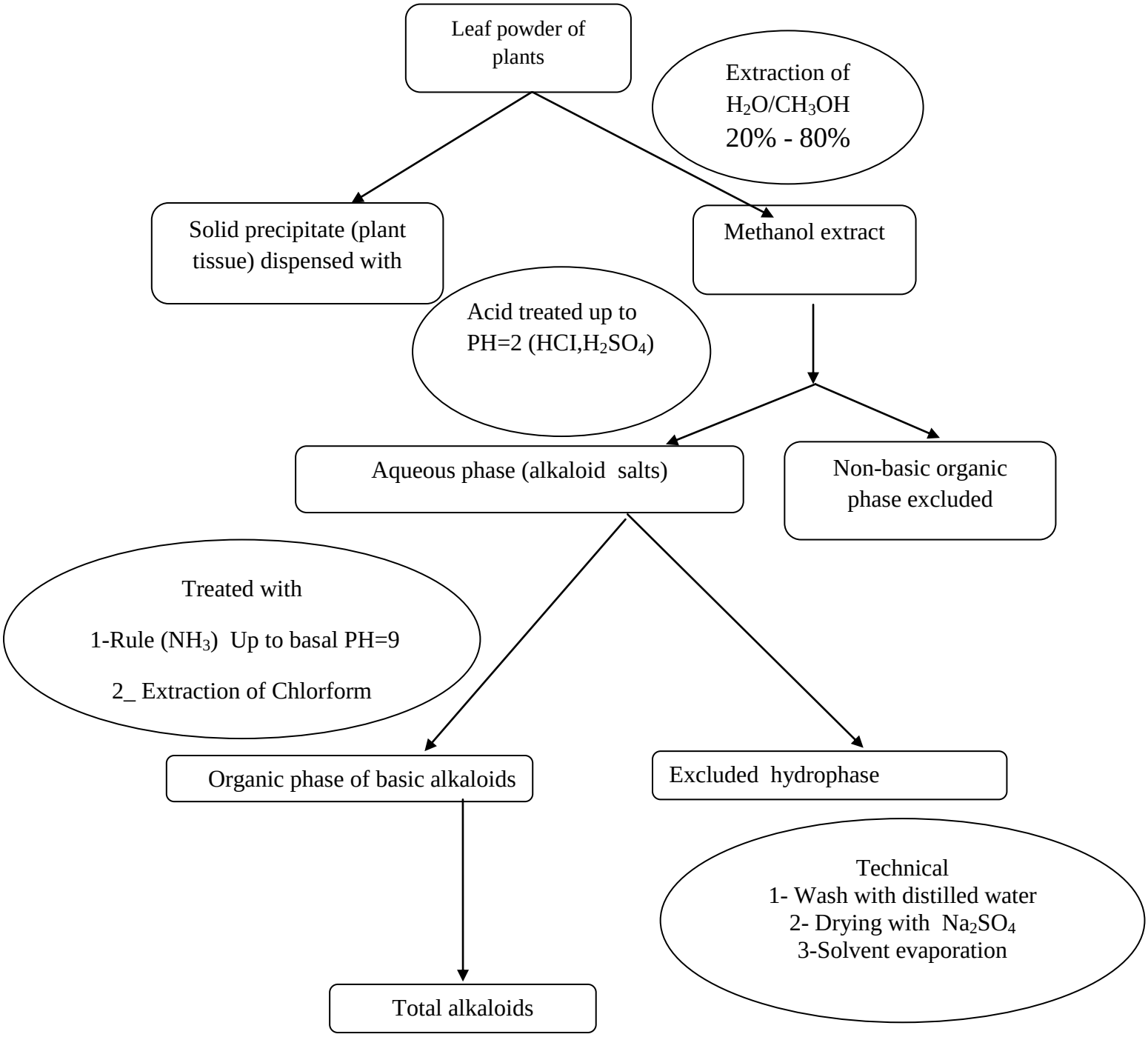


Fig. 20: Scheme of extraction of alkaloids with a polar organic

Explanation:

Alkaloids, as we mentioned previously, are found in plants in the form of salts, and this allows them to be soluble in water. The plants are initially ground in dry form and then treated with methanol (80%). This process ensures the separation of alkaloid salts from the plant tissue. The methanolic extract is then treated with acid until it becomes acidic, and this allows all the basic compounds to be transferred to the aqueous medium in the form of alkaloid salts. The non-basic organic compounds are liberated by washing the extract several times with chloroform (a non-basic solvent), and then we treat the aqueous phase with the base in the basic one. This allows us to extract the alkaloids with the solvent (chloroform). We concentrate the solution to obtain the total alkaloids in their organic form.

- ✓ **Extraction with a non-polar organic solvent:**

To extract alkaloids in this way, we follow the scheme shown in **Figure 21** below.

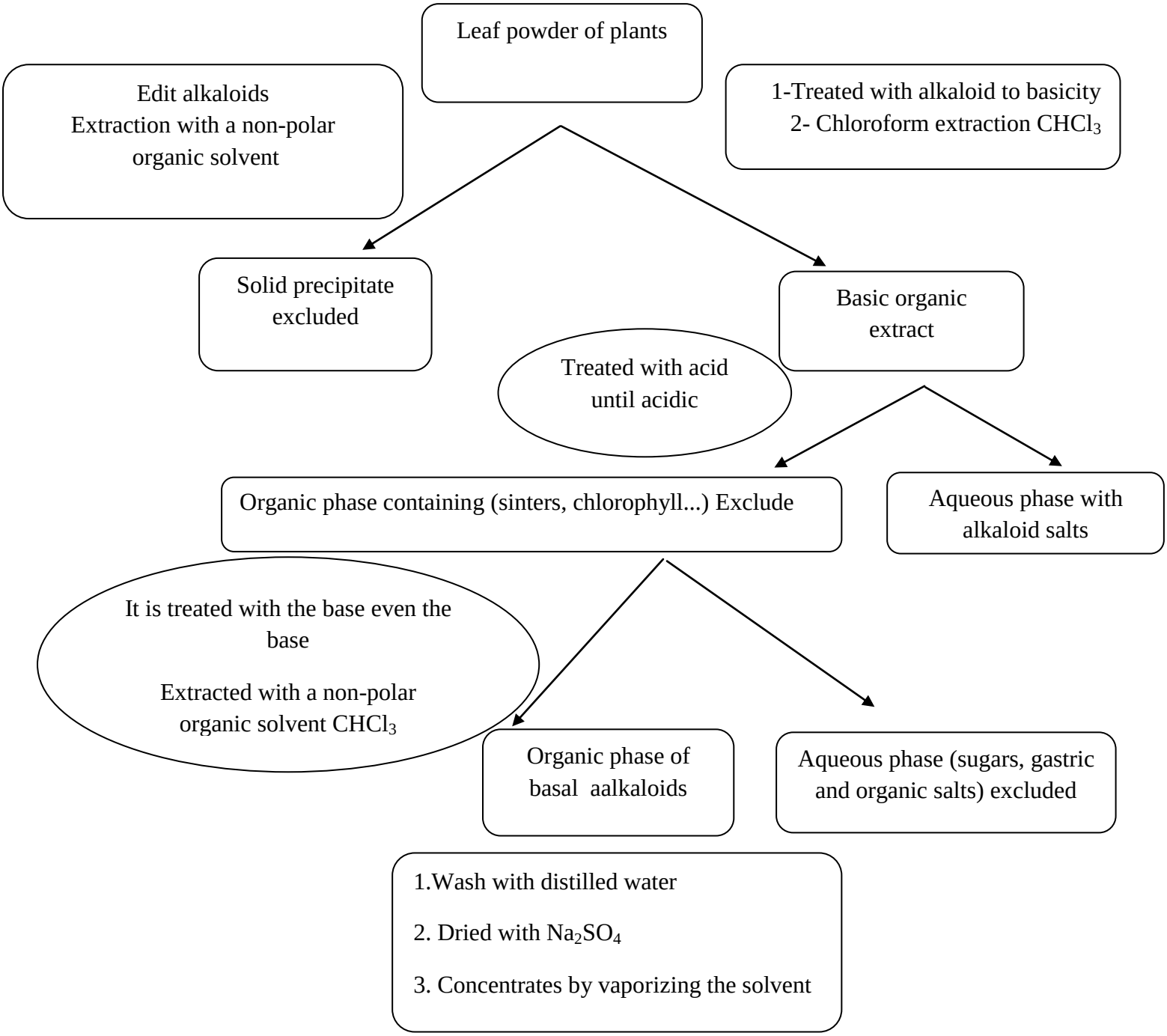


Fig. 21: Extraction of alkaloids with a nonpolar organic solvent

IV.6 Study of the organic preparation of isoquinoline:

Isoquinoline was isolated from coal tar, which represents a brown or black liquid extracted from coal. This was done in 1885 AD by the scientists Hoogewerf and Vandorp. It was prepared by the Pomeranz-Fritsh reaction method, and this reaction uses benzaldehyde and diethoxy ethylamine, which react in an acidic medium to produce isoquinoline, as shown in **Figure 22**.

