Separation of Plant Contents

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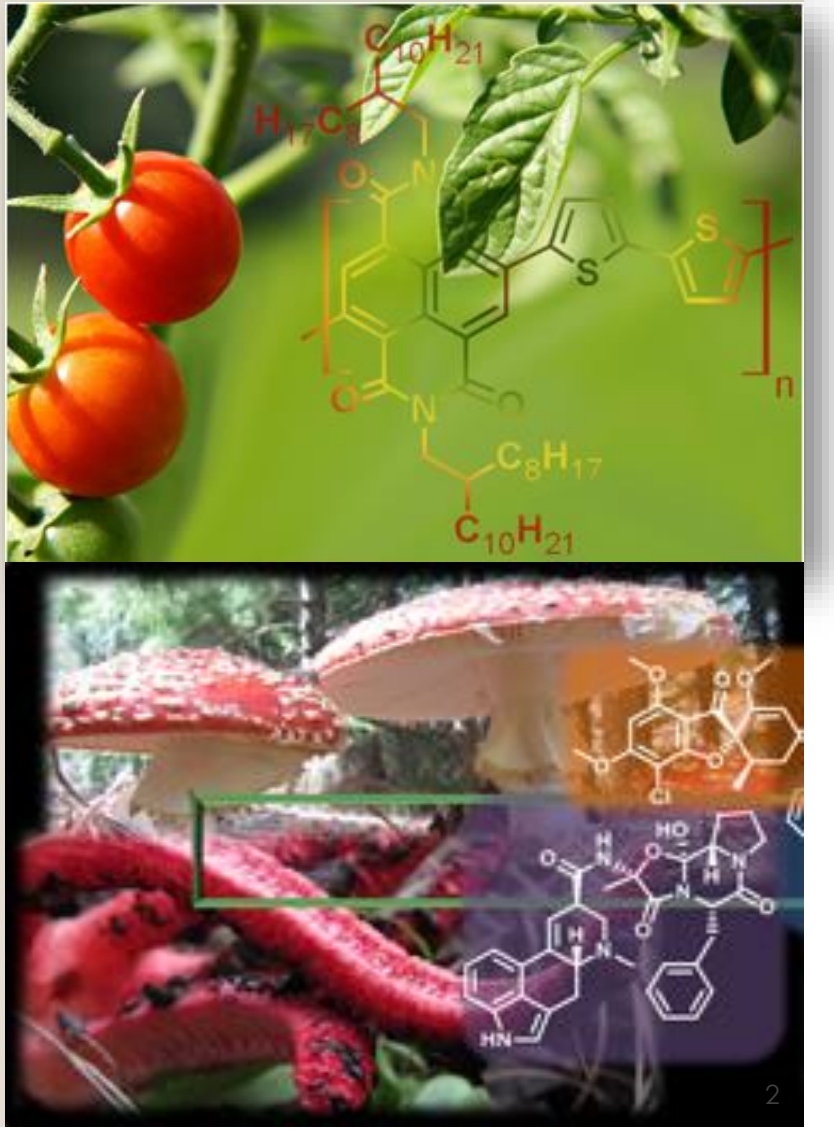
Introduction to Natural Products

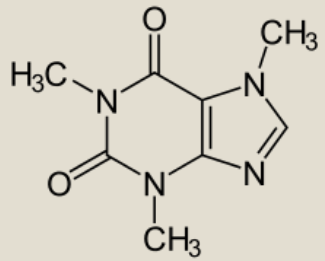
- Natural products are products from various natural sources, plants, microbes and animals.
- Natural products can be an entire organism (e.g. a plant, an animal or a micro-organism), a part of an organism (e.g. leaves or flowers of a plant, an isolated animal organ), an extract of an organism or part of an organism and an exudate, or pure compound (e.g. alkaloids, coumarins, flavonoids, lignans, steroids and terpenoids) isolated from plants, animals or micro-organisms.
- However, in practice, the term natural product refers to secondary metabolites, small molecules (molecular weight < 1500 amu), produced by an organism, but not strictly necessary for the survival of the organism.



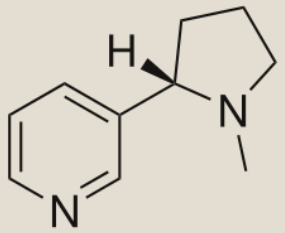
http://www.khalidshadid.com/chemistry-of-natural-products.html

The 18th century …

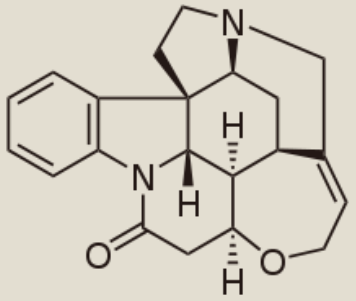
- At the end of the 18th century, crude drugs were still being used as powders, simple extracts, or tinctures.
- The era of pure compounds (In 1803, a new era in the history of medicine)
- Isolation of morphine from opium
- Strychnine (1817)
- Quinine and caffeine (1820)
- Nicotine (1828)
- Atropine (1833)
- Cocaine (1855)



