

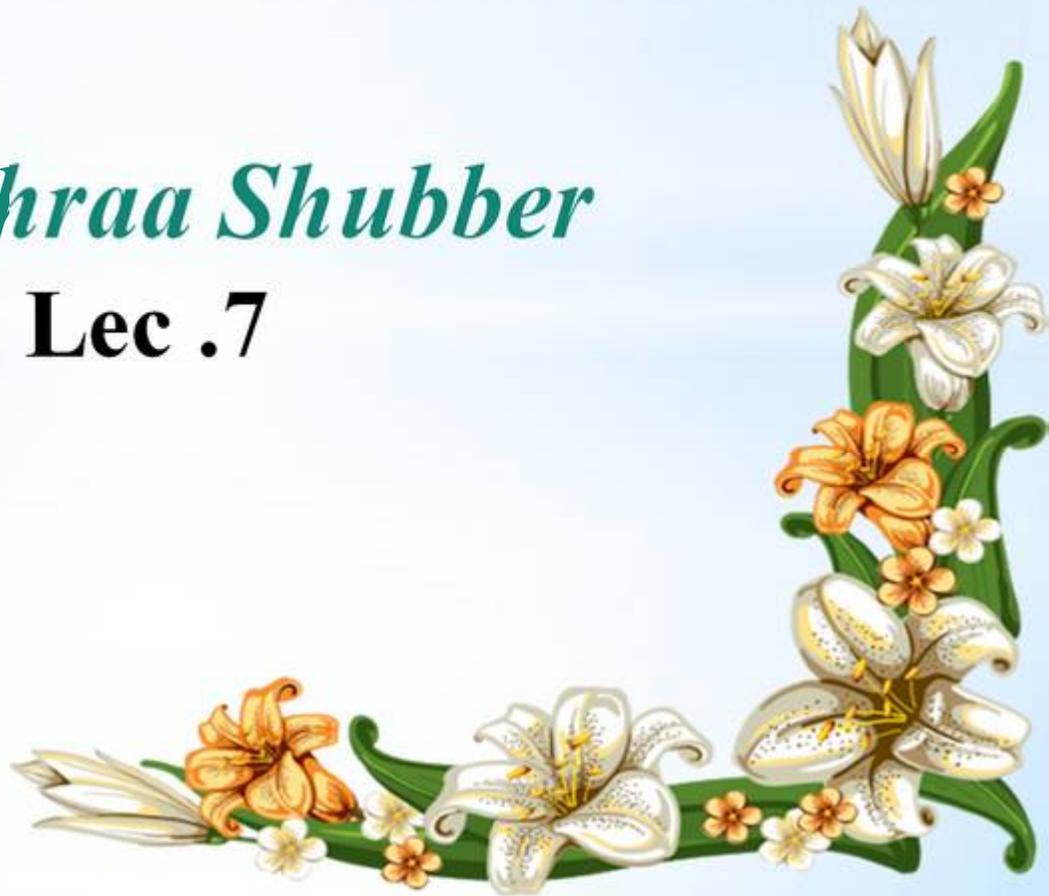
# pharmacognosy

3<sup>rd</sup> stage/1<sup>st</sup> term

## Cyanogenic Glycosides

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**Lec .7**



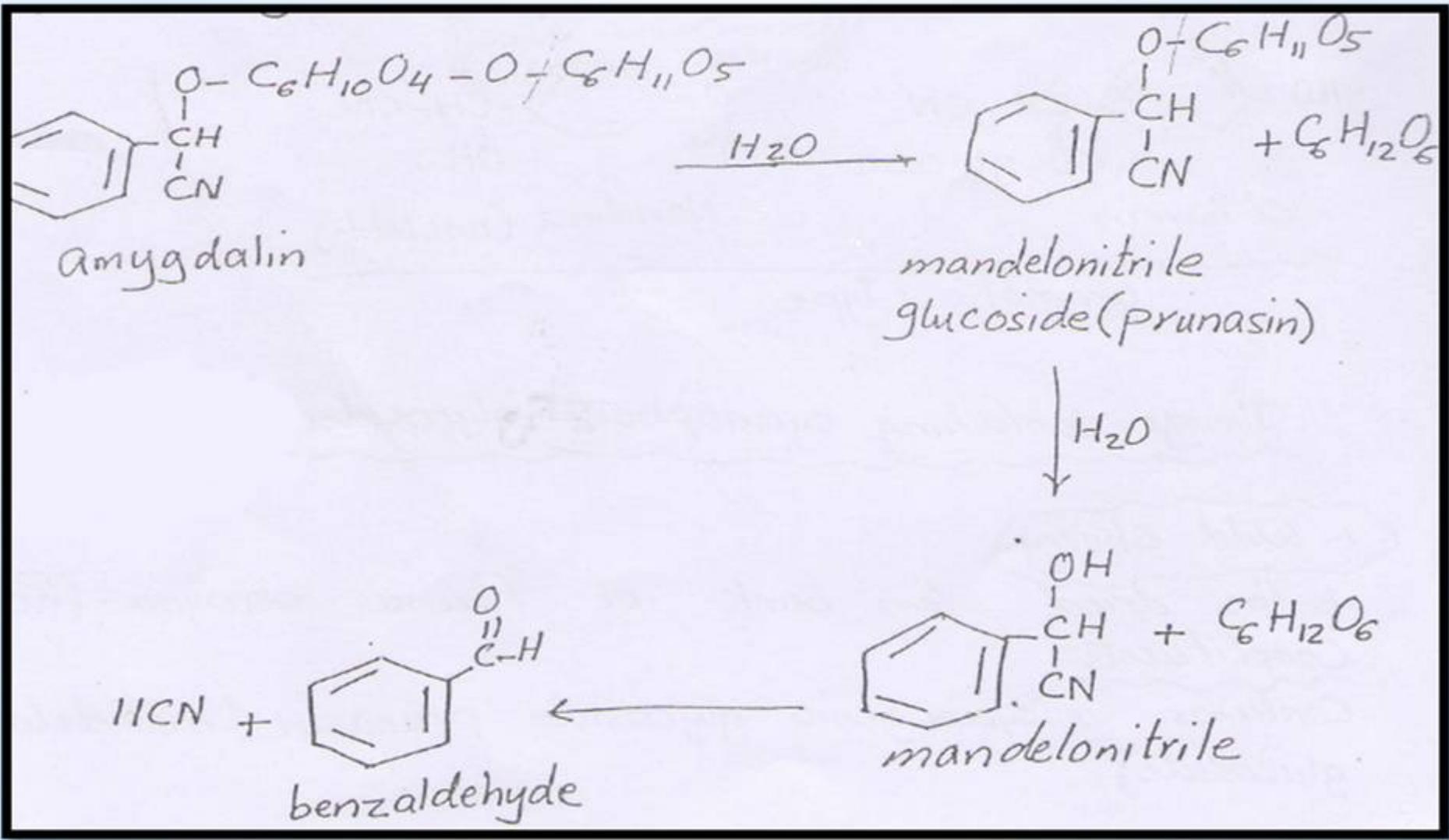
# Cyanogenic Glycosides

- These are glycosides that yield **hydrocyanic acid** as one of their hydrolytic products.
- The most common **cyanogenic glycoside** is **amygdalin**, which is found in large quantities in bitter almonds, in kernels of apricots, cherries, peaches and in many other seeds of the Rosaceae.
- And **prunasin** which occurs in *Prunus serotina*.
- When amygdalin is hydrolyzed it forms **two molecules** of **glucose** with **benzaldehyde** and **HCN**.

## **The hydrolysis takes place in three steps:**

1. Hydrolysis to give **one molecule of glucose** and **one of mandelonitrile glucoside**.
2. The **second molecule of glucose** is liberated with the formation of **benzaldehyde-cyanohydrin (mandelonitrile)**.
3. The mandelonitrile then breaks down with the formation of **benzaldehyde and hydrocyanic acid**.

- The hydrolysis steps are catalyzed by the presence of an **enzyme emulsin** found in almond kernels.



# Biosynthesis

- Evidences indicates that the biosynthesis of the majority of cyanogenic glycosides proceeds via common **amino acids precursors**.
- The **aromatic cyanogens** are derived from **phenyl alanine** and **tyrosine**; while the **non-aromatic** ones e.g. **linamarin** and **lotaustralin** are derived from **valine** and **isoleucine** respectively.

# Carbohydrate metabolism

Shikimic acid

Valine