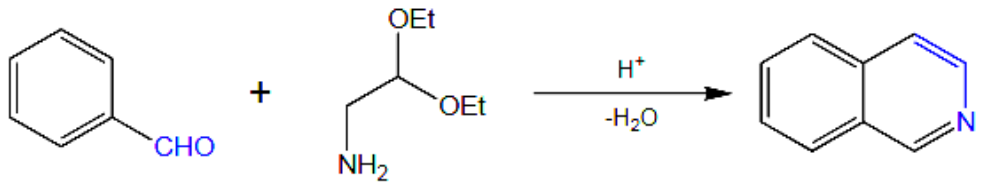
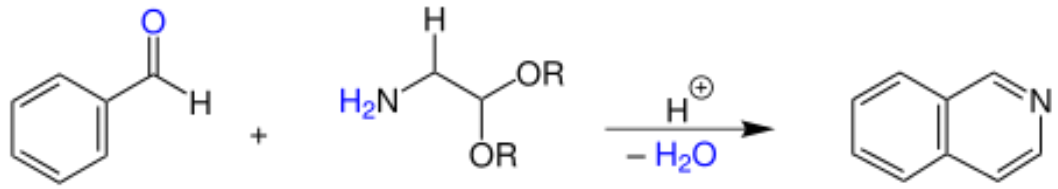


Fig.22: Organic preparation of isoquinoline

In general: The general Pomeranz-Fritsh reaction is as follows:



The reaction mechanism is shown in **Figure 23** below:

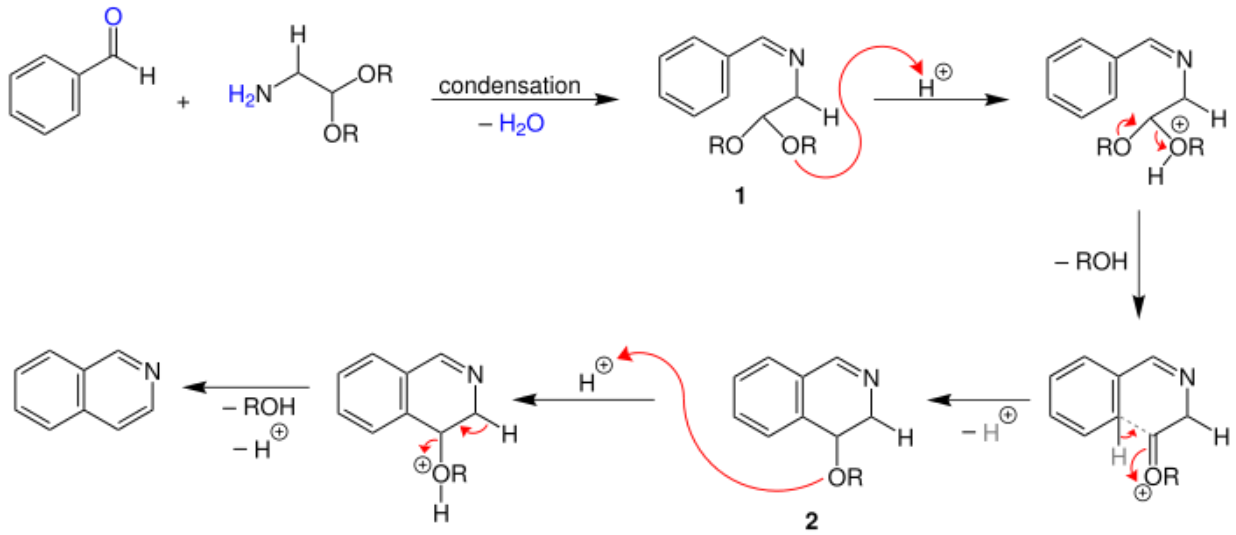


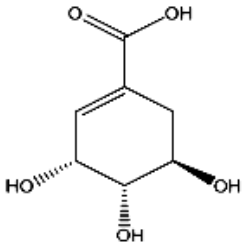
Fig. 23: Pomeranz-Fritsch reaction mechanism

The fifth axis
Phenolic compounds (polyphenol)

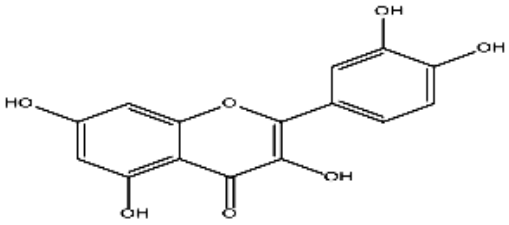
V. Phenolic compounds (polyphenol) :

V.1. Definition:

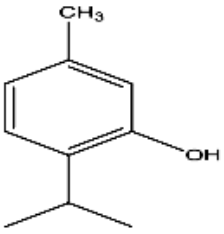
It is a group of secondary metabolic substances distinguished by containing one or several hydroxyl groups linked to aromatic ring nuclei. They are non-nitrogenic compounds that include thousands of molecules and are divided into several chemical sections, which have in common that they consist of at least one aromatic ring that is linked to a functional group. It may be a free hydroxyl, an ester function, an ether, or a sugar molecule. The biosynthesis of these parts is similar, as they are all produced from shikimic acid and from phenolic compounds as follows:



Acide shkimi



Quercetin



Thymol

V.2. Source:

The Phenolic compounds are considered healthy substances necessary for the body and are found in grape leaves and fruits, olive oil, pomegranates, tea, etc.

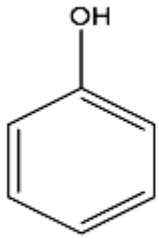
V.3. Effects :

Some types of polyphenols are considered antioxidants, soothe inflammation, and protect against cancer. It has been shown, after some tests of pomegranate juice, to limit the growth of cancer cells such as breast, lung, skin, intestine, and prostate cancer. Flavonoids protect the body's cells from free radicals. They are atoms or molecules with single electrons, which are often active. They play an important role in chemical reactions. They reduce the accumulation of fat in the blood vessels. Some studies also show that in atherosclerosis, the thickness of fat in the internal artery is reduced by 30%,, and this is after consuming pomegranates for three years. Phenols are also used to treat temporary strokes and cardiac shock.

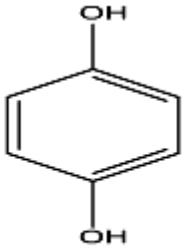
V.4. Category: Phenolic compounds are divided according to their coordination into:

V.4.1. Simple phenols (C_6) :

They consist of a hydroxyl group attached to an aromatic ring.



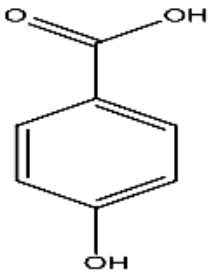
phénol



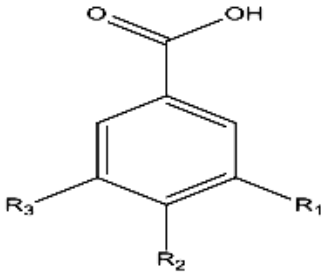
Hydroquinone

V.4.2. Phenolic acids structure (C_6-C_1):

It is considered one of the most common phenolic compounds. It consists of a benzene ring connected to a carboxyl group, such as:



acid phenolique (*p*-hydroxybenzoique)



(R_1=R_3=H, R_2=OH)

Acide phenolique (acid hydroxy 4-benzoique)

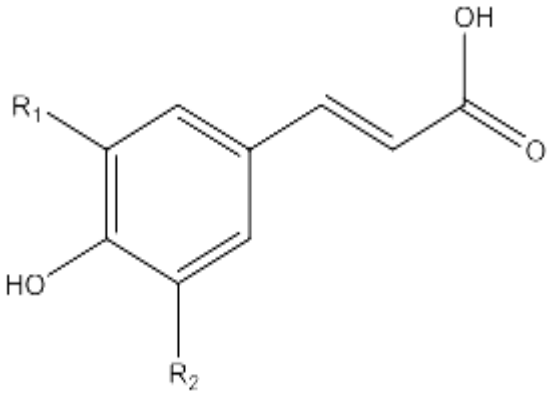
(R_1=R_2=R_3=OH) Acide gallique

(R_1=OCH_3, R_2=OH, R_3=H) Acide vanillique

V.4.3. Phenolic compounds with structure (C_6-C_3) :

It consists of two main sections:

A. hydroxycinnamic acid: They exist in the form of isomers (E‹Z) due to the presence of the double bond in the lateral root, and the E form is the most abundant because it is more stable. Hydroxycinnamic acids include four compounds that almost no plant organ is devoid of at least one of, which are:



Acids (ferulic, sinapic, caffeic, paracoumaric)

