



Phytochemistry (1)

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PhD

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Chapter 1



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Definition

- Phytochemistry is a branch of **Pharmacognosy**, deal with **chemical** and **biological** characters in order to obtain the **medicament**.

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Phytochemistry
has in view the
following
problems

Estimate the physical characters of raw material.

- Hygroscopic
- Amorphous

Determination of substance contents.

- Ingredient (s)
- Active principles

Determination of accompanying substance.

- Other chemical groups than the main one.
- Minerals
- Vitamins
- Amino acids

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Phytochemistry
has in view the
following
problems

Choosing the most suitable methods for extraction.

- Soxhlet
- Reflux
- Hot / Cold
- Lipophilic
- Hydrophilic

Isolation and purification the principal active.

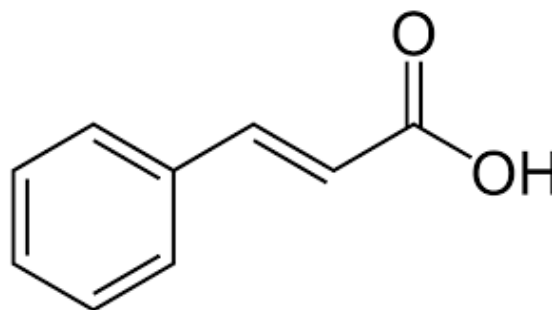
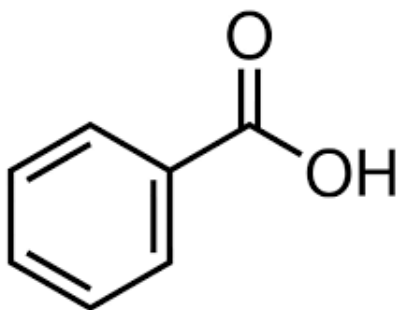
- Chromatography
- Gas-chromatography
- HPLC

Determination of the structure.

- NMR
- IR
- GC/Mass

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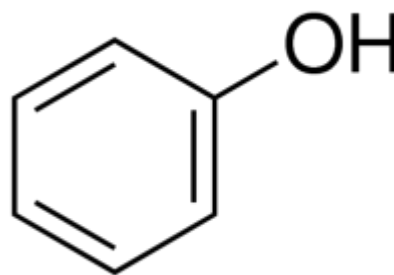
Chapter 2: Phenolic Acids



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Phenolic Compounds

- Phenolic compounds are chemically defined as compounds containing **hydroxylated aromatic rings**, the hydroxy group being attached directly to the phenyl, substituted phenyl, or other aryl group.
- They are secondary metabolites synthesized through the shikimic acid and phenylpropanoid pathways.
- It can describe a type of **resin** used to create various consumer items and is the name given to a class of plant-based chemical compounds.
- It can also refer to **carbolic acid**, an organic material that has been used in various medical and cleaning products.



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Phenolic Compounds

- Phenolic compounds possess numerous biological properties:
 - Phenolics able to act as **antioxidants**, which breaks the cycle of generation of new radicals.
 - Phenolic structures often have the potential to **strongly interact with proteins**, phenolics the ability to act as antioxidants by virtue of their capacity to inhibit some enzymes (*cytochrome P450 isoforms, lipoxygenases, cyclooxygenase and xanthine oxidase*).
 - phenolics can act as **pro-oxidants** by chelating metals in a manner that maintains or increases their catalytic activity or by reducing metals, thus **increasing their ability to form free radicals** (Menth).

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Phenolic Compounds

- Phenolic compounds possess numerous biological properties:
 - Carbolic acid** is another name for **phenol** or **phenic acid**, and is a natural substance that is solid, white, and crystalline.
 - It was originally derived from **coal tar**, and has been used in **soaps, cosmetics, and cleaning agents**.



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Main classes of phenolics

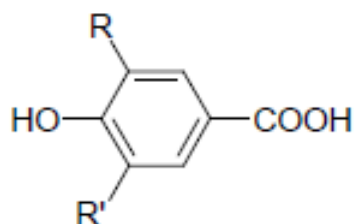
Benzoic Acid

- p-hydroxybenzoic acid ,
- Vanillic acid
- Syringic acid
- protocatechuic acids
- Gallic acids
- Lignin

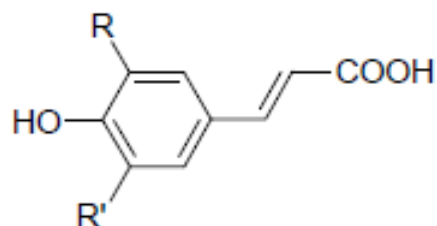
Cinnamic Acid

- p-coumaric acid
- Caffeic acid
- Ferulic acid
- Sinapic acid
- o-coumaric acid
- o-ferulic acid

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Benzoic acid derivatives

$R = R' = H$; *p*-hydroxybenzoic acid
 $R = OH$, $R' = H$; protocatechuic acid
 $R = OCH_3$, $R' = H$; vanillic acid
 $R = R' = OH$; gallic acid
 $R = R' = OCH_3$; syringic acid