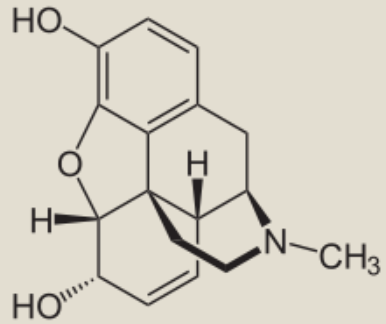
caffeine



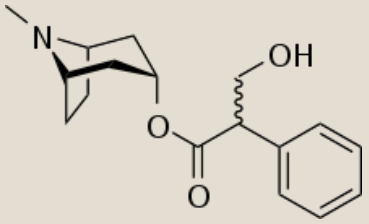
Nicotine



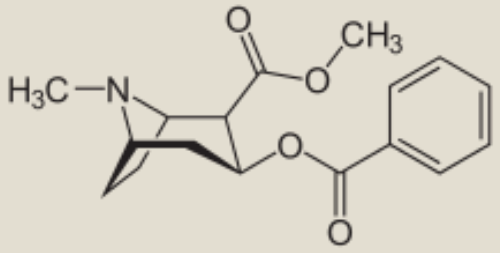
Strychnine



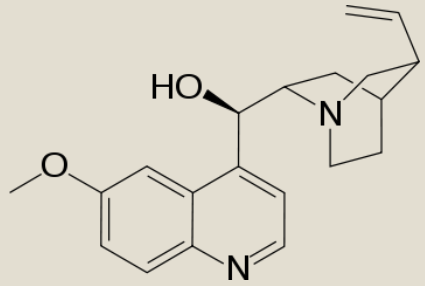
morphine



Atropine



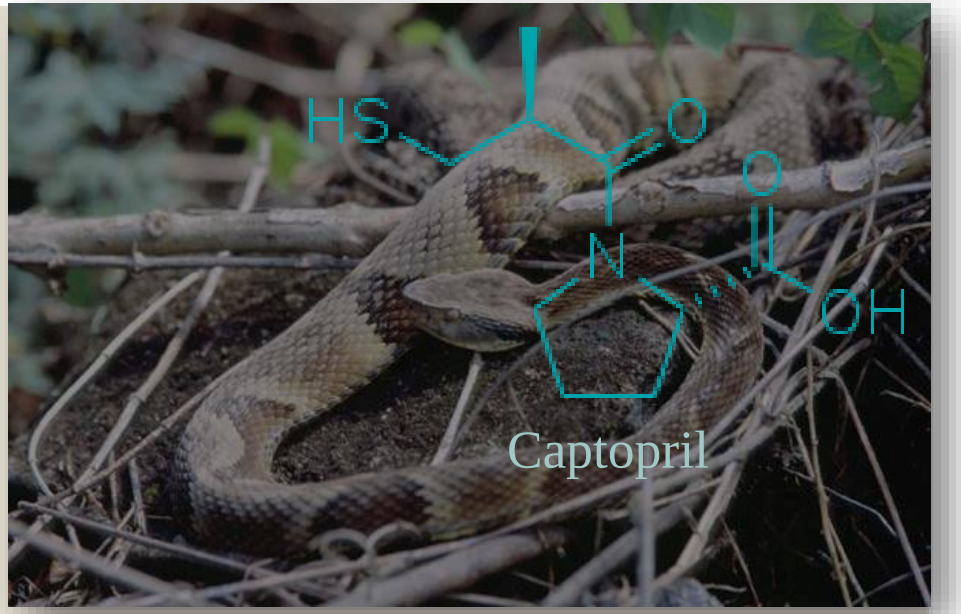
Cocaine

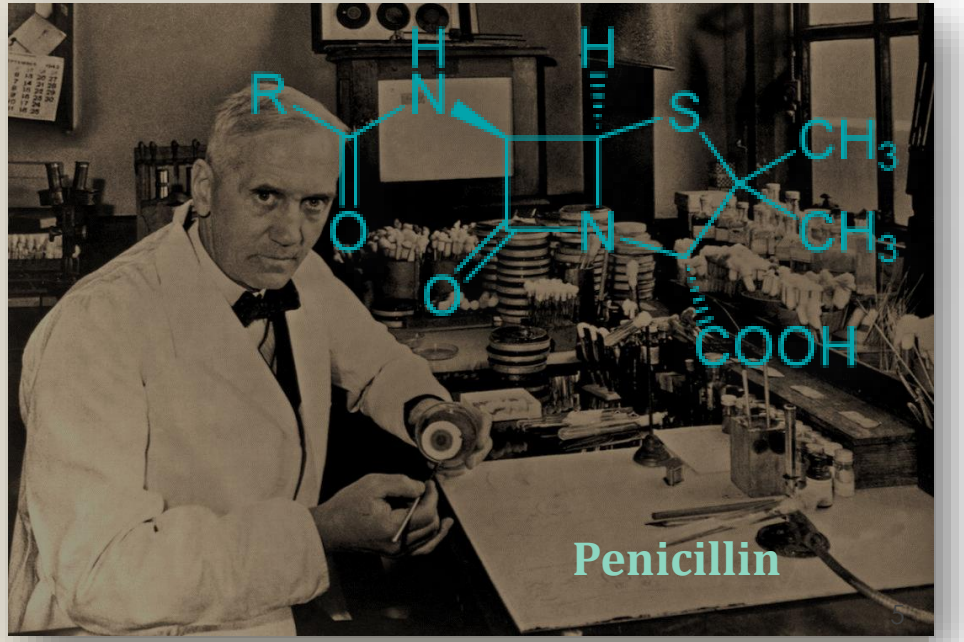


Quinine

- In the 19th century, the chemical structures of many of the isolated compounds were determined

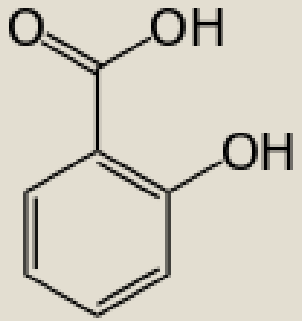
- In the 20th century, the discovery of important drugs from the animal kingdom, particularly hormones and vitamins. In addition, microorganisms have become a very important source of drugs