(R_1=R_2=H) Paracoumaric acid

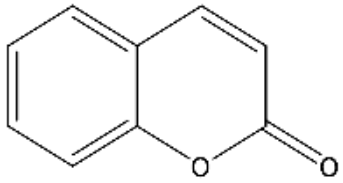
(R_1=OH, R_2=H) A. caffeic

(R_1=OCH_3, R_2=H) A.Ferulic

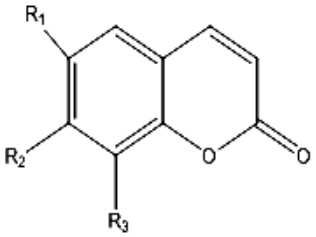
(R_1=R_2=OCH_3) A sinapic

B. Coumarines:

Coumarin was isolated in 1820, and this name was derived from the plant from which it was separated. It is composed of the basic structure (C3-C6). It is a benzene ring linked to a heteroatom containing an oxygen atom and a ketone function, as follows: Explained in the following figure: Examples of some coumarins



coumarine

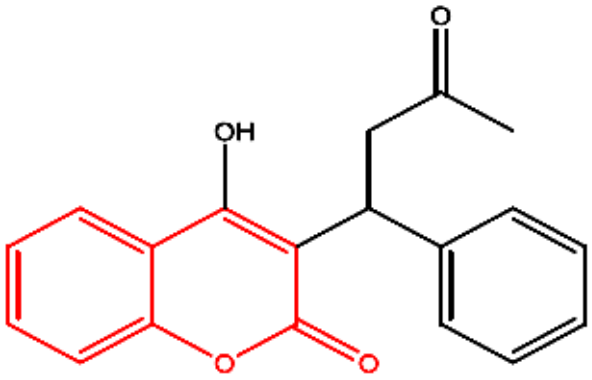


(R_1=R_2=R_3=H) ⟶ Coumarine)

(R_1=R_3=H, R_2=OCH_3) ⟶ Herniarine)

(R_1=R_2=OH ,R_3=H) ⟶ Esculétol)

Coumarin has a sweet smell like clover and is used in the pharmaceutical industry, such as in the formulation of a number of antibiotic drugs for clotting, such as:

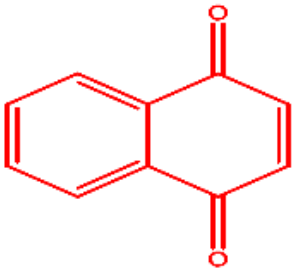


Coumaphéne

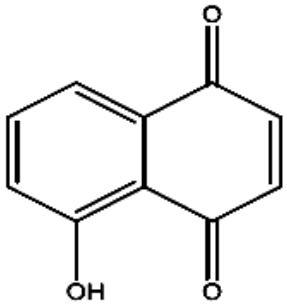
V.4.4. Phenolic compounds with structure (C_4-C_6):

It is an organic compound that forms yellow crystals with an irritating and pungent odor similar to benzoquinone and has antiseptic properties. For bacteria and tumors, examples of this include juglon (an extract from walnuts).

It also forms the central structure of many natural compounds, such as vitamin K.

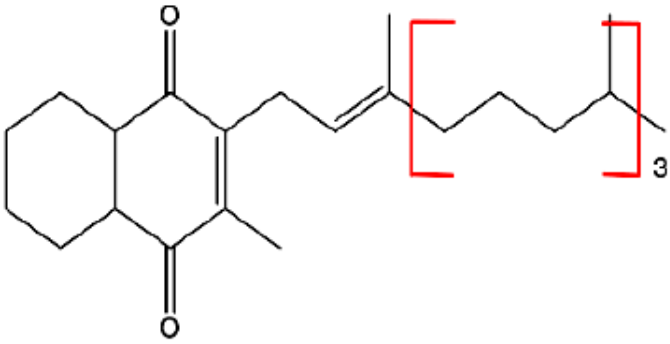


Naphoquinone



juglon

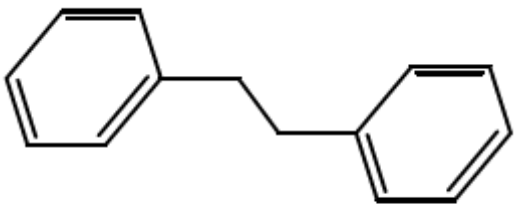
It also forms the central structure of many natural compounds, such as vitamin K_1.



V.4.5. Phenolic compounds with the structure C_6-C_2-C_6 Stelbenoides:

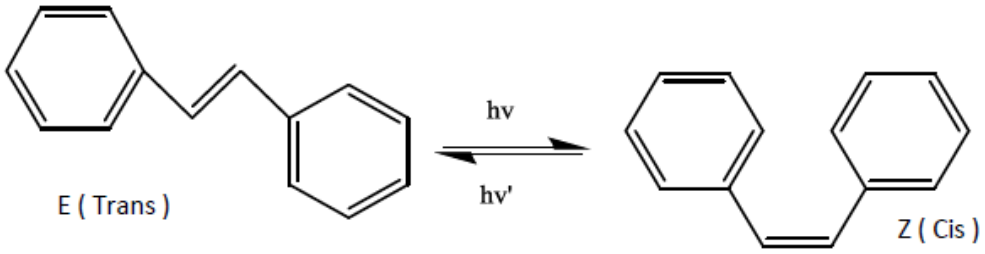
It consists of two Banzene rings linked by a bridge consisting of two carbon atoms, and it is one of the secondary metabolites produced by the plant when attacked by a plant pathogen. There are three categories, depending on the bridge connecting the aromatic rings:

• (Ethane) (C-C):



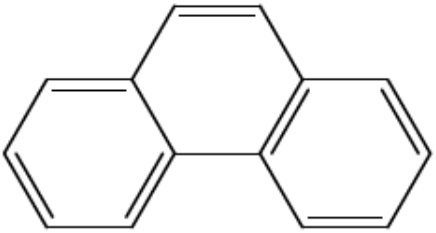
1,2-diphenylethane

• **(Ethène) (C=C):**



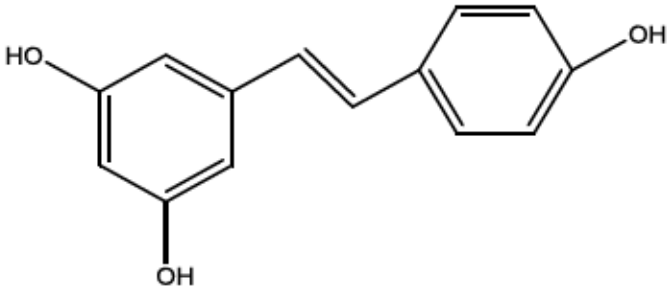
Stibénes(tras-cis)

• **Cyclic :**



Phénanthrénes

As an example of a trans-resveratrol compound (extracted from grapes),



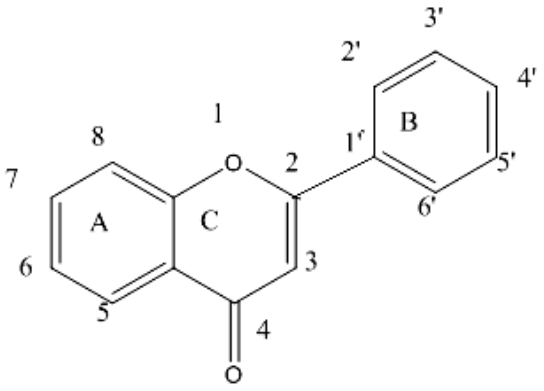
Trans- Resvératrol

V.4.6.Phenolic compounds with a structure (C_6-C_3-C_6): It is divided into several sections, including.

V.4.6.1 Flavonoid:

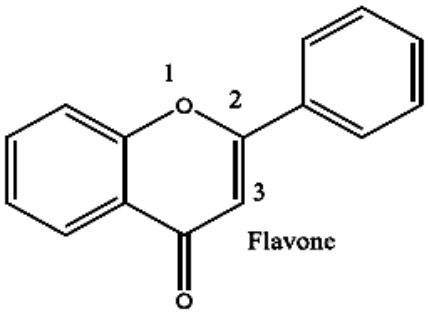
It has been known since 1952 by the scientist Geissmam; the origin of the word (flaves) is Greek, which means yellow color.

It is the most widespread phenolic compound. It is colored pigments that are concentrated, especially in the aerial part of the plant, with a sugar basis, or in the form of free compounds in the cytoplasm and fibrous membranes. The basic structure of flavonoids is the same as that of C_6-C_3-C_6, which is composed of 15 carbon atoms distributed over two rings A and B and connected by a heterogeneous ring. It contains an oxygen atom in position 1 and a ketone function in position 4, the connection point for ring B In loop C, starting from (C_2), which is as follows:

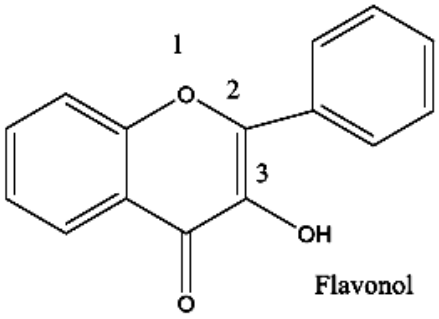


flavonoide

• Depending on the degree of oxidation of the C ring, it is divided into several other groups, such as flavone (flavones) if the C_3 position is not substituted, and flavonol (flavonol) if the C_3 site is substituted with an OH, as follows:

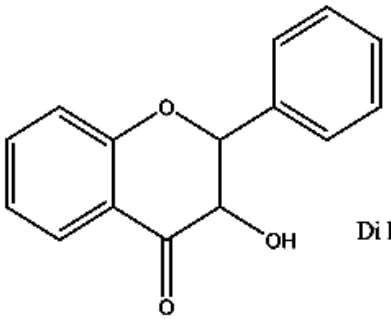


Flavone

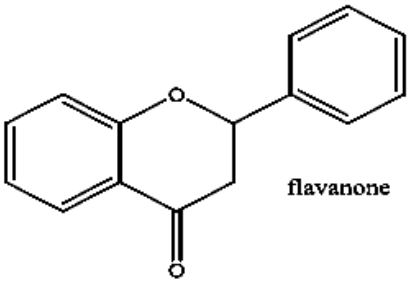


Flavonol

• While the bond between (C_2) and (C_3) is saturated, we get flavanone and flavanonol (dihydroflavonol) on Consecutively:



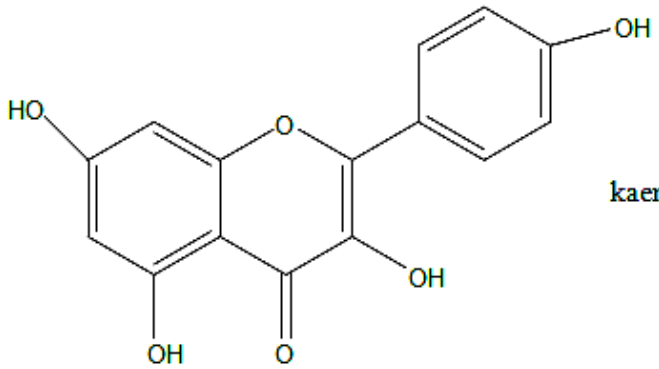
Di hyro flavonol (flavanonol)



flavanone

• As an example, kaempherol belongs to the class of flavonoids and the flavonol group. Kaemphèrol is extracted from strawberries.

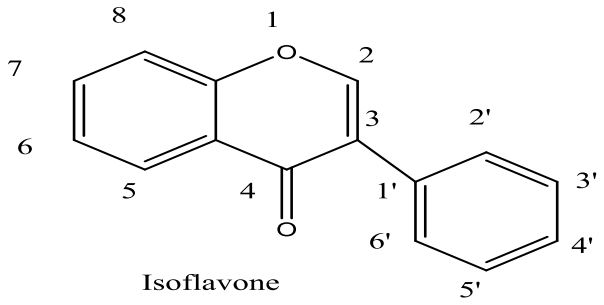
For example, kaempherol belongs to the class of flavonoids (flavonol group)



kaemphèrol

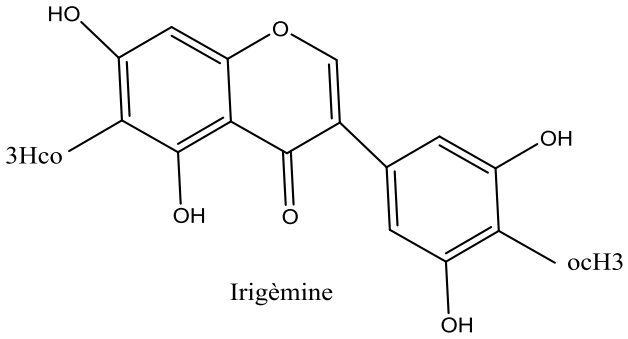
V.4.6.2. Isoflavonoids:

It is a plant-based substance that produces the hormone estrogen inside the body and is also known for its antioxidant effectiveness. It is found in abundance in beans and soybeans. It differs from flavonoids in terms of the connection between the B and C rings, where The bonding is at the carbon atom (C_3) as follows:



Isoflavone

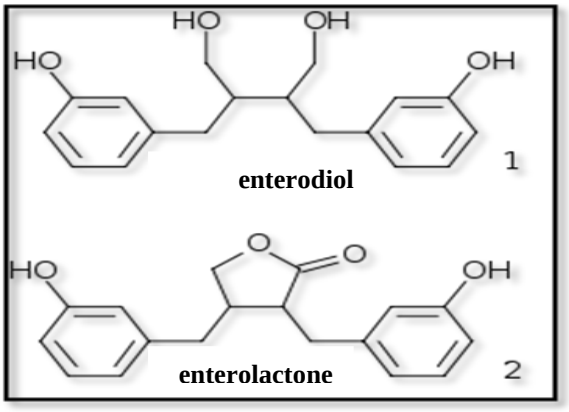
Example:



Irigèmine

V.4.7. Phenolic compounds with a lignan structure $(C_6–C_3)_2$ (lignans):

They are compounds consisting of two phenylpropane units and are produced by the dimerization reaction of substituted phenols derived from cinnamic acid. It explains as follows: .



V.4.8. Phenolic compounds with a (C_6–C_3)n structure (lignin):

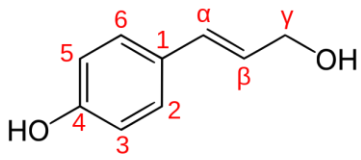
A complex chemical compound extracted from wood, which represents the secondary wall of the plant cell wall. The term lignin was first introduced by the Swiss botanist Augustin Pyramus de Candolle in 1819, who derived it from the Latin word lignum, meaning wood.

Lignin is one of the most common natural polymers on Earth after cellulose. As a biopolymer, lignin . They are all derived from phenylpropane:

1 - Alcool paracoumarylique. 2 – Aalcool conifférylique. 3- Alcool sinapylique

Alcool paracoumarylique.	**1**
Aalcool conifférylique.	**2**
Alcool sinapylique	**3**

1



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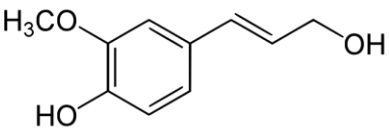

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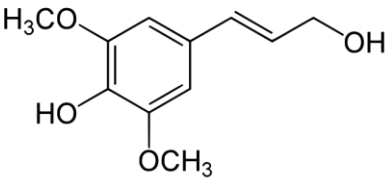
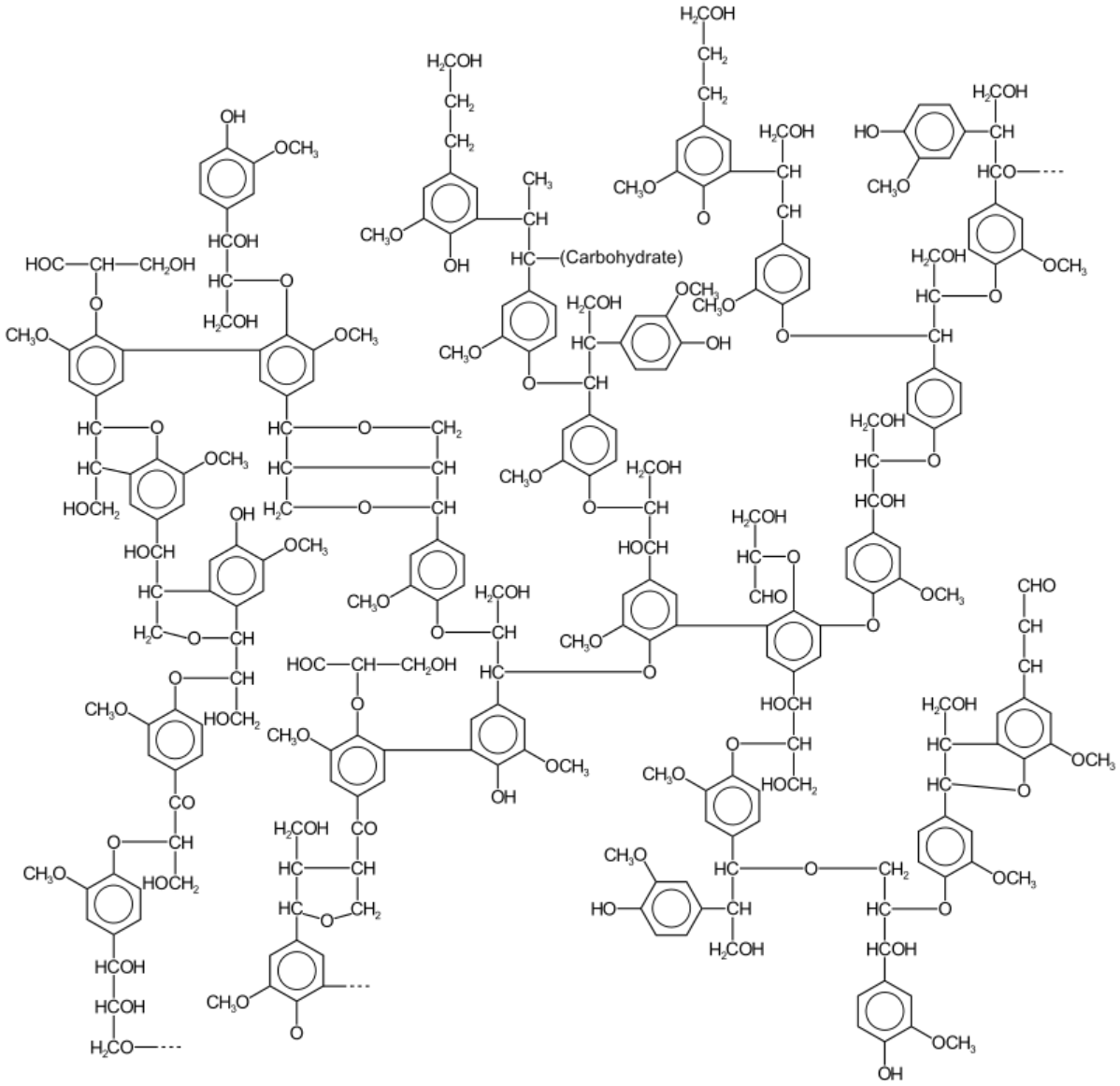


The following figure builds the structure Lignin



V.4.9. Tannins:

Tannins are found in vacuolar contents with phenolic properties. They are found intrinsically or deposited in the cells of connective or visceral tissue in many plant species. Their characteristics include protein precipitation and leather tanning. They are divided into two types: tannins Biodegradable and non-biodegradable condensed tannins.

biodegradable tannins:

They are complex molecules of sugar esters (polyhydroxy) and a variable number of phenolic acid molecules found in pomegranates and cloves.

