



FACULTY OF PHARMACY

# Resin lignans

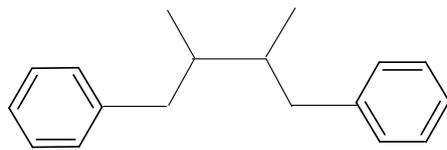
*Phytotherapy*



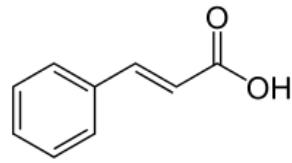
*Dr. Yousef Abusamra*

# Resin Lignans

- The lignans are a group of chemical compounds found in plants.
- Plant lignans are **polyphenolic** substances derived from **phenylalanine** via **dimerization** of substituted **cinnamic alcohols** to a dibenzylbutane.
- Example is podophyllotoxin.



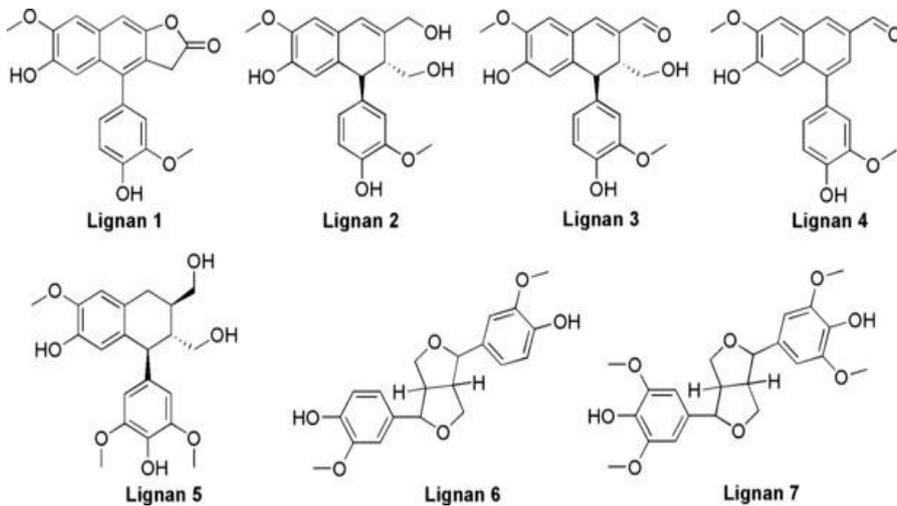
Dibenzylbutane



Cinnamic acid

1

## Examples of lignan structures



2

# Resins

- ❖ Resin is a "solid or highly viscous substance," which are typically convertible into polymers.
- ❖ Such viscous substances can be plant-derived or synthetic in origin.
- ❖ Are of great medicinal and industrial importance.
- ❖ They are often mixtures of organic compounds.
- ❖ Many plants, particularly woody plants (e.g. Conifers) produce resin in response to injury.
- ❖ The resin acts as a bandage protecting the plant from invading insects and pathogens.

3

# Resins

## Resins & resinoids

- Toxic plant resins = phenolic compounds
- Important naturally occurring phenolic resin in plants
- Exists as amorphous & brittle solids
- Insoluble in water, soluble in organic solvents (alcohol, chloroform & ether)

- I. Tetrahydrocannabinol
- II. Hypericin



**Amorphous:** without a clearly defined shape or form.

4

# Resin lignans

## Podophyllum: البيروح

- Podophyllum resin is obtained from the **rhizomes** or **roots** of *Podophyllum peltatum* (American podophyllum) or *Podophyllum emodi* (Indian podophyllum). **Berberidaceae** it is known as **May apple**.

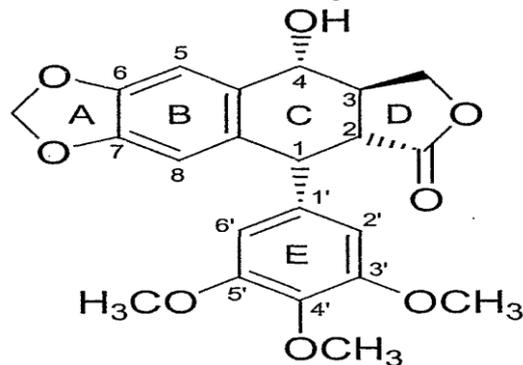


5

## Constituents:

- It contains 3.5 - 6% of resin. The active principle is the lignans, these include podophyllotoxin 20%,  $\alpha$ -peltatin 10%, and  $\beta$ -peltatin 5%. It contains also a number of lignan glycosides, they are water soluble and are lost during extraction of the plant.

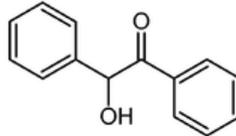
## Podophyllotoxin



- Uses:** The extract of the **roots and rhizomes** used as **purgative**, **caustic** مادة كاوية **antimitotic**.