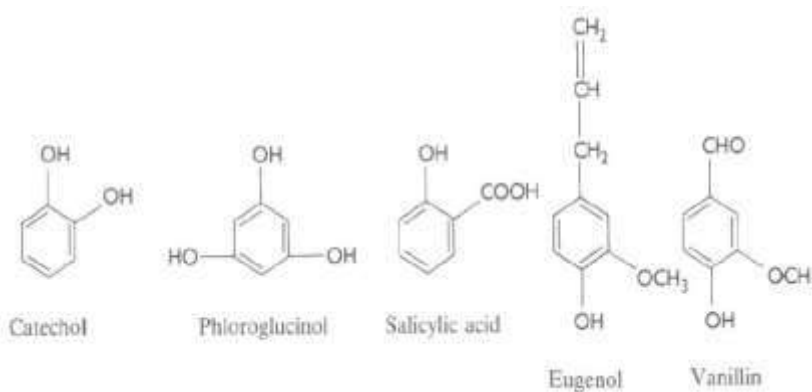
Cinnamic acid derivatives

$R = R' = H$; *p*-coumaric acid
 $R = OH$, $R' = H$; caffeic acid
 $R = OCH_3$, $R' = H$; ferulic acid
 $R = R' = OCH_3$; sinapic acid

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Simple phenols

- The simple phenols consist of a **singly substituted phenolic ring with alcoholic, aldehydes or carboxylic acid groups**. Main sources are:



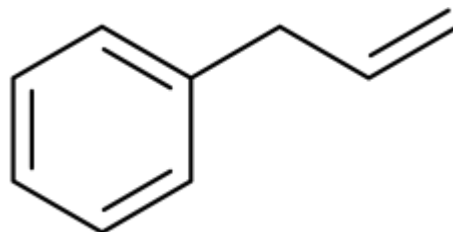
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Phenylpropanoids C₆-C₃

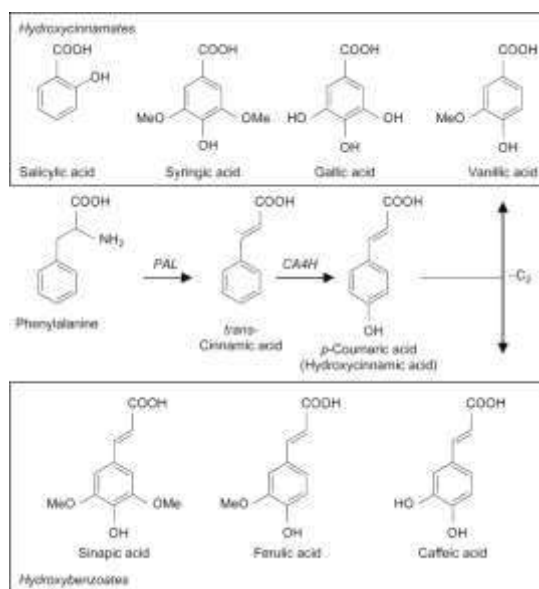
- The general phenylpropanoid metabolism generates a massive display of secondary metabolites based on the few intermediates of the shikimate pathway as the core unit.

- Phenylpropanoid are synthesized by plants from amino acid phenylalanine.**

- Their name is derived from the six-carbon, aromatic phenyl group and the three-carbon propene tail of cinnamic acid.

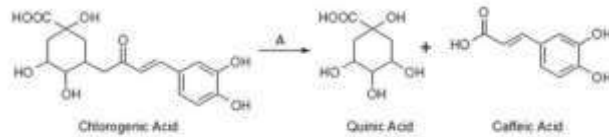
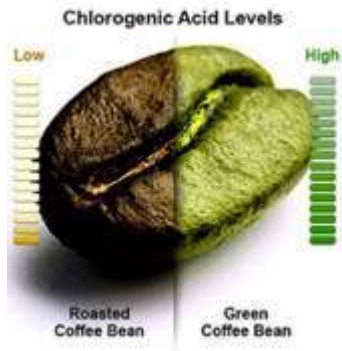


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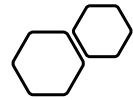


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Chlorogenic Acid



- Chlorogenic acid is an ester of caffeic acid and quinic acid. Chlorogenic acid is the major polyphenolic compound in coffee



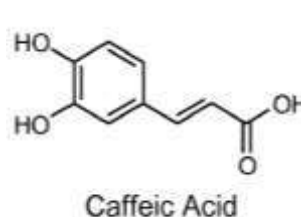
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Chlorogenic acid Benefits

- Chlorogenic acid (CGA)** lowers the blood glucose concentrations and inhibits G-6-Pase, the two main metabolic pathways responsible for the release of glucose from the liver.
- Green coffee became popular for weight loss by **reducing** the absorption of **fat** and glucose in the gut and lowering insulin levels to improve metabolic function.
- Affect blood vessels so that blood pressure is reduced.