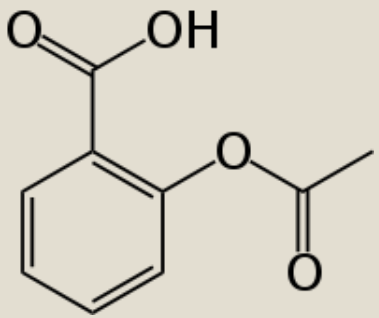


- ***Compounds from natural sources play significant roles in modern medicine:***

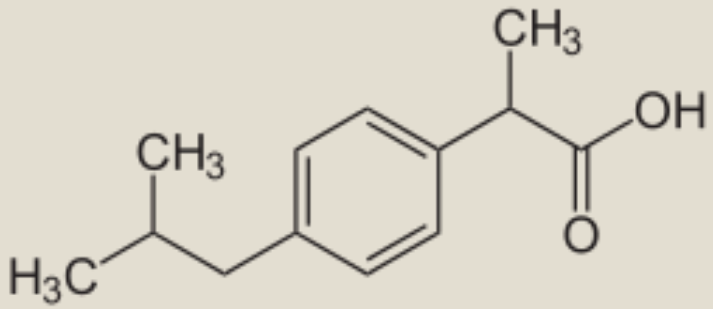
1. They provide a number of extremely useful drugs that are difficult, if not impossible, to produce commercially by synthetic means
2. Natural sources also supply basic compounds that may be modified slightly to render them more effective or less toxic
3. Their utility as prototypes or models for synthetic drugs possessing physiologic activities similar to the originals