Isoleucine

Tyrosine

- CO<sub>2</sub>  
+ Sugar

- CO<sub>2</sub>  
+ Sugar

Nandina (aromatic)

Linamarin

Lotaustralin

Non-aromatic

# Drugs containing cyanophore glycosides

**1. Wild cherry:** is the dried stem bark of **Prunus serotina** (Rosaceae).

**Constituents:** contains a cyanogenic glycoside prunasin (mandelonitrile glucoside).

**Uses:** wild cherry, in the form of syrup is employed as a flavored vehicle. It has been used as a **sedative expectorant**.



## 2. Bitter almond:

Is dried ripe kernel of **Prunus amygdalus**. (Fam: Rosaceae).

**Uses:** **anticancer** studies has been made for an amygdalin containing preparations known as laetrile or vitamin B17, and the possibility for **control of sickle cell** anemia with cyanogenic glycosides has been noted.



## Isothiocyanate glycosides

$\text{N}\equiv\text{C}-\text{O}-\text{H}$	Cyanic acid
$\text{H}-\text{N}=\text{C}=\text{O}$	<u>Isocyanic acid</u>
$\text{R}-\text{N}=\text{C}=\text{O}$	<u>Isocyanates</u>
$\text{R}-\text{N}=\text{C}=\text{S}$	<u>Isothiocyanate</u>

- The seeds of several mustard family plants contain glycosides, the aglycones of which are isothiocyanates.
- The most important glycosides are **sinigrin** from black mustard, **sinalbin** from white mustard and **gluconapin** from ripe seed.
- When hydrolyzed by the enzyme **myrosinase**, they yield the mustard oils which are responsible for activity.

## Biosynthesis

- Aglycones of isothiocyanate glycosides may consist of either aliphatic or aromatic derivatives.
- The aliphatics are derived from acetate while the aromatics from shikimic acid.