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Caffeic Acid

- Caffeic acid (3,4-dihydroxycinnamic acid) is an organic compound that is classified as a **hydroxycinnamic acid**.
- It is found in all plants because it is a key intermediate in the biosynthesis of lignin.
- Caffeic acid is **antioxidant, anti-inflammatory, antiviral and anti cancer properties, prevent toxicity associated with chemotherapy and radiation**.
- The most common source of caffeic acid in the human diet is **from drinking coffee, turmeric, basil, thyme, oregano, sage, cabbage, apple, mushroom, kale, olive oil and strawberries**.
- **Despite its name, caffeic acid is unrelated to caffeine.**

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Physico-Chemical Properties, Characterization & Extraction

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Physical Properties of Phenol

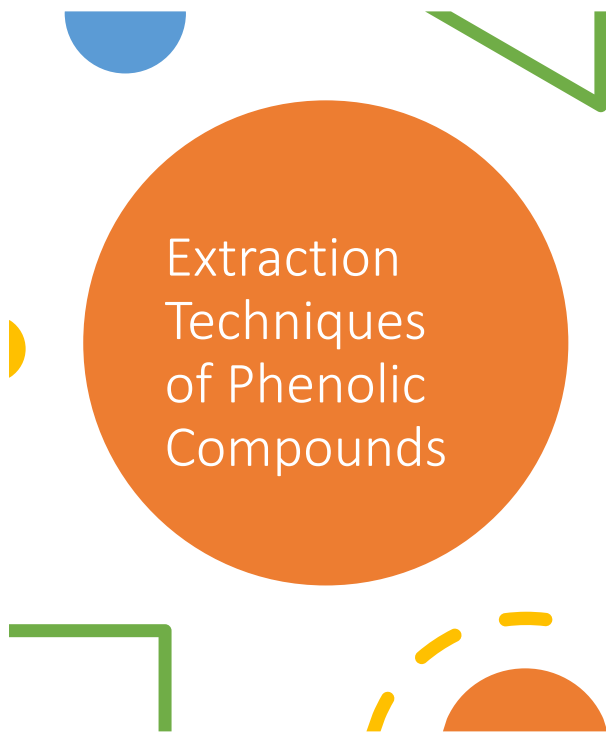
- Phenols are colorless liquids or crystalline solids but become colored due to slow oxidation with air.
- Due to the presence of strong intermolecular hydrogen bonding, phenols have a higher boiling point than the corresponding hydrocarbon or aryl halides.
- Due to their ability to form hydrogen bonds with water, phenols are moderately soluble in H_2O and in polar organic solvents
- The phenols are acidic in nature and stronger acids than alcohols. This is due to the fact that the sp^2 hybridised carbon of phenol to which $-OH$ is attached, is highly electronegative which causes a decrease in electron density on oxygen. This increases the polarity of $O-H$ bond and results in an increase in ionisation of phenols than that of alcohols.

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Chemical Properties of Phenols

- Chemical properties of any organic compound largely depends on the functional group attached to it.
- The hydroxyl group ($-OH$) determines most of the chemical properties of alcohols and phenols.
- The following types of reactions are seen in $-OH$ derivatives :
 - Reactions involving the cleavage of the **oxygen-hydrogen** bond ($R-O\cdots H$).
 - Reactions involving the cleavage of the **carbon-hydroxyl** bond ($C\cdots OH$).
 - **Dehydration** and **oxidation** reactions.
 - **Electrophilic** substitution reactions in phenols.

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Extraction Techniques of Phenolic Compounds

- Various extraction methods of phenolic compounds from plants were presented with advantages and disadvantages.
- According to the structure and extraction source of these compounds, different extraction methods can be recommended. Suggested methods need to be simple and rapid with a high.
 - Thin Layer Chromatography (TLC)
 - Liquid-liquid extraction (LLE)
 - Supercritical fluid extraction (SFE)
 - High performance liquid chromatography (HPLC)
 - Gas Chromatography (GC)

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Phenol, resorcinol, Ortho cresol, Para cresol	Violet or blue coloration
Catechol	Green coloration
Hydroquinone	Violet or transient blue color
Pyrogallol	Blue rapidly changing to red

Identification

- Compounds with a phenol group will form a blue, violet, purple, green, or red-brown color upon addition of aqueous ferric chloride. This reaction can be used as a test for phenol groups:

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Biosynthesis

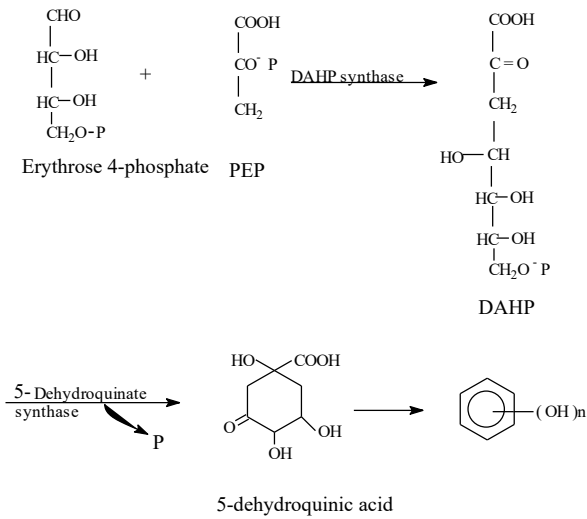
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Shikimic Acid Pathway

- Plant phenolics arise from two main aromatization pathways
 - The most common pathway is the one which, via **Shikimic acid**, (synonym: *Illicium religiosum*) leads from monosaccharide to aromatic amino acid [phenylalanine and tyrosine] then, by **deamination** of this latter, to **cinnamic acids** and their numerous derivatives, including **benzoic acids**, acetophenones, lignans and coumarins.
 - The other pathway begins with **acetate** and leads to **poly- β -ketoesters** of variable length (fatty acids and alcohol's), which afford, by cyclization (Claisen or aldol condensation), products that are often polycyclic, including chromones, iso-coumarins, xanthenes and quinones.