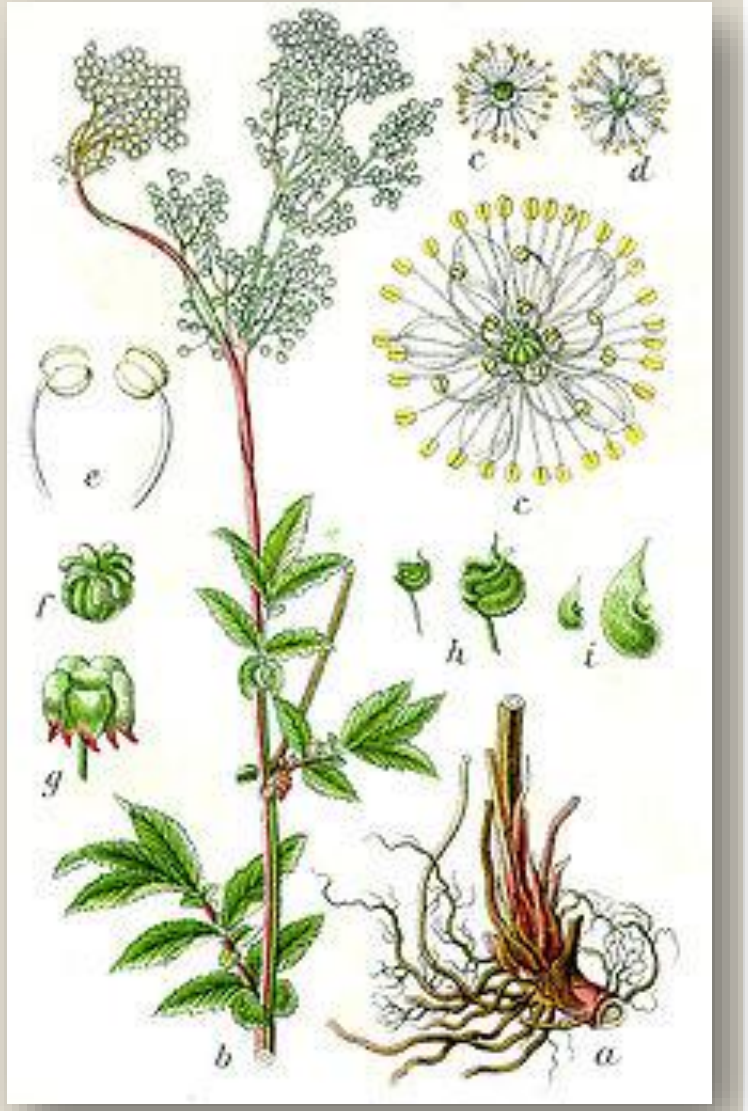
salicylic acid



Aspirin

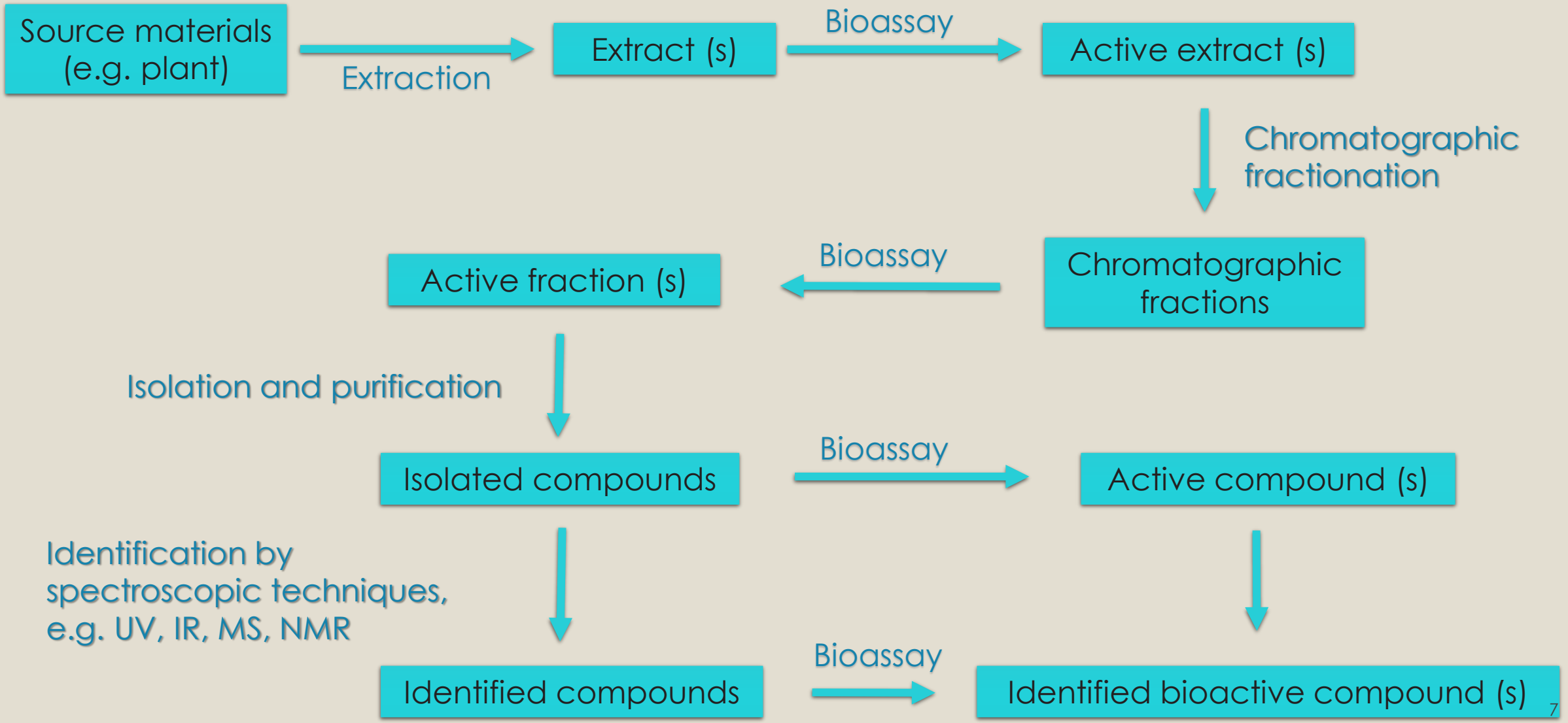


Ibuprofen

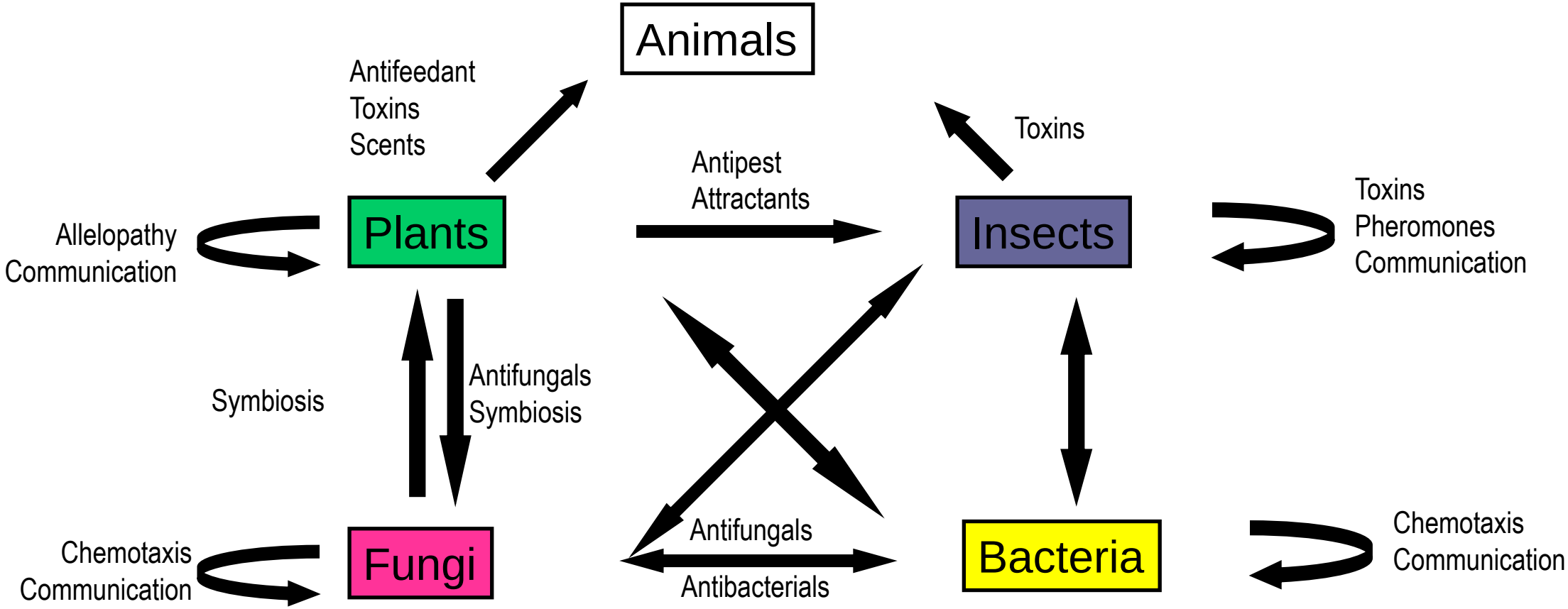