Their hydrolysis produces a sugar moiety, most often glucose, and a phenolic moiety consisting mainly of gallic acid. Or ellagic acid, as shown in **Figure 24** below.

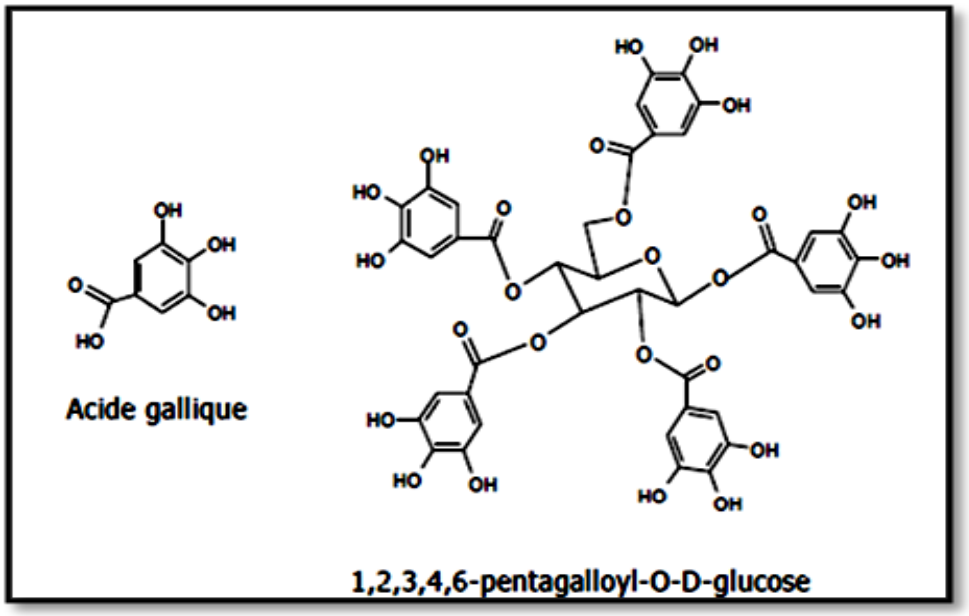


Fig. 24: Biodegradable tannin

Condensed tannin :

They are condensed flavonoid compounds that are not bound to glucose .
They are in the form of a polymer and are found in cinnamon and tea. They consist of flavanol units (chatechine). These units are linked at carbon C_4 of the unit and carbon C_8 of the unit that is its hill, as in **Figure 25** .

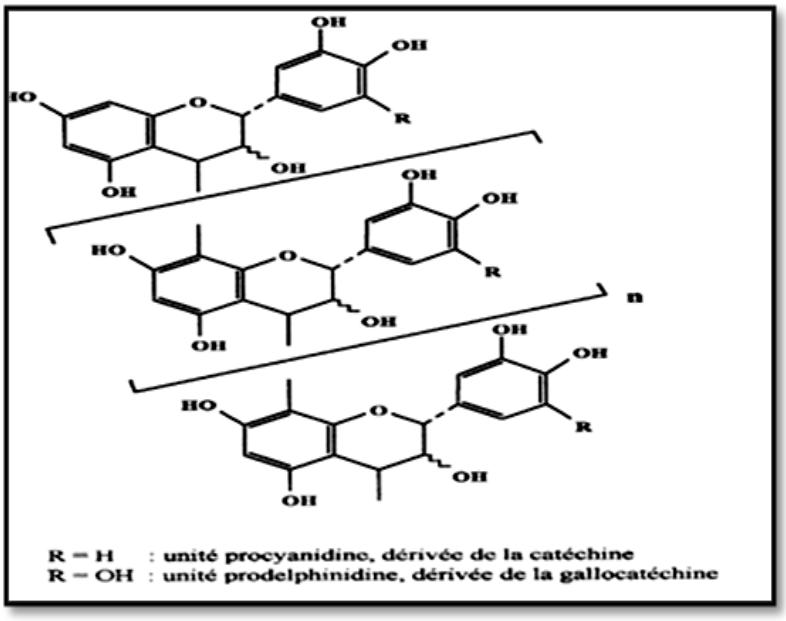
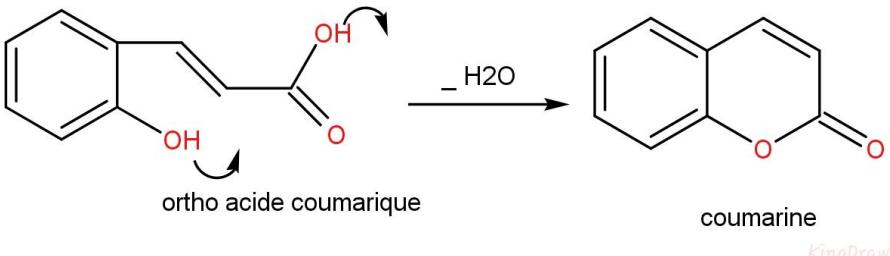


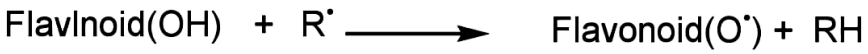
Fig. 25 Condensed tannin

Physical and Chemical Properties of Polyphenols:

- Phenols are dissolved in polar organic solvents and in solutions of sodium hydroxide and sodium carbonate.
- All substituted formulations of phenolic compounds partially dissolve in water.
- Easily oxidizable, especially in alkaline mediums.
- Cinnamic acid circulates easily when it contains hydroxyl in the ortho position of the side chain.
- The lactone ring is formed with the removal of the water molecule, which forms coumarin, which is the most physiologically active of the phenols.



- Examination with CCM and ultraviolet rays of coumarins is represented by colored spots that are more evident in the presence of ammonia (NH_3).
- Flavonoids are colorful compounds and are the cause of plant coloration.
- Flavonoids with a weak acidic character dissolve in strong bases as they dissolve in organic polar solvents because they contain free or sugary hydroxyl groups.
- Less polar compounds, such as isoflavones with the lowest number of methoxy groups, are dissolved in chloroform or ether.
- Flavonoids are compounds capable of capturing many oxidizing species.



- Phenols contain a hydroxyl group, which makes them form hydrogen bonds within molecules in complex phenolic compounds, which makes them change many properties such as melting point,solubility, UV spectra,IR, etc.
- Phenols with minerals (Fe,Al) form complexes.

- **Chemical Study:**
- **Flavonoids Detection:**

We take 2 g of dry powder and put it in 30 ml of water with chloric acid (HCl %1) and leave it for 24 hours. We filter and then perform the following tests:

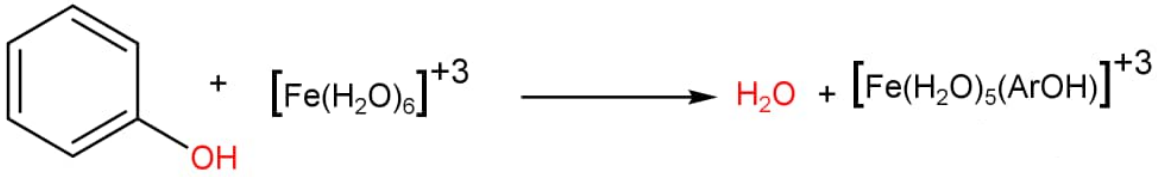
We take 5 ml of leachate and add ammonium hydroxide (NH_4OH) to it until the base, and we notice the appearance of a light yellow color as evidence of the presence of flavonoids.

We add a small amount of magnesium (Mg) to the sour extract when we notice the appearance of a red color as evidence of the presence of sugar flavonoids.

- **Phenol Detection: (Reaction with $FeCl_3$)**

Most phenols react with iron chloride to produce a colored complex. Where 1 ml of it is dissolved in a mixture of water and alcohol, to which three drops of an aqueous solution of iron hloride are added, we notice the formation of a precipitate or discoloration (red, blue, purple,purple ,.... etc.).

This is evidence of the presence of phenol .