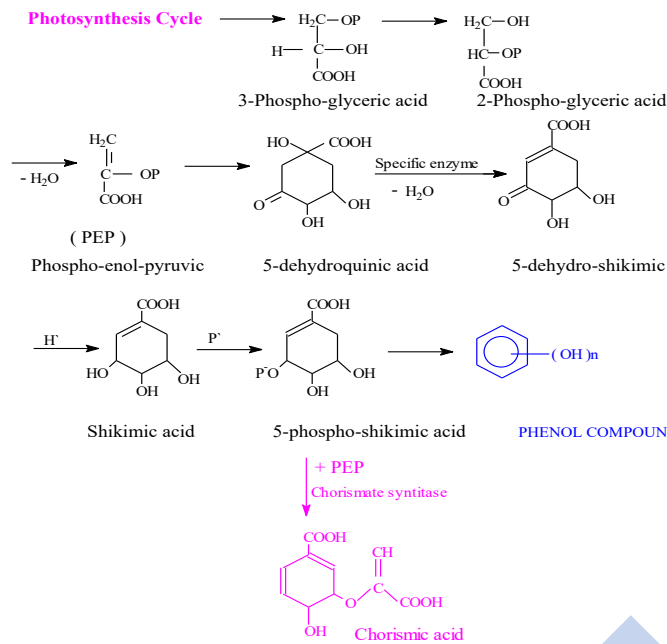
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Shikimic Acid Pathway

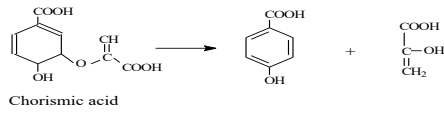
**** DAHP = D-arabinoheptulosonate-7-phosphate**

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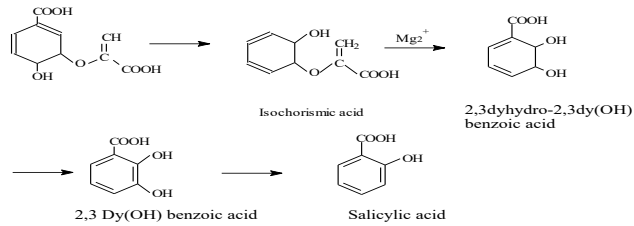


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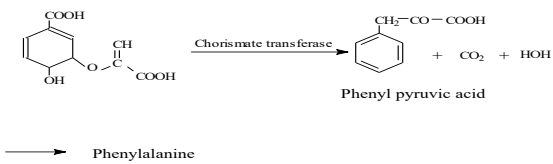
1. Formation of P-hydroxy benzoic acid