6

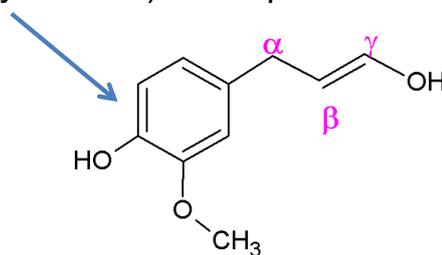
- Podophyllum resin known also as podophyllin and it is used as **1. caustic** for some papillomas [a small wart-like growth on the skin or on a mucous membrane, derived from the epidermis and usually benign.].
- It is applied topically as 25% dispersion in compound benzoin [a hydroxy ketone attached to two phenyl groups]tincture or 70% alcohol.



- The resin is also used as **2. purgative** in doses of 10 mg.
- A number of lignans with lactone rings in the *trans*-configuration are the tumor inhibiting constituents of podophyllum like **podophyllotoxin** and **α & β-peltatin**.

7

- **Biosynthesis** of these lignans by **dimerization** of two C<sub>6</sub>-C<sub>3</sub> units (coniferyl alcohol) at the β-carbon of the side chains.

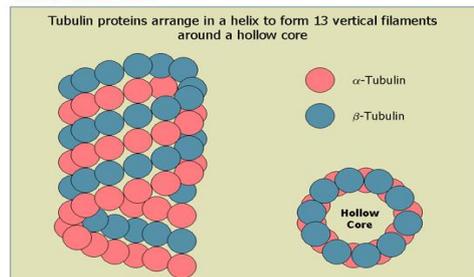


- **Etoposide**: is a lignan derivative obtained semi-synthetically from podophyllotoxin and used for treatment of **small-cell lung cancer**, **testicular cancer** as well as **lymphomas** and **leukemias**.
- Podophyllotoxin is a naturally occurring lignan (not lignin) from the rhizomes of *Podophyllum hexandrum* Royle (**Berberidaceae**).
- Has an important anti-neoplastic and antiviral properties.

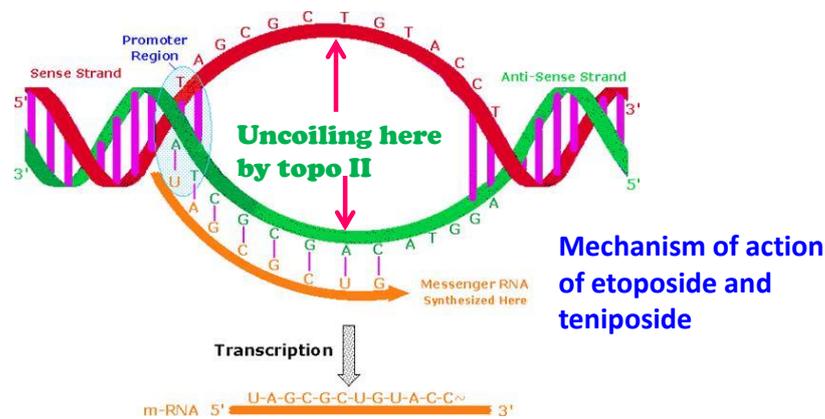
8

- Podophyllotoxin and their glycosidic derivatives (Etoposide and Teniposide) have different mode of action.
- Podophyllotoxin inhibits the microtubules preventing assembly, but its glycosidic derivatives like etoposide and teniposide inhibit DNA topoisomerase II by stabilizing the covalent topo II-DNA cleavable complex (preventing unwinding during replication).
- Accordingly, glycosidic derivatives of podophyllotoxin reduce the side effects.

Microtubules



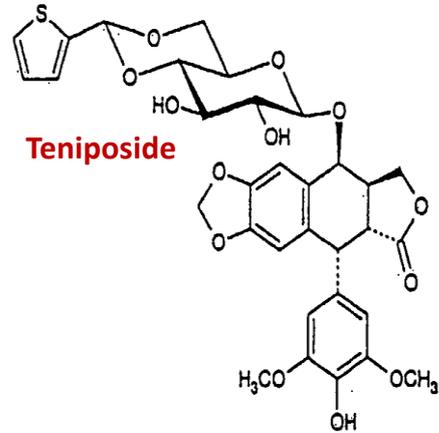
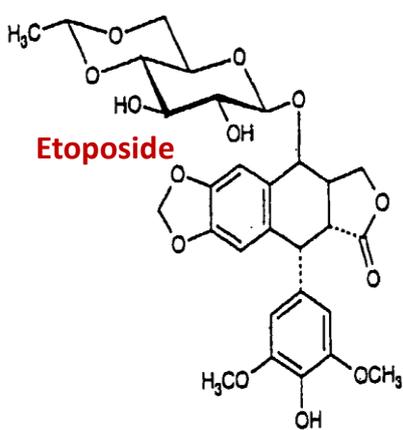
9