1: Total Phenols Extraction:

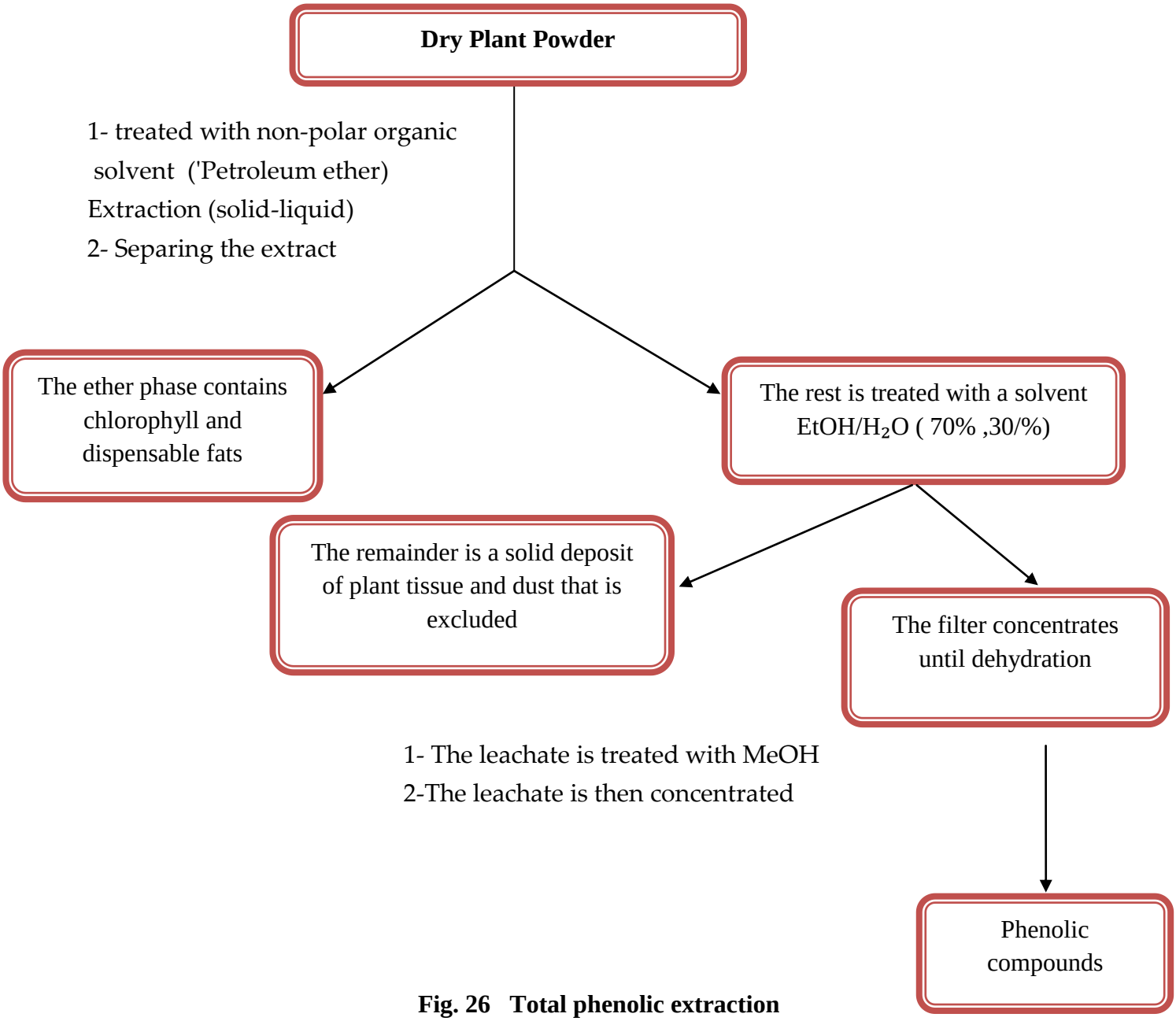


Fig. 26 Total phenolic extraction

2-Extraction of flavonoids and Glycoflavonoids:

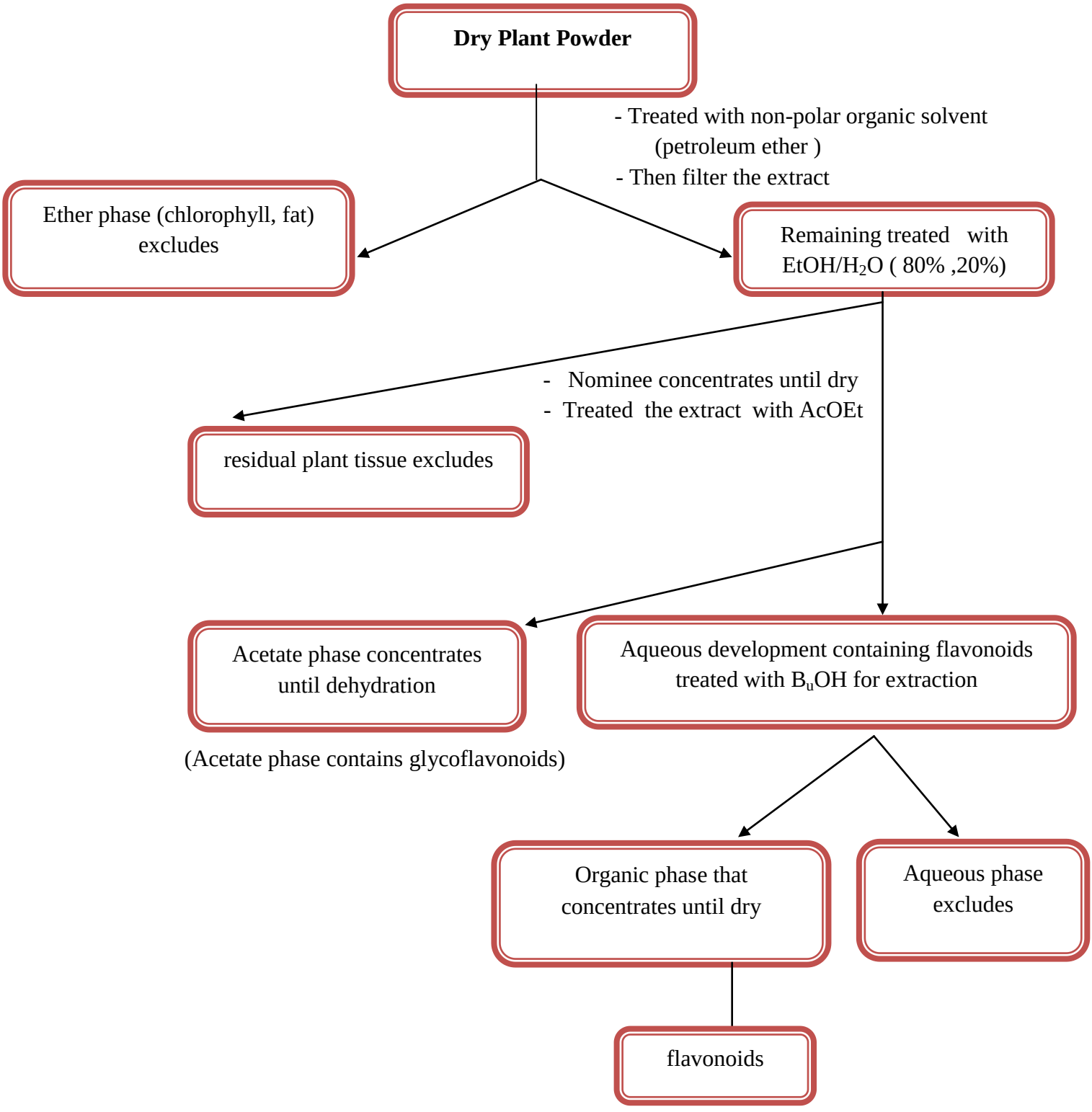


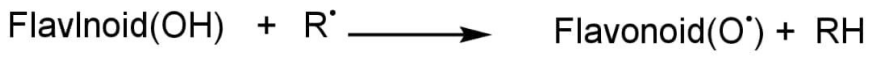
Fig. 27 Glycoflavonoids and Free Flavonoids Extraction

- **The importance of phenols:**

It has been proven that phenol has many health benefits. It is an antioxidant. It is known that plant compounds that contain phenol are antioxidants. This means that they can stop the interaction of free radicals with other molecules in your body, which prevents damage to your DNA. It is found in tea. And fruits and vegetables. Among the most important phenolic compounds with biological activity are flavonoids. Interest in flavonoids has increased in recent years, such that the results of extensive research in the fields of medicine and biology have shown their anti-cancer, anti-allergic, anti-viral, anti-bacterial, antioxidant, and other activities.

- **The importance of flavonoids as antioxidants:**

Flavonoids are characterized by their comparative properties to oxidation due to the presence of (OH) groups, which are:

- This depends on the ability to edit protons
- On flavonoids, and in general, the hunting of these roots depends on the chemical formula of flavonoids and their replacements.
- 

- **The use of flavonoids in the pharmaceutical industry:**

- Interest in flavonoids has increased in recent years, as the results of extensive research in the fields of medicine and biology have shown their anti-cancer, anti-allergic, antiviral, and antibacterial efficacy.

- **Anti-cancer effect:**

- Numerous and extensive experiments have proven the preventive role of flavonoids against the appearance of cancer. The antioxidant activity of these compounds is one of the first mechanisms to be studied. Flavonoids work to scavenge free radicals that lead to DNA abnormalities. Deoxyribonucleic acid (ADN) leads to mutations in tumor or tumor-suppressing genes. Tumors, which are considered a precursor to the emergence of this disease.