# Mustard

■ **Black mustard** is the dried ripe seeds of varieties of **Brassica nigra** (Fam:Brassicaceae)



**Constituenets:** although black mustard consists of fixed oil 30-35%, its principal constituent is the glycoside sinigrin, which is accompanied by the enzyme myrosinase. Upon the addition of water to the crushed or powdered seeds, the myrosinase causes hydrolysis of **sinigrin**.

**Uses:** black mustard is a **local irritant** and an **emetic**.

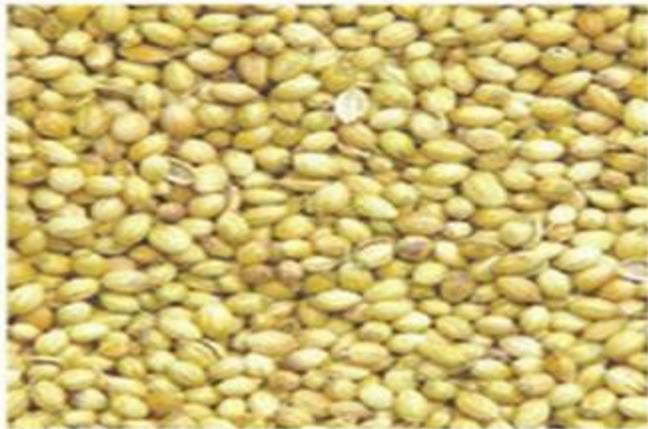
Externally, the drug is a **rubefacient**.

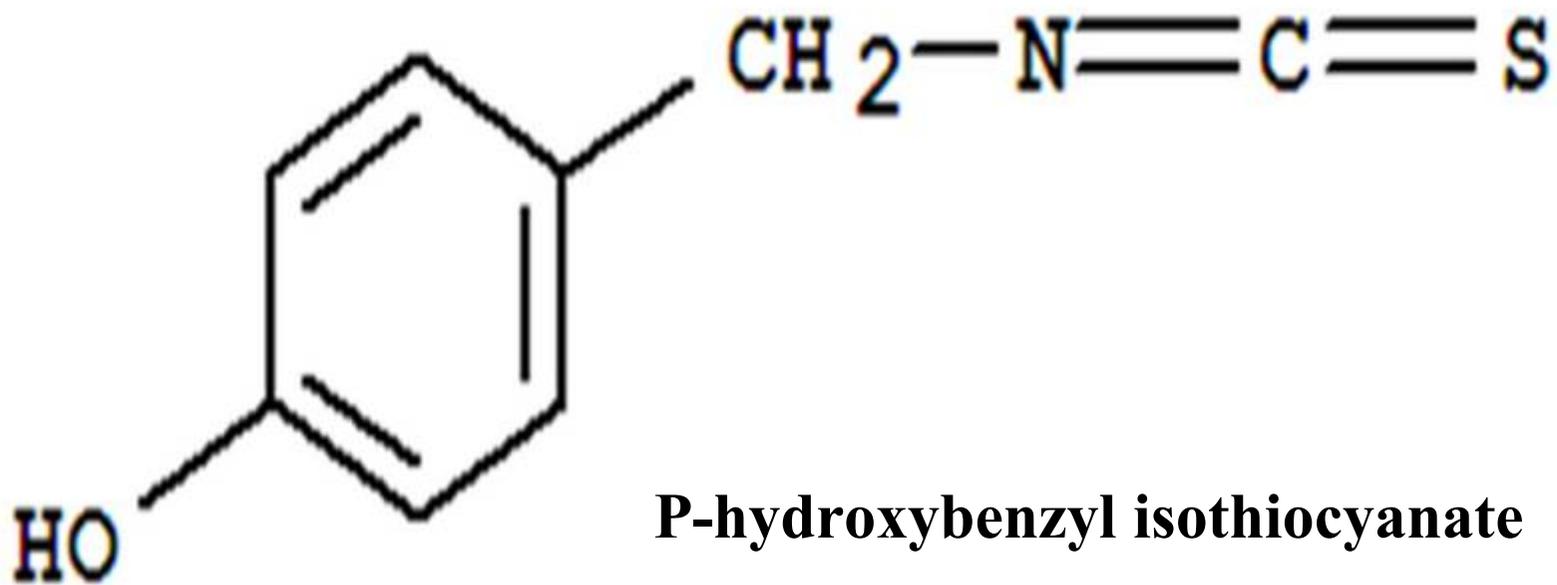
It's used as a **condiment**.



## ■ White mustard

- Is the dried ripe seeds of **Brassica alba** (Fam: Brassicaceae).
- It contains the enzyme myrosinase and a glucoside, **sinalbin**, which upon hydrolysis yields p-hydroxybenzyl isothiocyanate, a pungent-tasting but almost odorless oil.
- It also contains 20-25% of fixed oil.





**p-hydroxybenzyl isothiocyanate**

# Alcohol Glycosides

## Biosynthesis

- Because of the close relationship between this group and others like aldehyde, lactone and phenol, the biosynthesis of all these groups will be discussed together.
- Available evidence indicates that the aromatic nuclei of these compounds derive from precursors formed from **shikimic acid pathway**:

Shikimic acid → Phenylalanine → Cinnamic acid

→ Helicin → Salicin (Alcohol)

→ Ferulic acid → Glucovanillin(Aldehyde)

→ O-coumaryl Glucosides → Coumarin (Lactone)

→ Hydroquinone (Arbutin (Phenol))

## Salicin

- is an alcohol glycoside obtained from several species of **salix** and **populous** (Fam: salicaceae).
- The principal sources are **salix purpurea** and **S.fragilis**. Salicin is hydrolyzed by emulsin into D-glucose and saligenin (salicyl alcohol).