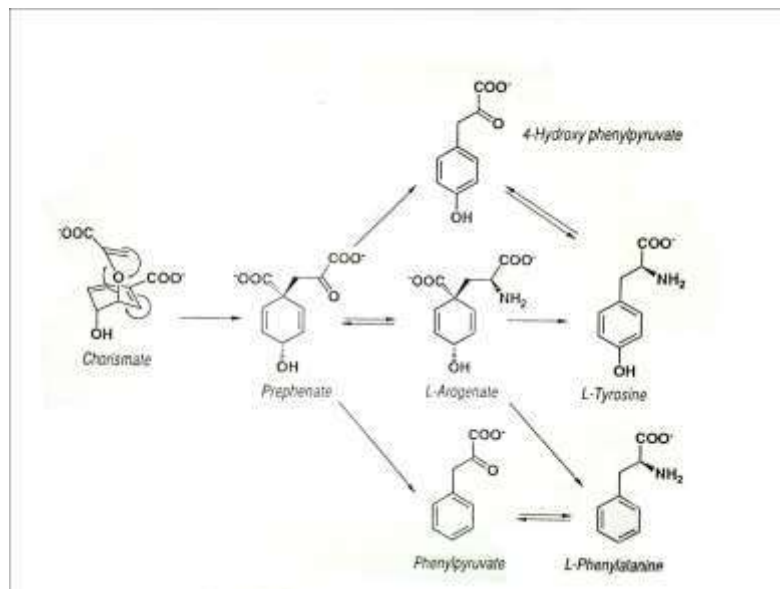
2. Formation of Salicylic acid



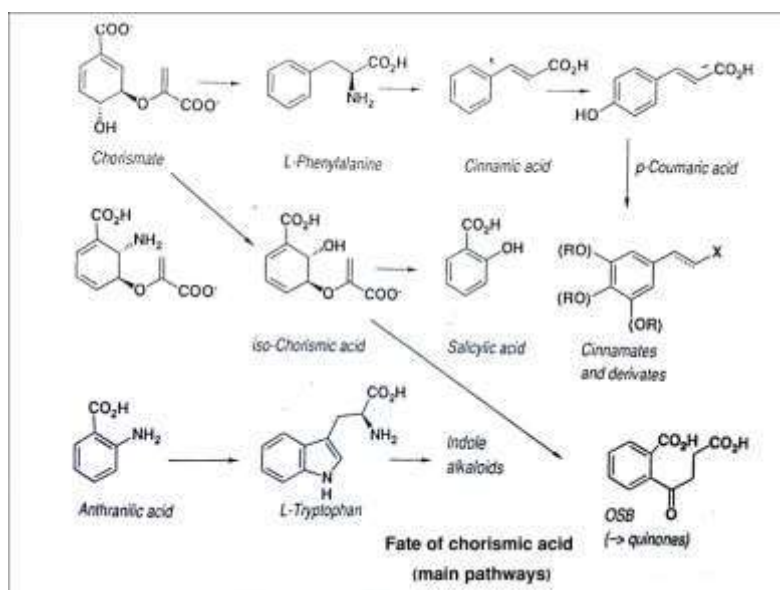
3. Formation of Phenylalanine



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Pharmacological Properties

- Phenolic compounds have **two main actions**:
 - First** is **urinary antiseptic** properties of arbutin, and
 - Second** is **anti-inflammatory** properties of salicylates.
- Glycosidic **phenylpropanoids esters** have **interesting anti-inflammatory** potential activity such as verbascoside, which **inhibit 5-lipoxygenase** in human granulocytes.



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Simple Phenol Containing Drugs

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Oregano

- Scientific name: *Oregano vulgare*
- Family: Lamiaceae
- Traditional name: أوريغانو
- It is native to temperate Western and Southwestern Eurasia and the Mediterranean region.

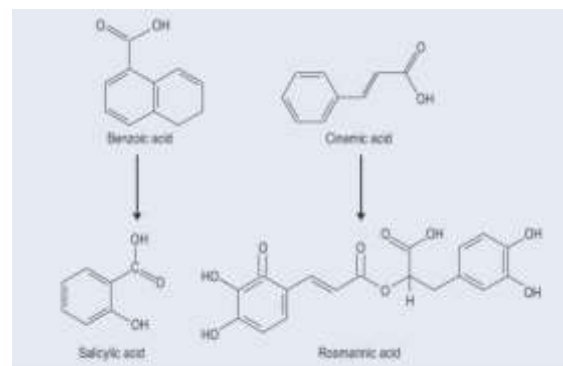
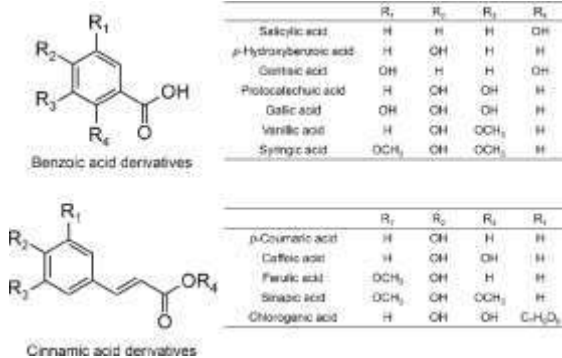


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Phytochemicals

- **Phenolic acids:** Rosmarinic acid, Benzoic acid, caffeic acid, chlorogenic acid, gentisic and p-coumaric acids
- **Flavonoids**
- **Volatile oils:** Thymol, Carvacrol
- **Triterpenes:** Ursolic acid, oleanolic acid, β -Sitosterol
- **Minerals:** Potassium, Calcium, Magnesium, Phosphorous,
- **Vitamins:** Vitamin A, B1, B6
- **Macronutrients:** Protein, Fat, Carbohydrates & fibers

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Biological Properties

- **Traditional Medicine:**
 - Oregano has been used as a culinary and medicinal herb upon the digestive and respiratory systems and is also used to promote menstruation.
- **Effect:**
 - Strong antioxidant, antimicrobial, natural antibiotic & anti-inflammatory
- **Action:**
 - The plant is taken internally in the treatment of colds, influenza, mild feverish illnesses, indigestion, stomach upsets and painful menstruation.
 - It is strongly sedative and should not be taken in large doses, though mild teas have a soothing effect and aid restful sleep.
 - Oregano is the best natural antiseptics because of its high thymol content.
- **Contraindication:**
 - In pregnancy planning & Pregnant woman.