Effect of Flavonoids on Diabetes :

- Flavonoids have an important impact on diabetes. These compounds may help and give a positive behavior in people with diabetes, including :
- Reducing the chances of developing type 2 diabetes, especially heart attack .
- Lowering cholesterol levels.
- Keep blood sugar levels under control .
- Lower levels of insulin resistance.

The Sixth axis
Saponins

VI. Saponins

VI. 1. Definition:

They are heterogeneous substances of sterols or terpenes that have foaming properties for their aqueous solutions, or what is known as tensioactives that is, reducing the surface tension between two liquids and they are defined as compounds from aphrogénes, that is, foam activators.

Most saponins have hemolytic properties; hemolysis is the destruction of red blood cells that release hemoglobin (Hb) into the blood plasma and is a normal physiological state. In healthy individuals, RBCs are destroyed after a 120-day life span. However, in some cases, hemolysis is exaggerated, which reduces the lifespan of erythrocytes; this is called excessive hemolysis. Eventually it develops into anemia, which is toxic in cold-blooded animals.

VI. 2. Distribution of the areas in which the plant is found:

Saponins are abundant in plants:

- **Les saponosides stéroidique**: EX; Liliaceae, Agavaceae, Dioscoreaceae

They are found exclusively in monocotyledon angiosperms

- **Les saponosides triterpénique:** EX; Araliaceae, Caryophyllaceae, Curcubitaceae, Renunculaceae…

They are found in dicotyledon angiosperms.
In general, saponins are found in all parts of the plant, especially in roots, seeds and follicles .

VI. 3. Chemical Composition:

High molecular weight glycosides, released by hydrolysis of one or more **génine** and called **Sapogénine.**

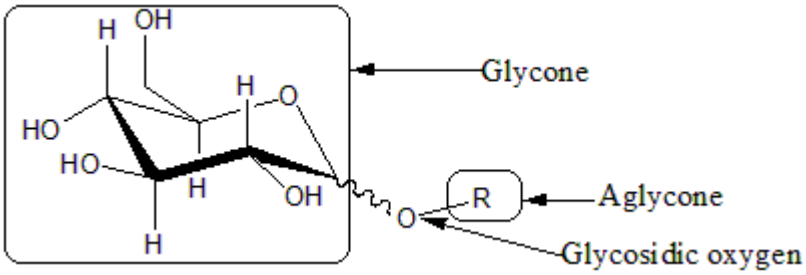
VI. 4. Definitions:

Sapogénine : is one of the aglycone parts of a group of natural compounds.

Glycosides : are a group of organic compounds in which a sugar group is linked with another group by an O-glycosidic bond.

Glycosides play an essential role in biology, and many plant glycosides are used as medical drugs. It is a sugar molecule associated with a non-diabetic part, called the glycone, while the non-diabetic part is called the aglycone, or the basic part, which we call the genin.

Glycone : can consist of a single sugar group (monosaccharide) or several sugar groups (oligosaccharide)

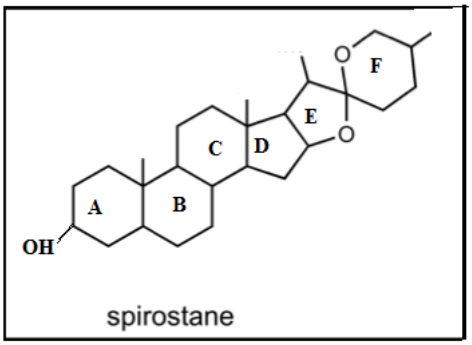


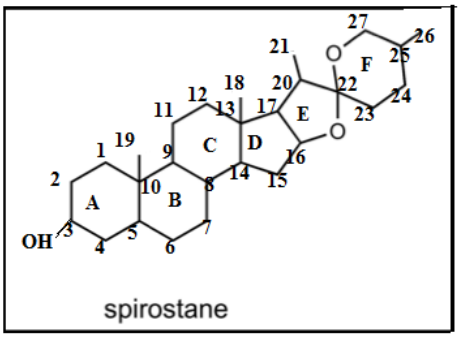
Glycoside

Génine : It belongs to two different types of organic structures, Stéroïde and Triterpène.

1. Genin steroid :

- that has an organic structure of 27 carbon atoms for the SPIROSTANE nucleus comprising 6 rings A,B, C, D, E,F.
- The A,B,C,D rings are for the steroid nucleus.
- In position C17 there are two heterogeneous rings, the E ring (furanique) and the F ring (pyranique).
- In position C3 forms a secondary alcohol.

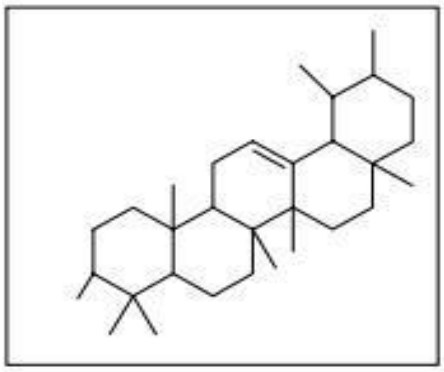




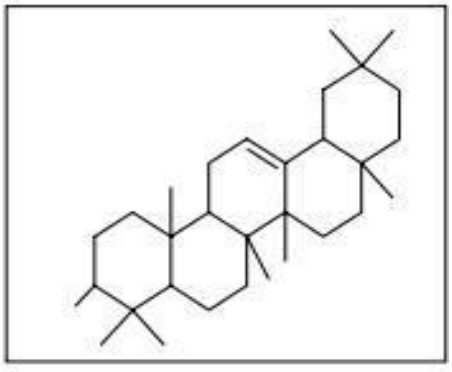
Génine stéroidiq

2. Genine Triterpenic:

The triterpenes of Genine have a basic organic structure composed of C_{30}, forming a core of four rings of the Dammarane type, which is an intermediate compound evolving towards pentacyclic organic structures of the Naneael type (amyrine- β) or the Ursane type (amyrine- α).



amyrine- α



amyrine- β

VI. 5. Biological synthesis of saponins:

Steroidal saponins and triterpenoid saponins have the same source, which is Squalene.

VI. 6. Physical and chemical properties of saponins:

Extraction, characterization, and quantitative study

- **Physical and chemical properties:**

- Saponins are soluble in hot water, foamy solution, and alcoholic solutions but do not dissolve in non-polar organic solvents.
- Sapogenin dissolves in non-polar organic solvents and does not dissolve in water.

- **Extraction of saponins:**

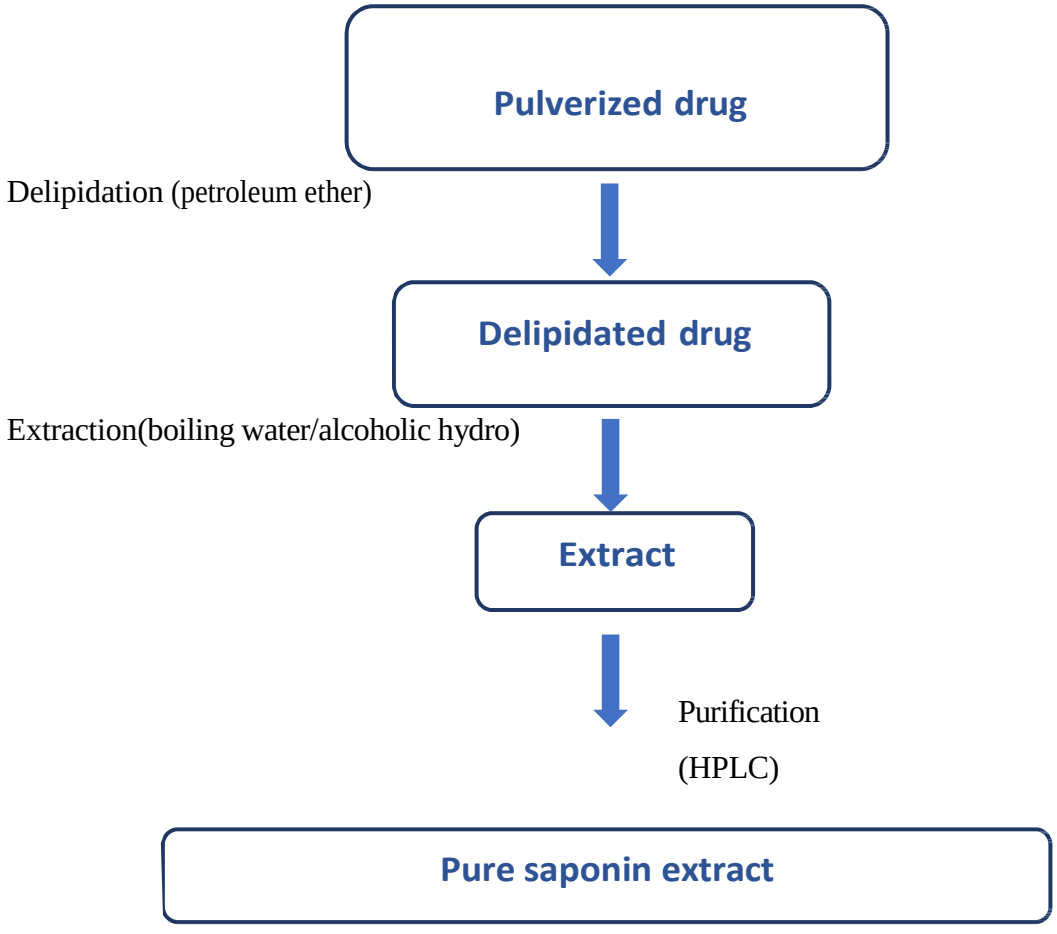


Fig. 28 Saponin extraction scheme from a plant drug

➢ **Description:**

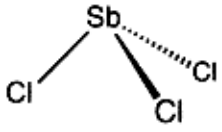
1- Indicators:

Hemolytic index: It is a degree of dilution for the preparation that under certain conditions causes complete hemolysis of red blood cells.