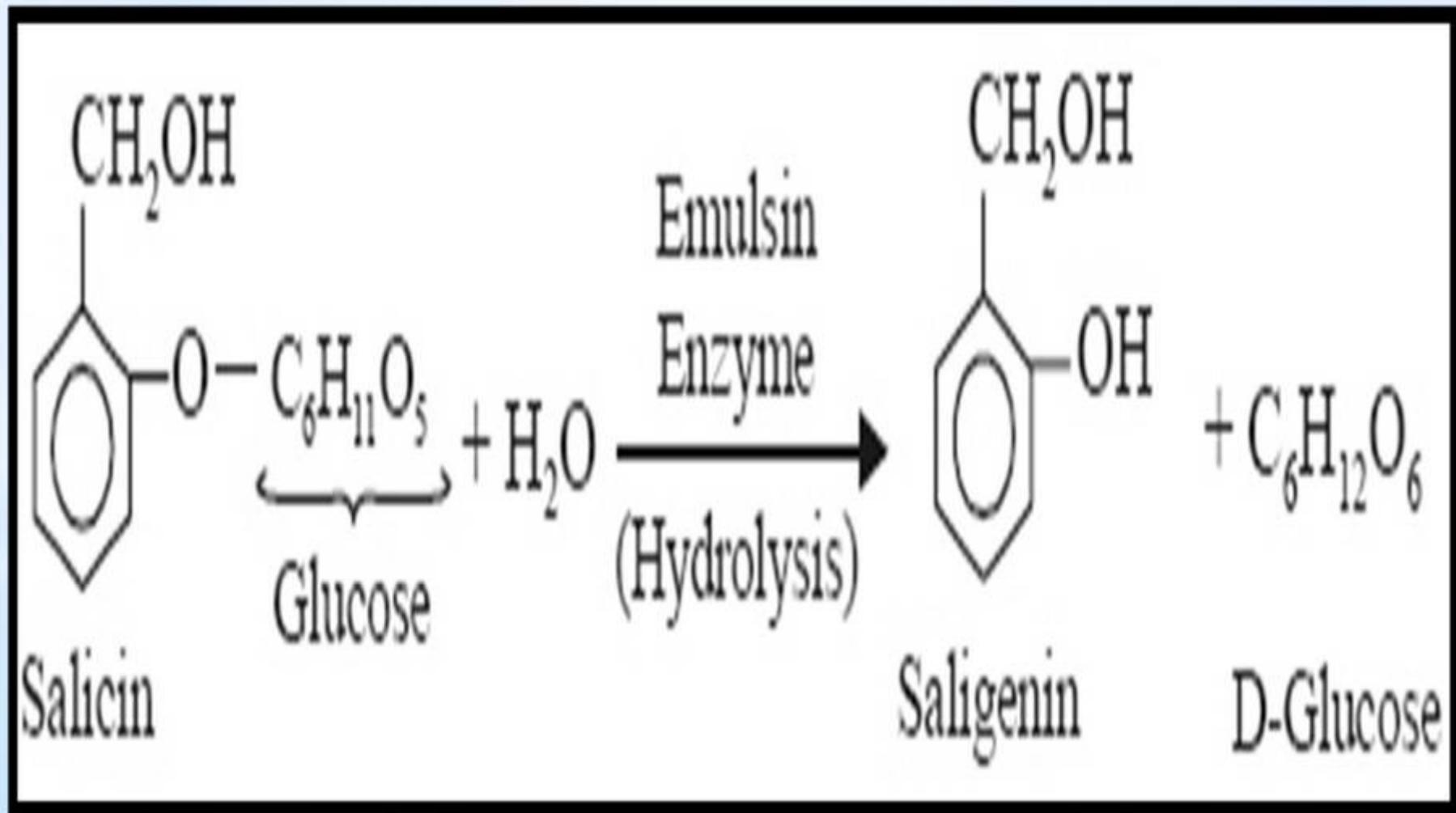
## Populous



## salix



- Salicin is used as **antirheumatic**, probably through the formation of **salicylic acid**.



# Aldehyde Glycosides

- **Vanillin** is the aglycone developed during the curing of vanilla beans.
- Vanillin is methylprotocatechuic aldehyde.
- **Vanilla or vanilla** bean is the full grown unripe fruit of **Vanilla planifolia** often known in commerce as Mexican or of **Vanilla tahitensis**, known in commerce as Tahiti vanilla (Fam: Orchidaceae).



**Constituents:** vanilla contains two glycosides:

**1. Glucovanillin:** upon hydrolysis with enzyme gives vanillin and glucose.

**2. Glucovanillic alcohol:** upon hydrolysis gives vanillic alcohol and glucose. Vanillic alcohol may oxidize to vanillic aldehyde (vanillin).