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Biological Properties

- **Indication (Target Patient(s)):**
 - Urinary tract infection (UTI) (antibacterial)
 - Low LDL- Cholesterol level (anti-inflammatory)
 - Protect the body from damage cells (Antioxidant)
 - Treat candida (Yeast infection) (antimicrobial)
 - Antiparasitic (antimicrobial)
 - Diarrhea (antimicrobial)
 - Colitis (anti-inflammatory)
 - Painkiller (Sedative properties)
 - Skin sores (anti-inflammatory, antioxidant)
 - Cancer fighting (antioxidant)
 - Lose weight (chlorogenic acid)
 - Indigestion (chlorogenic acid)
 - Hair loss (anti-inflammatory + nutritive)
 - Regulate blood pressure (rich in potassium)
 - Flu, common cold

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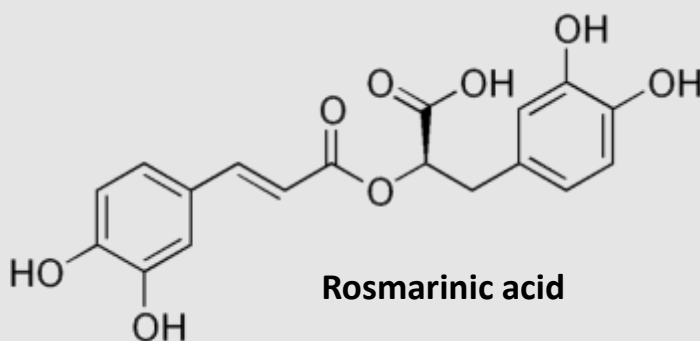
Rosemary



- **Scientific name:** *Rosmarinus officinalis* L.
- **Family:** Lamiaceae
- **Traditional name:** إكليل الجبل / روزماري
- *Rosmarinus officinalis* L. (rosemary) is a medicinal plant native to the Mediterranean region and cultivated around the world.
- **Rosemary** was traditionally **used** to help alleviate muscle pain, improve memory, boost the immune and circulatory system, and promote hair growth.

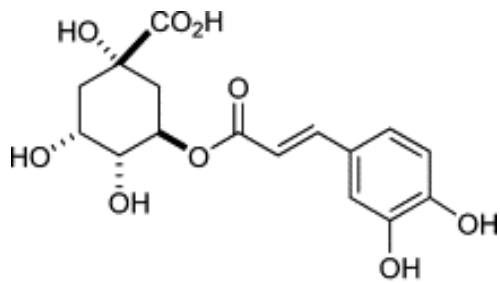
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Phytochemicals

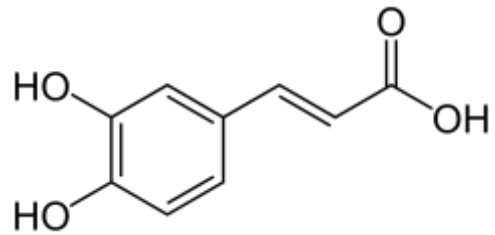


- **Phenolic acid:** Rosmarinic acid, caffeic acid, chlorogenic acid
- **Flavonoids:** hesperidin
- **Volatile oils:** 1,8-cineole (Eucalyptol), alpha-pinene, camphor.
- **Diterpenes:** Carnosic acid.
- **Triterpenes:** Oleanolic acid, Ursolic acid
- **Minerals:** K, Ca, Mg, Cu, Mn, Fe
- **Vitamins:** A, B6, C

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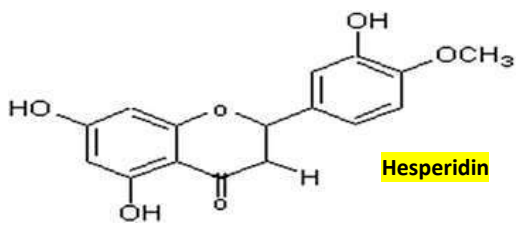


Chlorogenic acid

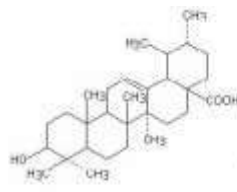


Caffeic acid

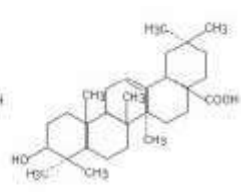
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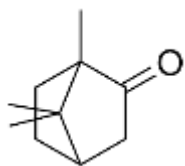
Hesperidin



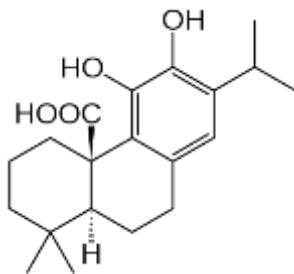
Ursolic Acid



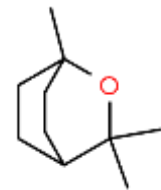
Oleanolic Acid



Camphor



Carnosic acid



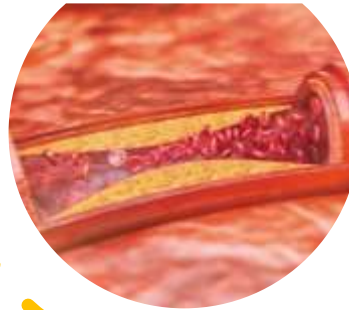
Eucalyptol

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Biological Properties

• Effect:

- Antibacterial & antiviral
- Ability to attenuate asthma, atherosclerosis, cataract, renal colic, neuroprotective, hepatotoxicity, peptic ulcer, inflammatory diseases.
- Control of hypercholesterolemia and oxidative stress and relief of physical and mental fatigue
- Lipid peroxidation reduction in heart and brain
- Glycemia reduction
- Muscle relaxant



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Indication (Target Patients)