Spirea

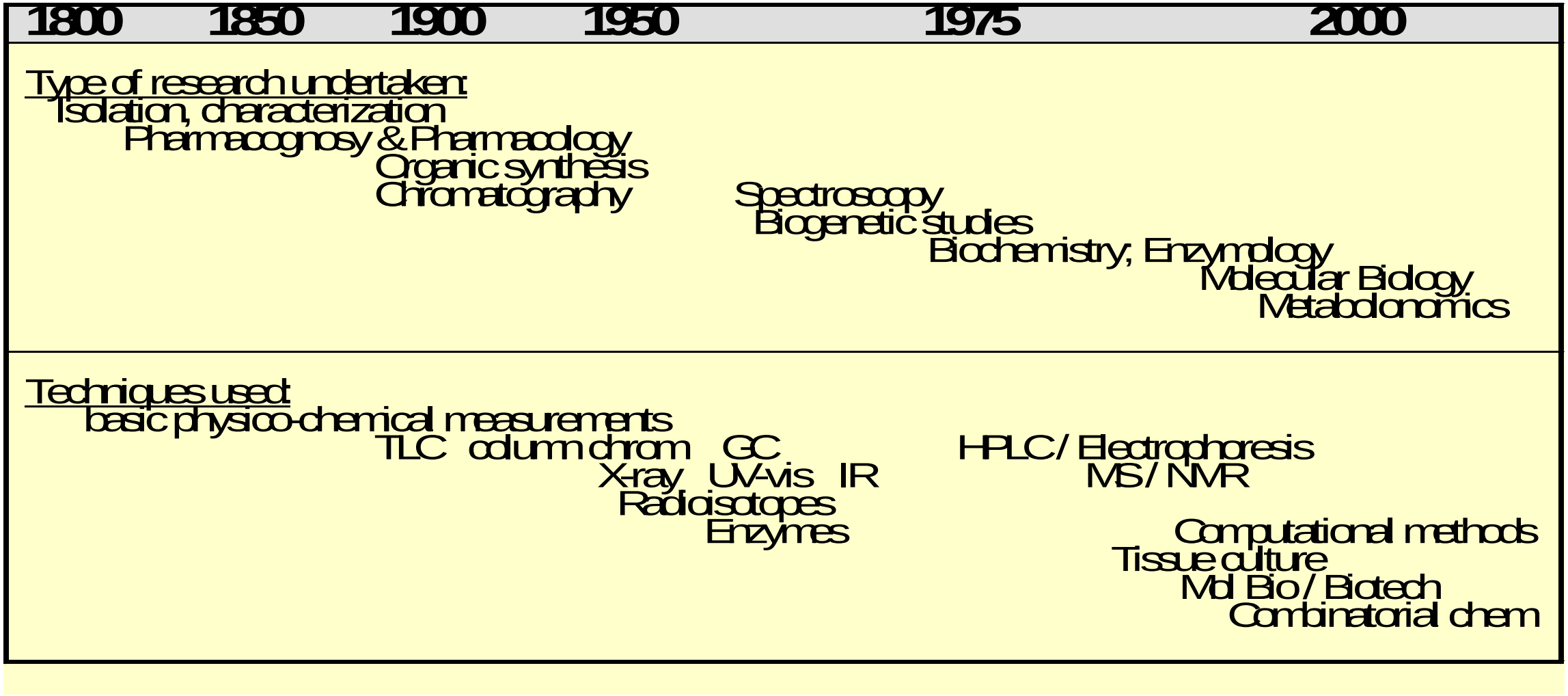
Overview of a bioassay-guided traditional natural product drug discovery process