- Podophyllotoxin has been widely used in traditional herbal medicine of many diverse cultures as remedies as purgative, snakebites, periodontitis التهاب اللثة, skin disorders, coughs, various intestinal worm disease, venereal (sexual) wart condyloma acuminatum, lymphadenopathy اعتلال العقد اللمفية and certain tumors, but
- **Its glycosidic derivatives are mainly used in the treatment of cancer disease.**

10

**\*\* They are glycosides.**



11

## Cannabinoids:

### Indian hemp (marijuana):

- *Cannabis sativa* (Cannabaceae) is indigenous to central and western Asia, cultivated widely in India and many tropical countries for its fibers (**hemp fibers are used in industry for example**) and seeds (**for seed oil that has many benefits for health, it is devoid of the psycho-active components**).
- **Note:** hemp has very low psycho-active constituents and is cultivated for fibers, while marijuana is rich in these psycho-active ingredients, like tetrahydrocannabinol (THC).



**Hemp**

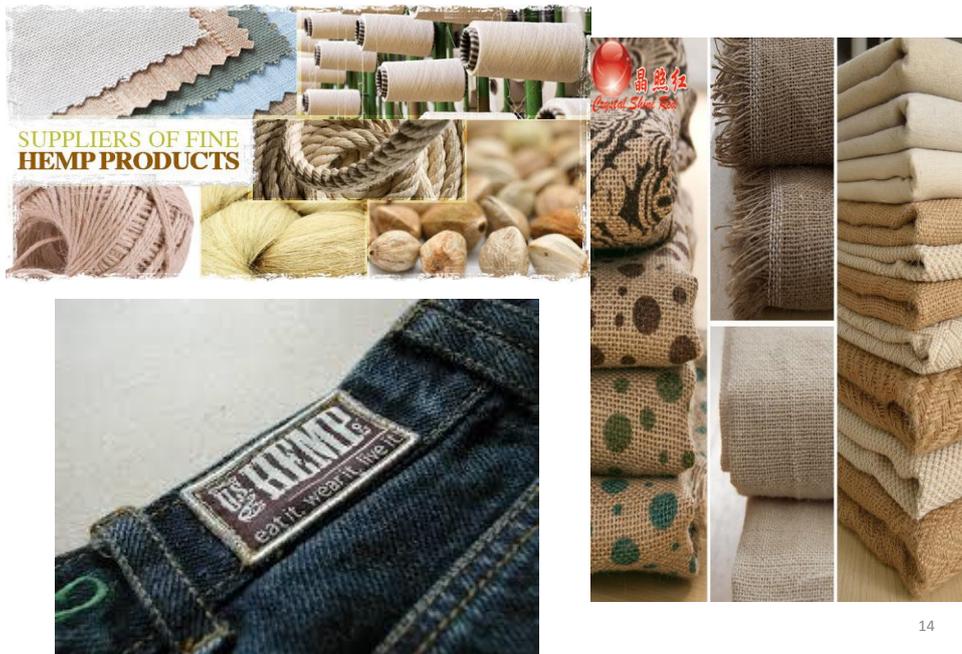
12

## Some hemp industry products



13

## Some hemp industry products



14



- In many countries, its consumption and possession is **illegal**.
- If it is cultivated in **cold countries**, it will be tall and used for its fiber, while if it is cultivated in **tropical** and **subtropical** countries, for sake of its use as a drug.
- The active principles are secreted as a **resin** by glandular hairs from the time first flowers appear until the seeds reach maturity.
- It is more concentrated in the leaves and flowering tops.
- Indian cannabis (tropical) produces about 15-20% of the resin, while plants in the temperate region produce less amount of the resin with less quality (less quality and quantity).