- Skin/mouth infections (Acne, dermatitis, Psoriasis, eczema) (Rosmarinic acid & vitamin A)
- Flu, common cold, cough, sinusitis, asthmatics (Rosmarinic acid)
- Myocardial blood pressure reduction (Rosmarinic acid)
- Stomach ulcer (Rosmarinic acid)
- Cancer (Rosmarinic acid and vitamin C)
- Improve memory (Carnosic acid, carnosol & vitamin B6)
- Mood swing/ depressive behaviors/ headache (Carnosic acid, carnosol and minerals)
- Brain performance (Camphor & Eucalyptol)
- Joint arthritis (Carnosic acid, carnosol & minerals)
- Hair growth (Rosmarinic acid, Fe, C)
- Regulate the blood sugar level.

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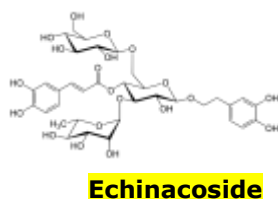
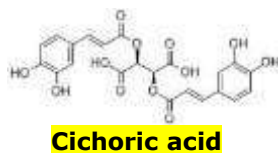
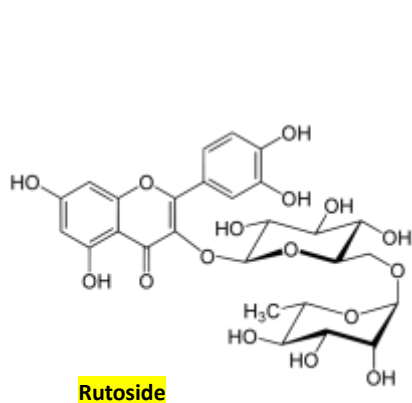


Echinacea

- **Scientific name:** Echinacea purpurea
- **Family:** Asteraceae
- **Traditional name:** القنفذية / الأرجوانية / زهرة القمح
- It is native to eastern North America and present in United States as well as in the Canadian Province of Ontario.

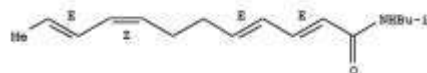
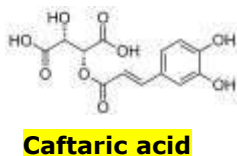


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Phytochemicals

- **Caffeic acid derivatives:** cichoric acid, caftaric acid and chlorogenic acid
- **Phenylpropanoids:** Echinacoside
- **Alkamides:** dodeca-2E,4E,8Z,10E/Z-tetraenoic acid
- **Polysaccharides**
- **Flavonoids:** Rutoside
- **Essential oils:** Borneol



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Biological activity

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Effect

- Strengthens your immune system by stimulating the production of T-cells. *(T cells are lymphocyte immune cells that protect the body from pathogens and cancer cells. T cells originate from bone marrow and mature in the thymus and the activation of immune cells to fight infection).*
- It also increases the ability of your white cells to fend off pathogenic invaders.
- Shorten the Symptoms of Illness
- Used as a Topical Disinfectant
- Powerful antioxidants
- Benefit Psoriasis and Eczema
- Good for Slow-Healing Wounds
- Heal Sunburn
- Resolve Recurrent Infections



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Indication / Target Patients

- Common cold Colds & flu
- Influenza Respiratory tract infection
- Upper respiratory tract infection
- Urinary tract infection (UTI)
- Chronic fatigue syndrome (CFS), Rheumatism,
- Migraines, Acid indigestion,
- Pain, Dizziness,
- Attention deficit-hyperactivity disorder (ADHD).

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Precaution

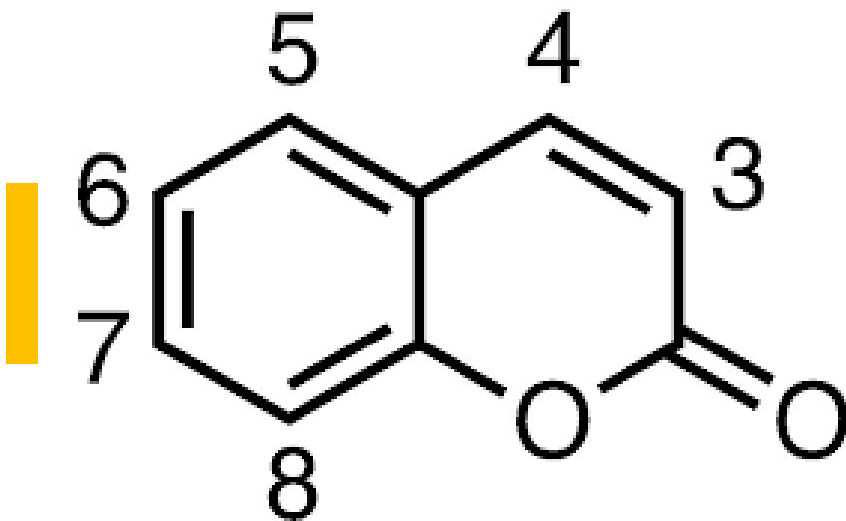
- It might not be a good idea to use Echinacea supplements in any form, including tea, daily for longer than **eight consecutive weeks**.