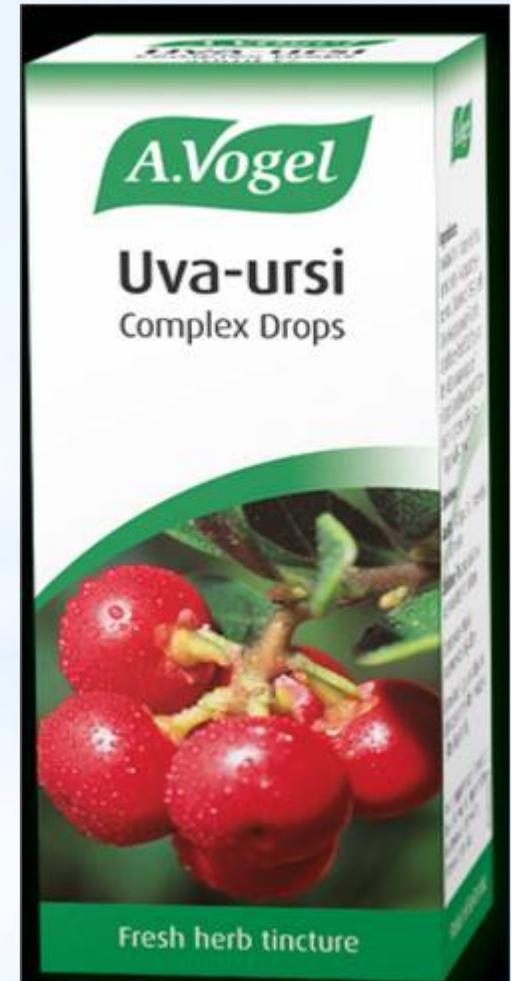
**Uses:** vanilla in the form of vanilla tincture, is used as **flavoring agent**, also as a source of vanilla.

# Phenol Glycosides

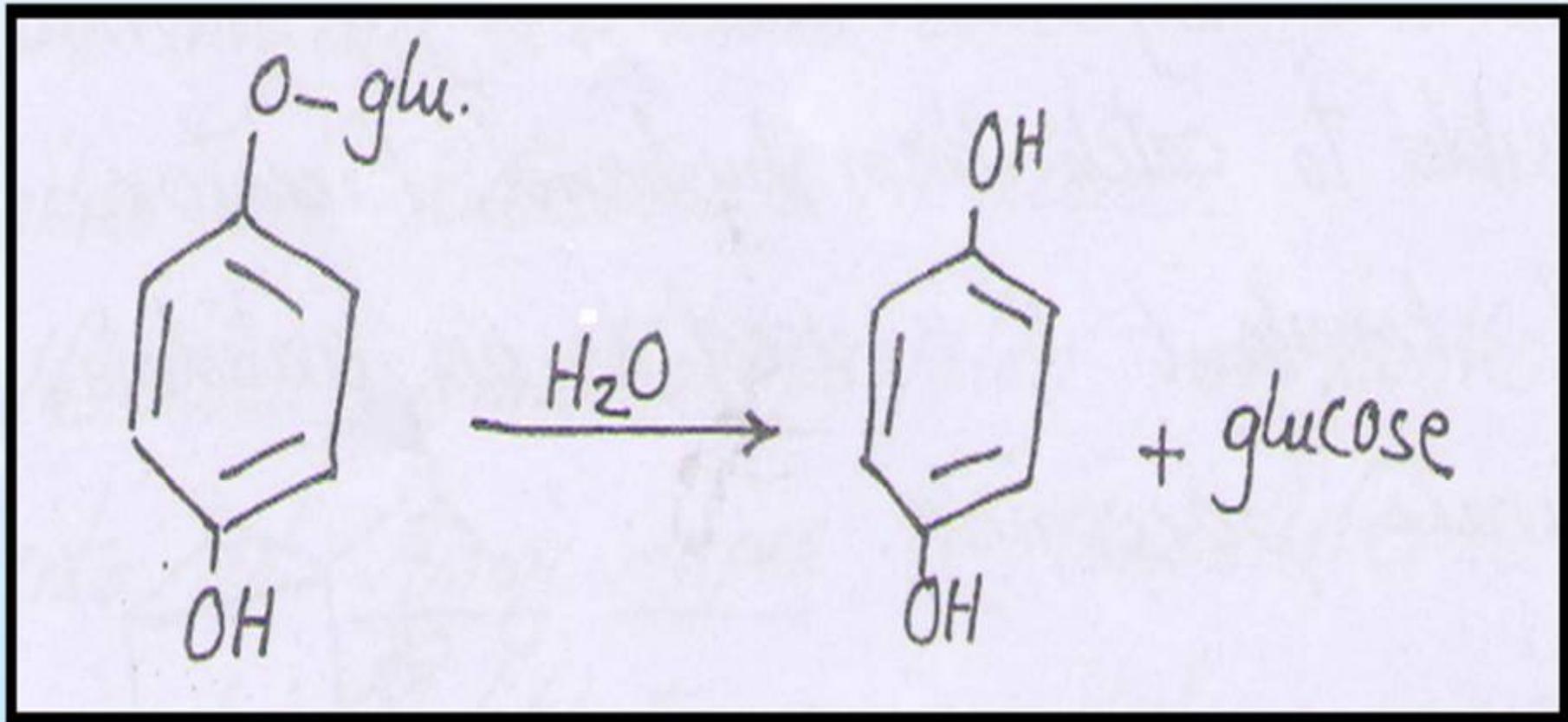
- Upon hydrolysis gives phenolic compounds and sugar.
- Uva ursi: is the dried leaf of *Arctostaphylos uva-ursi* (Fam: Ericaceae).