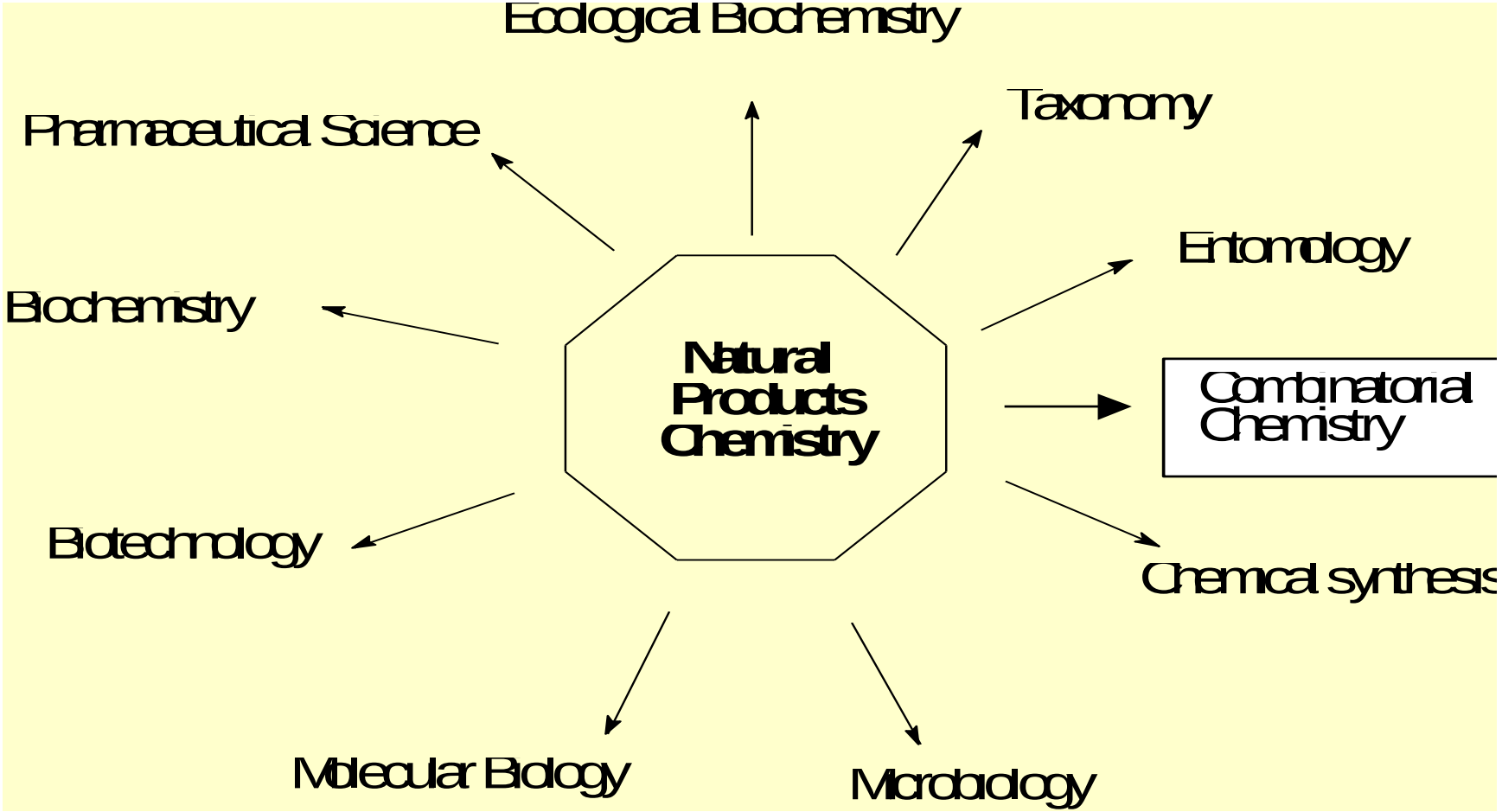
Natural products and Ecology



Techniques used in natural products chemistry



Natural products chemistry is at the intersection of many fields:



Classification of natural products based on chemical structural

Generally four classes

1- Open chain aliphatic compounds, Amino acids and fatty acids

2- Alicyclic compounds, Terpenoids and Steroids

3- Aromatic compounds, Phenolics and Quinones.

4- Heterocyclic compounds, Coumarins, Flavonoids and Alkaloids.

- Classes of Natural products
- There are many classes of natural products such as:

- Coumarins
- Terpenoids
- Flavonoids
- Carbohydrates
- Alkaloids,
- Steroids
- Amino acids
- Proteins
- Fatty acids and lipids

On the other hand natural products could be divided into two major classes

- Primary metabolites

- Secondary metabolites

Principles of Phytochemistry

- **Plant selection**
- **Plant collection**
- **Extraction using different solvents**
- **Isolation of the chemical constituents by using a suitable method of chromatography**
- **Structural elucidation** of the isolated compounds using chemical and physical conventional methods e.g chemical reaction, MS, UV, IR, NMR

- **Chromatography**

- **Chromatography may be described as the processes which allow the resolution of mixtures by affecting isolation of some all components**

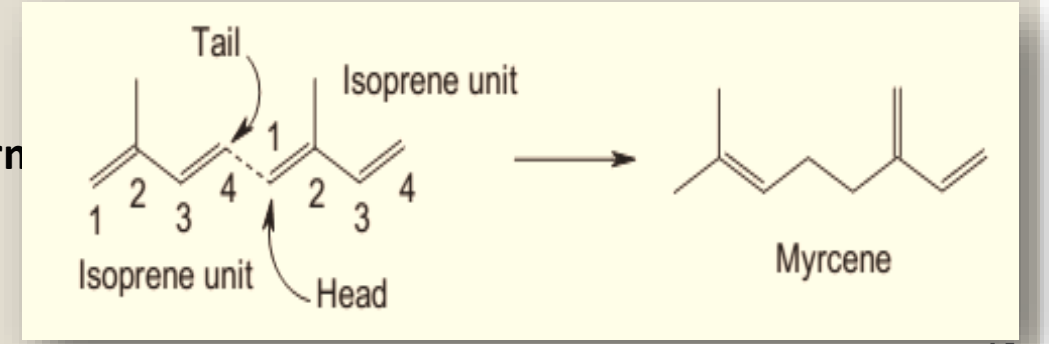
a. Solution chromatography

b. Gas chromatography

Terpenoids

- The odor of a freshly crushed mint leaf, like many plant odors, is due to the presence in the plant of volatile C_{10} and C_{15}, compounds, which are called terpenes.

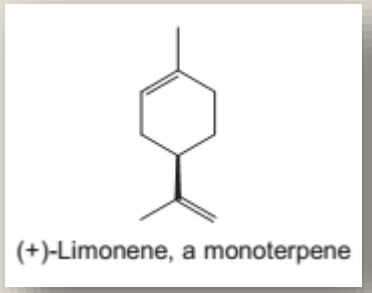
- Terpenoids are compounds derived from a combination of two or more isoprene units. Isoprene is a five carbon unit, chemically known as 2-methyl-1,3-butadiene.
- According to the isoprene rule proposed by Leopold Ruzicka, terpenoids arise from head-to-tail joining of isoprene units. Carbon 1 is called the 'head' and carbon 4 is the 'tail'.
- For example, myrcene is a simple 10-carbon-containing terpenoid form from the head to-tail union of two isoprene units as follows.