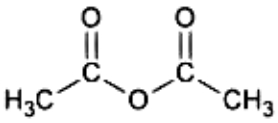
Foam index: It is a degree of dilution of aqueous solution for the preparation under certain conditions, gives stable foam.

2- Color reactions: Non-specific reactions, for example:

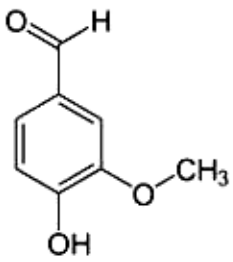
- **Libermann Reaction:** in the presence of acetic anhydride in sulfuric medium:
  - ✓ With triterpenic genins **pink** to **red** coloration
  - ✓ With steroidal genins **blue-green** coloration
- **Vanillin or Anisic Aldehyde Reaction** in strong acidic medium:
  - ✓ Strongly colored product
- **Carr and Price Reaction:**With antimony trichloride in acetic anhydride medium, a blue or pink coloration is obtained.



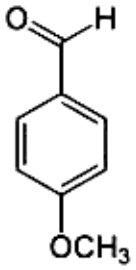
Antimony Trichloride



Acetic Anhydride



Vanillin



Anisic Aldehyde

Chromatographic Separation Methods:

CCM: used for monitoring saponin plants, in the presence of witnesses and expecting and identifying them (Revelation) by colorimetric reagents.

❖ **Quantitative Dose Study:**

- ✓ **Indices :** inaccurate dosage
- ✓ **Gravimetric (weight measurement):** by precipitation of sapogenins after hydrolysis and weighing of the residue
- ✓ **Colorimetric and spectrophotometric**
- ✓ **Chromatographic methods:** HPLC.

VI. 7. Therapeutic Properties:

➢ **Harmful effect on cells resulting in:**

- Fever at the lung level from the effect of expectorant (phlegm or mucus).

These secretions come from the respiratory system and the oral cavity such as mucus, which is one way of transmitting infections to some bacteria or viruses that affect the respiratory system (influenza virus in particular).

They should not be confused with secretions from the digestive system (in the presence of blood, comparing two colors of blood is sufficient to determine the source if it is digestive system or respiratory system).

- Impact on kidney cells (diuretic)
- Impact on red blood cells through hemolytic process.

- **Toxicity in cold-blooded animals:** Other therapeutic properties of saponins: It is antifungal, antiviral, and anti-inflammatory.

VI. 8 . Saponins Uses :

- Saponin plants are used as anti-inflammatory, expectorant, antidote, and diuretic medications, etc.
- In industry, saponin extracts are used for several purposes including:
- Raw Materials for Semi-synthesis of Steroid Derivatives: Sapogenin was the first molecule used in the synthesis of steroid hormones.

Examples: **Diosgenin** extracted from various tubers from Dioscorea plant and **Hecogenin** that extracted from Aloe Vera plant, the latter is the most important in semi-synthesis.

- As foaming agents: like Panama wood.

Plant-based raw materials for the semi-synthesis of steroid derivatives:

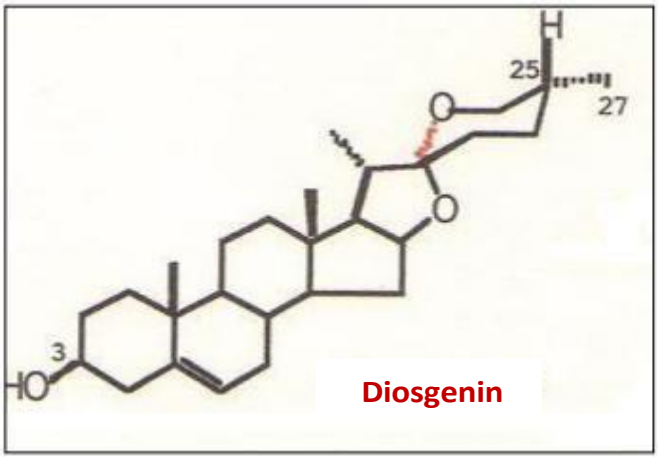
1) Diosgenin:

Source: Tubers of Dioscorea Species (Dioscoreaceae) with a diosgenin content of over 2%:

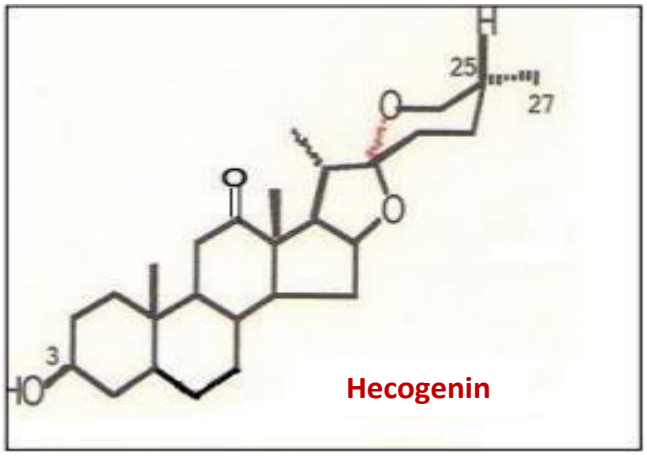
Dioscorea composita, D floribunda, D mexicana, D spiculiflora...

2) Hecogenin:

Source: Leaves of agaves (Agavaceae): Agave sisalana, A fourcroydes.



Diosgenin



Hecogenin

Principles Drugs with Saponosides:

1- Licorice: *Glycyrrhiza glabra* L, Fabaceae

- **Plant:** Large perennial herbaceous plant

✓ Very developed underground parts

✓ Compound imparipinnate leaves - violet flowers Varieties:

  - Typica (Spain, Italy, Turkey)
  - Glandulifera (Central and Eastern Europe)
  - Violacea (Iran, Iraq)

- **Drug:** root - stolon, fluid extract.

✓ Production:

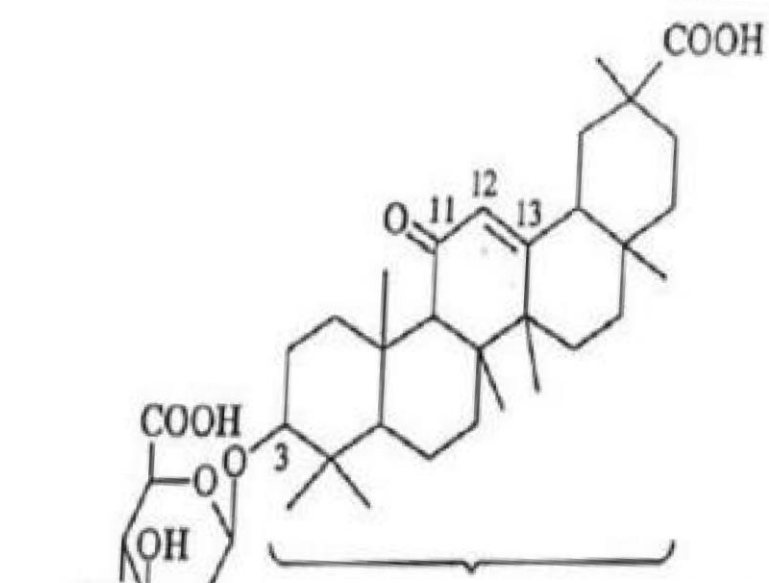
  - Wild and cultivated plants - harvested in autumn

✓ Characteristics:

  - Cylindrical gray-brown sticks with bright yellow section - sweet taste
  - Anatomy: fibers accompanied by cells with calcium oxalate prisms.

✓ Chemical Composition:

  - Saponosides: glycyrrhizin (6-12%), mainly glycyrrhizic acid.



glycyrrhetic acid = glycyrrhetinic acid

(ENOXOLONE)

2 D-glucuronic acids

glycyrrhizic acid

Flavonosides: (1.5%): liquiritoside, isoliquiritoside

- ✓ Physiological action:
  - Mineralocorticoid (excess -> edema)
  - Anti-inflammatory
  - Anti-gastric ulcer
  - Hypocholesterolemic
  - Various properties: antispasmodic, diuretic, expectorant, sweetener...
- ✓ Tests:
  - Botanical
  - Physio-chemical characterization and dosage of glycyrrhizin
- ✓ Use:
  - Galenic forms: sweetener, anti-gastric ulcer, antispasmodic
  - Extraction of glycyrrhizin => glycyrrhetinic acid (enoxolone) local anti- inflammatory, treatment of oral inflammations and infections (Arthrodont), anti-hemorrhoidal (Sédorrhoïde)
  - Semi-synthetic product: carbenoxolone: anti-gastric ulcer.

List of references

List of references

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