## Constituents:

contains the glycoside **arbutin**



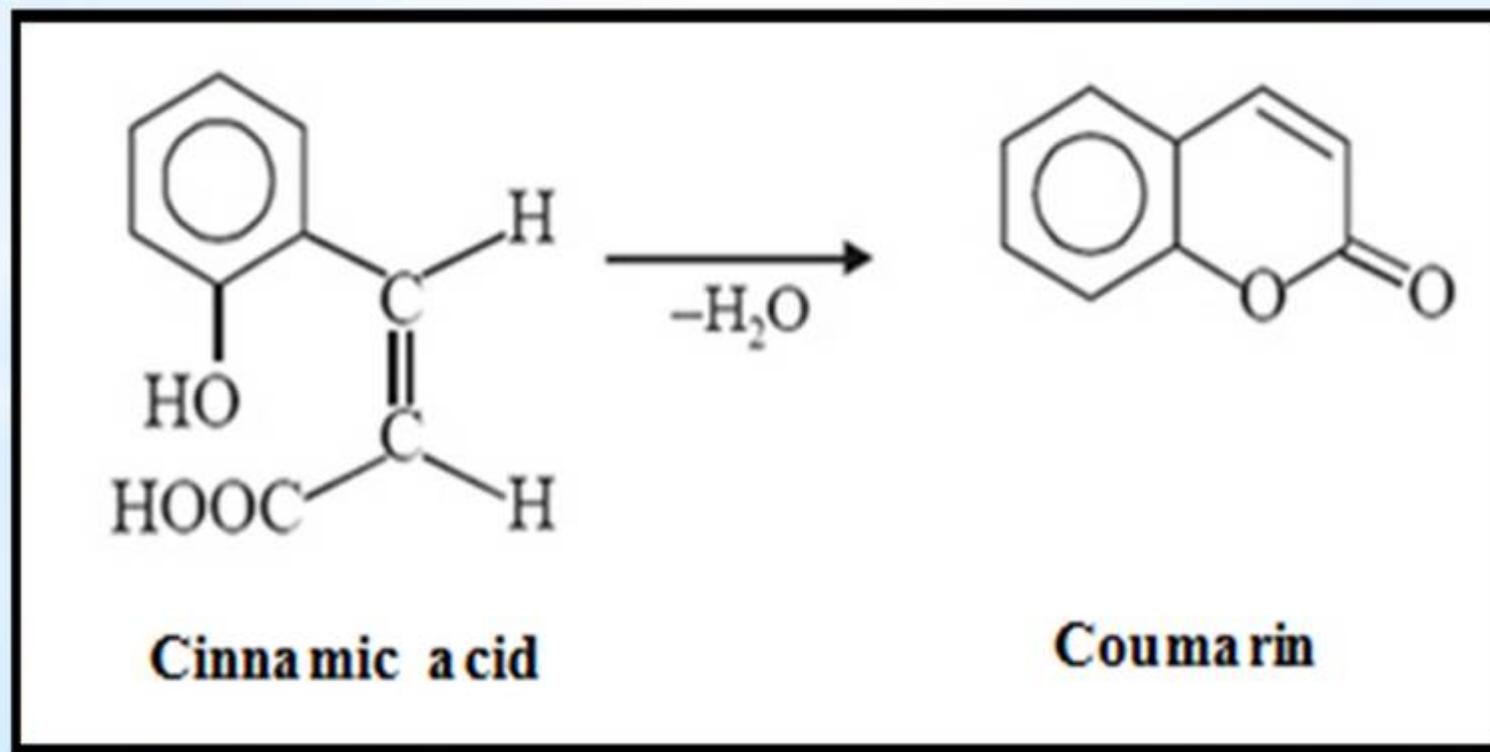
**Uses:** urva ursi has been used for many years as a **diuretic** and as an **astrigent**.



# Lacton Glycosides

## Coumarins

They are lactons derived from O-hydroxy cinnamic acid by ring closure between ortho hydroxyl group and carboxyl group of side chain formed coumarin.



Coumarin occurs as colorless crystals and has a characteristic fragrant odor and bitter, aromatic, burning taste. Its soluble in alcohol.

**It is widely distributed in nature, it occurs in:**

**1. Tonka beans:** in the dried seeds of *Dipteryx odorata*, and *Dipteryx oppositifolia*. Family: Lamiaceae.

**2. Sweet vernal grass:** *Anthoxanthum odoratum*.  
Family: poaceae.



- Coumarin and extracts of tonka beans were formerly used as **flavoring agents**.
- However, because of coumarin hepatotoxicity and coumarin-drug interactions that occur in a number of therapeutic substances, the FDA has banned the use of coumarin and coumarin containing materials for flavoring purposes.
- Some coumarin derivatives still find application for their **anticoagulant properties**.