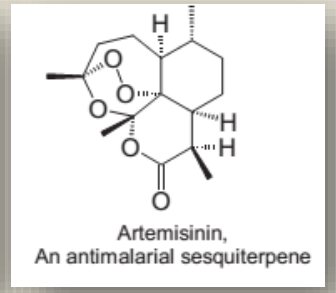


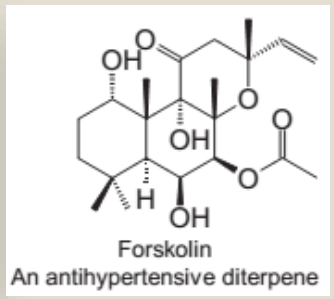
Classification

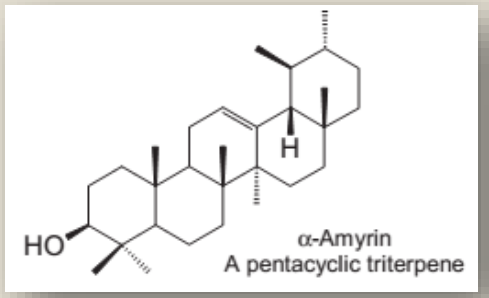
- **Terpenoids are classified according to the number of isoprene units involved in the formation of these compounds.**

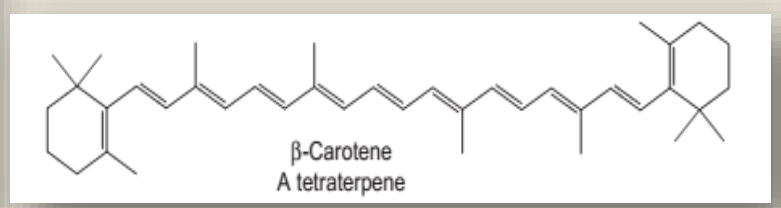
Type of terpenoids	Number of carbon atoms	Number of isoprene units	Example
Monoterpene	10	2	Limonene
Sesquiterpene	15	3	Artemisinin
Diterpene	20	4	Forskolin
Triterpene	30	6	α-amyrin
Tetraterpene	40	8	β-carotene
Polymeric terpenoid	Several	Several	Rubber

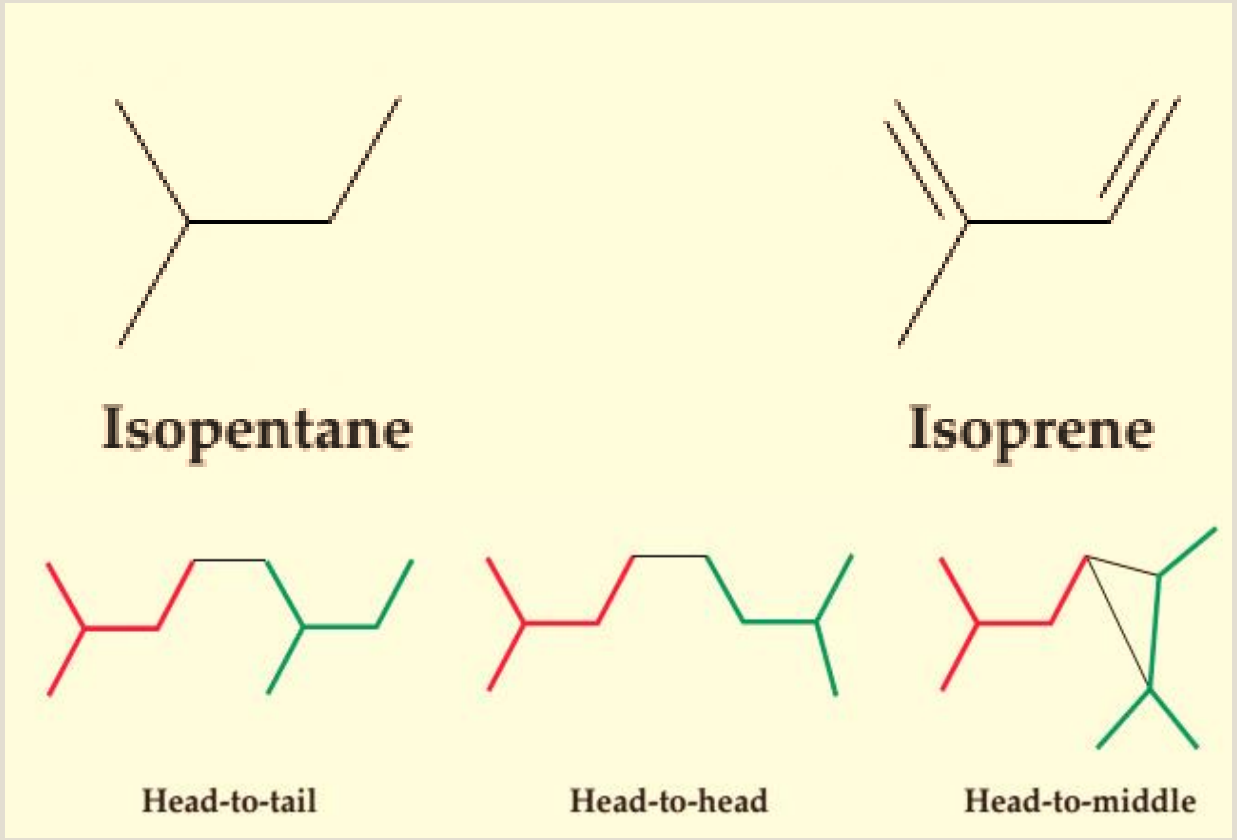

(+)-Limonene, a monoterpene


Artemisinin,
An antimalarial sesquiterpene


Forskolin
An antihypertensive diterpene


α-Amyrin
A pentacyclic triterpene


β-Carotene
A tetraterpene


Isopentane
Isoprene
Head-to-tail
Head-to-head
Head-to-middle

Classification of Terpenoids

- **Most natural terpenoid hydrocarbon have the general formula $(C_5H_8)_n$. They can be classified on the basis of value of n or number of carbon atoms present in the structure.**

S.No.	Number of carbon atoms	Value of n	Class
1.	10	2	Monoterpenoids($C_{10}H_{16}$)
2.	15	3	Sesquiterpenoinds($C_{15}H_{24}$)
3.	20	4	Diterpenoids($C_{20}H_{32}$)
4.	25	5	Sesterpenoids($C_{25}H_{40}$)
5.	30	6	Triterpenoids($C_{30}H_{48}$)
6.	40	8	Tetraterpenoids($C_{40}H_{64}$)
7.	>40	>8	Polyterpenoids(C_5H_8)n

- **Each class can be further subdivided into subclasses according to the number of rings present in the structure:**

i) Acyclic Terpenoids: They contain open structure.

ii) Monocyclic Terpenoids: They contain one ring in the structure.

iii) Bicyclic Terpenoids: They contain two rings in the structure.

iv) Tricyclic Terpenoids: They contain three rings in the structure.

v) Tetracyclic Terpenoids: They contain four rings in the structure.