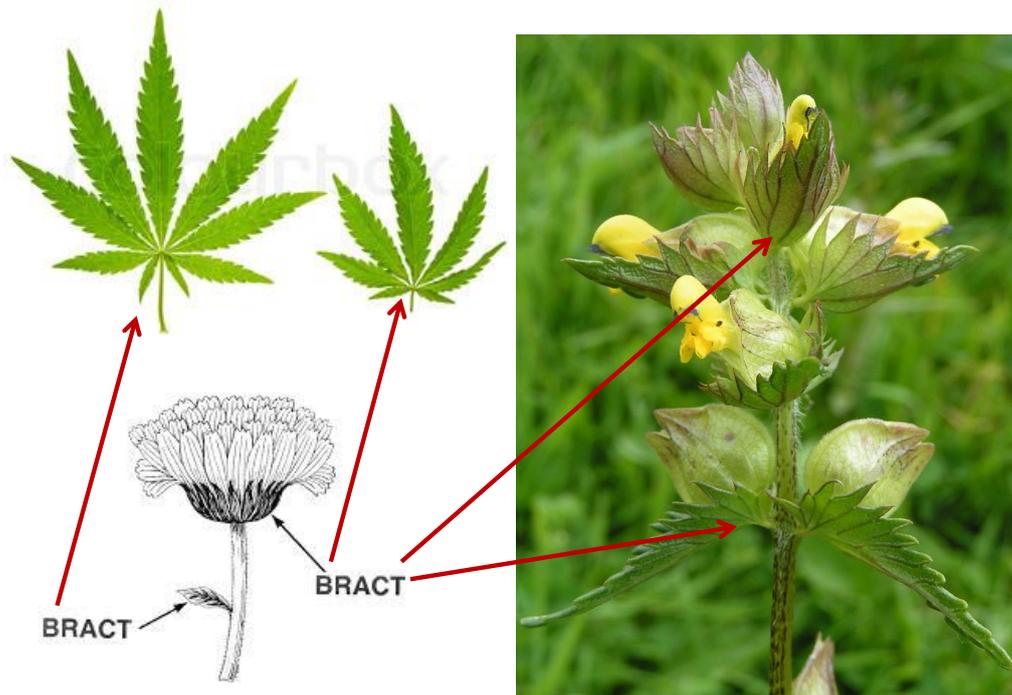
15

- The major constituents are called cannabinoids.
- The principle psychoactive agents are
  - 1. Tetrahydrocannabinol (THC)** or  $(-)$ -*trans*- $\Delta^9$ -tetrahydrocannabinol or ( $\Delta^9$  - THC),
  - 2. Cannabinol (CBN).**
  - 3. Cannabidiol (CBD).**
- Other compounds are: **cannabidiolic acid** – **tetrahydrocannabinolic acid** and **cannabichromene**.

❖ The quantity of THC increases in **flowering tops** up to 3-7% and 5-10% for the **bracts** and 60% for **cannabis oil**.

❖ **[A bract** is a modified leaf, especially one associated with a flower or inflorescence. Bracts are usually different from normal leaves. They may be smaller, larger, or of a different color, shape, or texture].

16



17

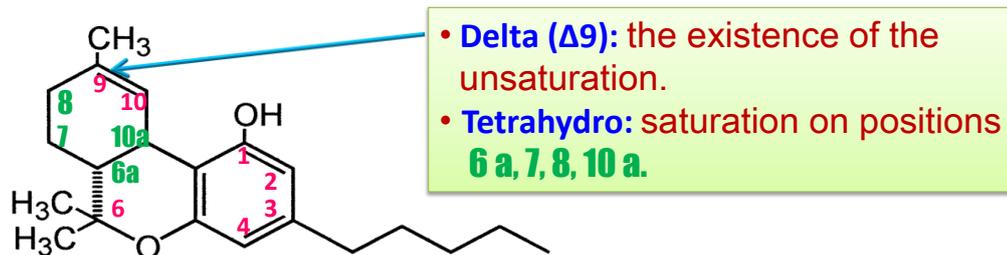
- Smoking of cannabis produces mild euphoria [شعور بالخفة - نشوة] والنشاط] with relaxation and changes in perception of sound and color.
- It reduces the ability to concentrate with short loss of memory.
- This may lead to hallucination, depression , anxiety and panic with risk of bronchitis and lung cancer.

- Uses and pharmacological activity:

1. It was used as an **analgesic** and **tranquillizer**, but nowadays, safer drugs are used for this sake.
2. In recent times, cannabis has been found to have a valuable **antiemetic** effect which helps reduce **the side effect of nausea and vomiting caused by cancer chemotherapy**.
3. Also, it is **helpful for appetite** in HIV patients and in cases of weight loss.

18

4. Has **antioxidant activity**.
5. **Muscle spasms** caused by multiple sclerosis.
6. **Seizure disorders**.
7. **Crohn's disease** [ belongs to a group of conditions known as **Inflammatory Bowel Diseases (IBD)**. Crohn's disease is a chronic inflammatory condition of the gastrointestinal tract. It is characterized by **ulcers and fistulae**, **Fistula**: an abnormal or surgically made passage between a hollow or tubular organ and the body surface, or between two hollow or tubular organs ]



$\Delta$ -9-tetrahydrocannabinol (THC)

19

- There has never been a documented human fatality solely from overdosing of tetrahydrocannabinol or cannabis in its natural form.
- However, numerous reports have suggested an association of cannabis smoking with an increased risk of myocardial infarction.
- Information about the toxicity of THC is primarily based on results from animal studies.
- The toxicity depends on the route of administration and the laboratory animal.

20