# Coumarin derivatives

1. Hydroxycoumarin

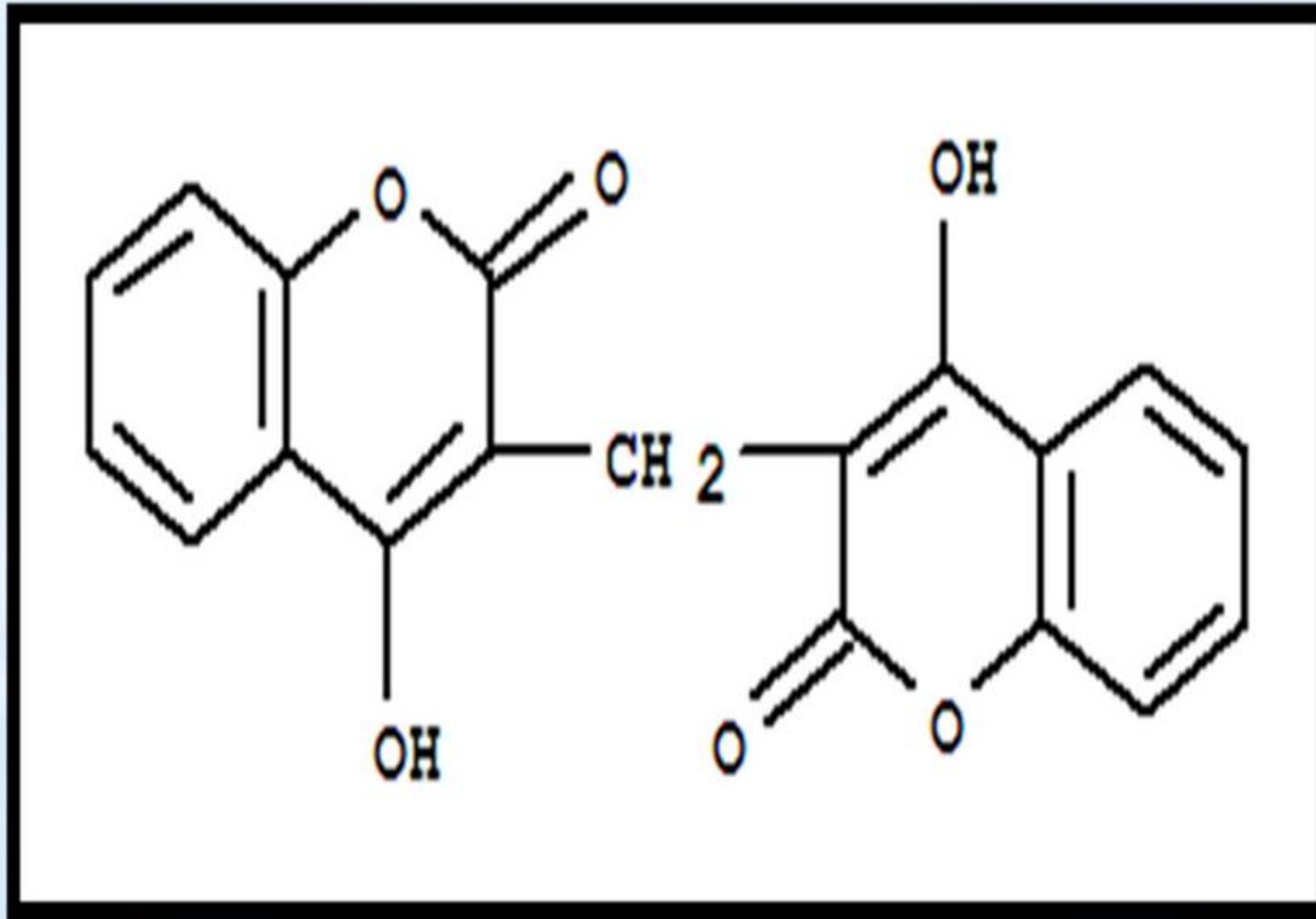
2. Furocoumarin

1. Hydroxycoumarin: examples

**A. Scopoletin** : obtained from the barks of **Viburnum pronifolium**. Family: Caprifoliaceae. Has **antispasmodic activity**.