General methods of determining structure

1- The molecular formula is determined by usual methods and also by means of Mass spectrometry

2-If oxygen is present in molecule, its functional nature is determined , it is present as hydroxyl, aldehyde, ketone, etc.

3- The presence of olefinic bonds is determined by means of bromine and the number of double boned is determined by analysis of bromine or by quantitative hydrogenation

- 4- Degradation oxidation, the reagent used for this purpose are Ozone, acid or alkaline permanganate, chromic acid , degradation oxidation has been the most powerful tool for elucidation the structures of terpenes.

5- Dehydrogenation of terpenes by sulphur

a. Heating the compound with the calculated amount of sulphur hydrogen eliminated as hydrogen sulphide.

b. Heating the compound with the calculated amount of seleniumHydrogen is eliminated as hydrogen selenide

c. Heating the compound with palladium or platinum-charcoal , hydrogen is eliminated

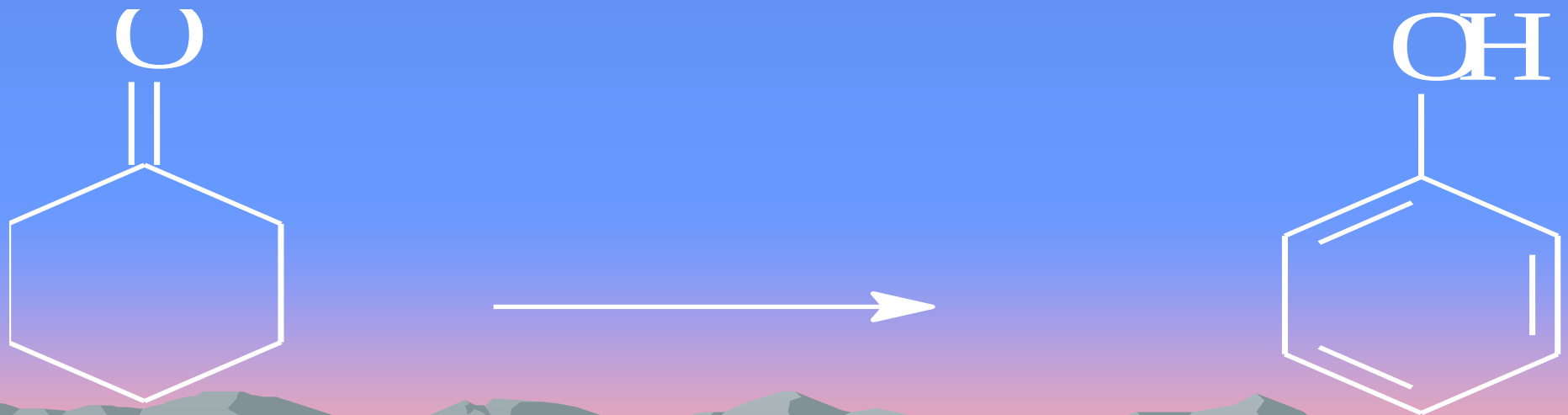
Cyclohexan Benzen

Hydrindene indene

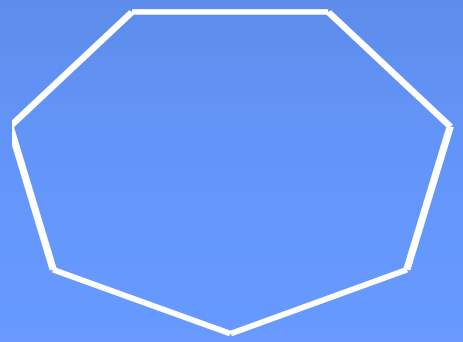
d. Alcoholic group may be eliminated with the formation of unsaturated hydrocarbones

e. Phenolic hydroxyl groups and methylated phenolic groups are usually unaffected by degedrogenation with sulphur

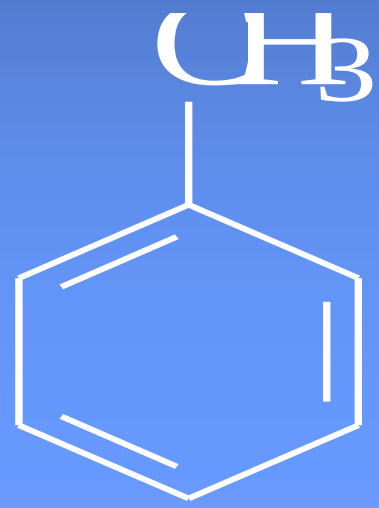
f. The products obtained from ketones depend on wheter the keto group is in ring or in an open ring, cyclic ketones are dehydrogenated to phenols



In some cases dehydrogenation is accompanied by rearrangement of carbon Skelton, this occur at higher temperature



at higher temp.



Cycloheptane

Side chain large than methyl may remain intact, or be eliminated or be degraded.

Dehydrogenation may produce new rings

Measurment of UV, IR, NMR spectra and mass spectrometry have been also used

After the analytical evidence has led to tentative structure, the final conformation the structure depened on the synthesis.

Monoterpenes

a. Acyclic
b. Monocyclic
c. bicyclic