## B. Bishydroxycoumarin or dicumarol:

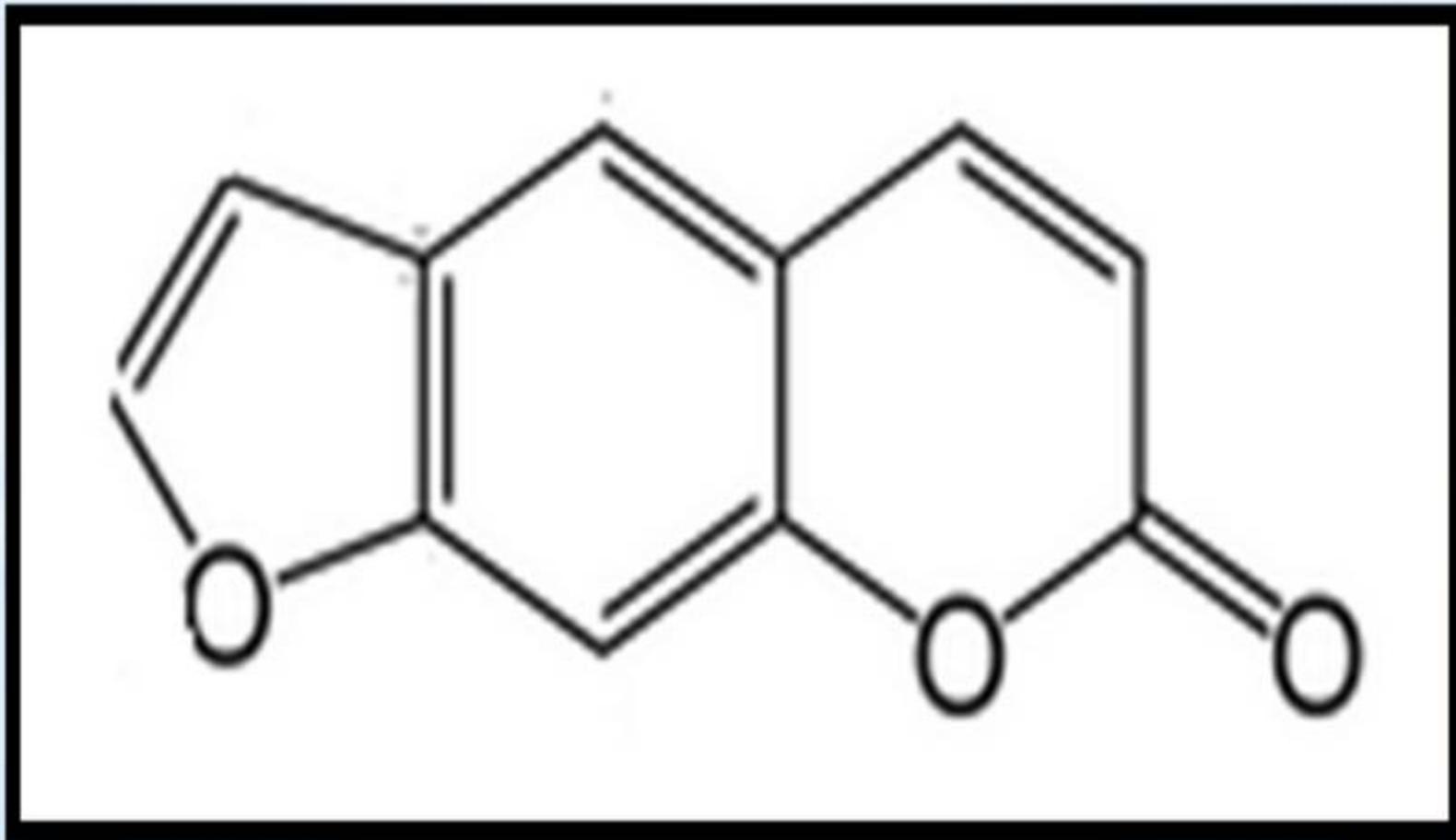


- Related to coumarin. It was obtained originally from improperly cured leaves and flowering tops of **Melilotus officinalis**. Family:Lamiaceae.
- A number of synthetic analogs of bishydroxycoumarin like warfarin also are used in anticoagulant therapy and used for the prophylaxis and treatment of venous thrombosis and pulmonary embolism.



## 2. Furocoumarins: example: psoralens

are photosensitizing furocoumarins that occur in a number of plant families, including the Apiaceae and Rutaceae, where they are a common cause of phototoxicity.



## Methoxsalen,

- a constituent of **Ammi majus**, is used to facilitate **repigmentation** in idiopathic vitilligo and for symptomatic control of sever psoriasis.
- Methoxsalen may be applied topically or taken orally.



In general, coumarins have antimicrobial and antifungal activity, photosensitizing, blood thinning, antispasmodic, antiasthmatic, hypotensive properties. Warfarin also used as rat poison.

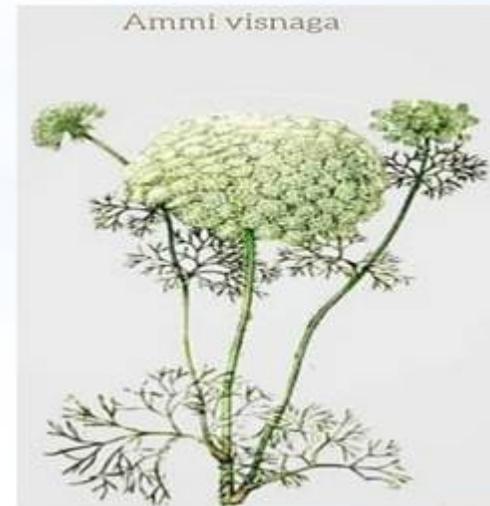


## Chromones

Represent a small group of plant phenolics that are isomeric with coumarins. The best known chromones is the furochromone khellin, which is a **potent coronary vasodilator**.

## Khellin:

- is a furochromone found in the fruit of **Ammi visnaga**, family: Apiaceae.
- It has been used for **urethral spasm and renal colic**.
- It is a potent **coronary vasodilator** and **bronchodilator** in the treatment of coronary insufficiency, angina pectoris, and bronchial asthma.
- It is an **antiasthmatic, antiallergic** agent that acts locally in the lung to which it is applied by inhalation.



*Thank You*