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Drug-Drug interaction

- Echinacea is often taken together with **goldenseal**.
- Echinacea and **corticosteroids**

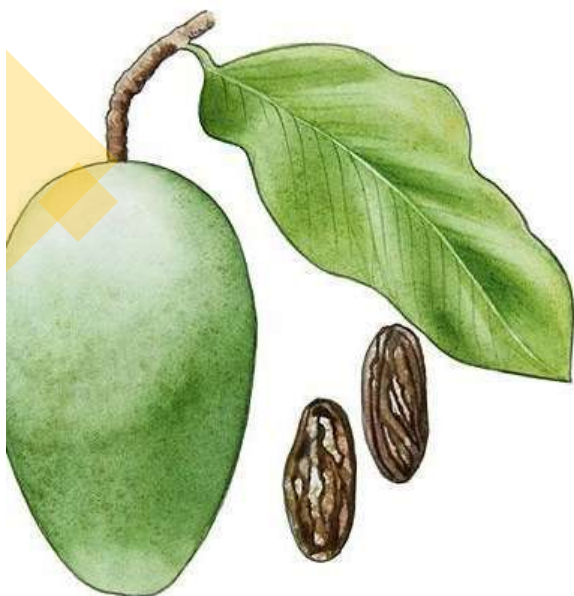
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Chapter 3
Coumarins

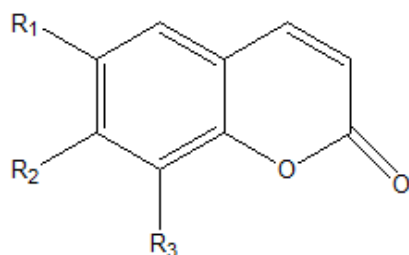
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Coumarins



- Coumarins are a family of **benzopyrones** (*1,2-benzopyrones* or *2H-1-benzopyran-2-ones*) widely distributed in the nature.
- The name coumarin comes from a French term for the **Tonka bean**, *coumarou*, seeds of ***Coumarouna odorata*** (*Fabaceae/Leguminosae*), one of the sources from which coumarin was first isolated as a natural product in 1820.
- Coumarin has been used in perfumes since 1882.

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R ₁	R ₂	R ₃	Compound
H	OH	H	Umbelliferone
OH	OH	H	Aesculetin
OCH ₃	OH	H	Scopoletin

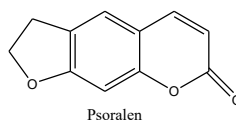
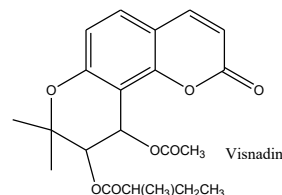
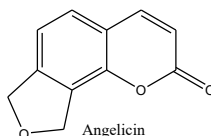
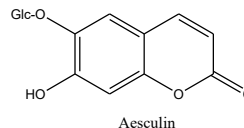
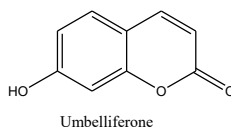
Chemistry & Classification

- Coumarins are benzo-alpha-pyrones (lactones of *o*-hydroxycinnamic acid) formed via the shikimic acid pathway.
- Except for a few rare cases, including coumarin itself which is unsubstituted,
- All plant coumarins contain **hydroxy or methoxy groups in position 7**.
- These substituted simple coumarins, such as **scopoletin**, **aesculetin** and **umbelliferone**, are common and widespread in higher plants and often occur as **glycosides**.

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Prenylation

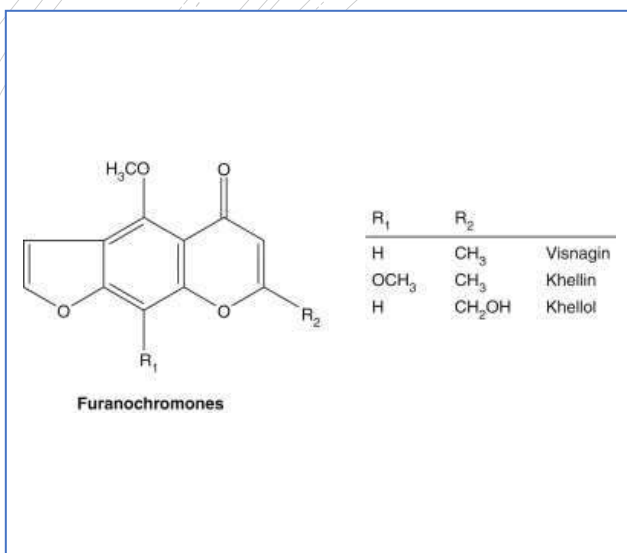
- Prenylation on the ring in the 6 or 8 position of umbelliferone.
- Prenylation is also the origin of polycyclic coumarins, furano and pyrano coumarins, **linear** (Psoralen) and **angular** (angelicin, visnadin) coumarins.



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Furanochromones

- The furanochromones such as **khellin** from **Ammi visnaga** are structural derivatives of benzo-gamma-pyrone (furanobenzo-gamma-pyrone) and therefore are as much related to flavonoids as coumarins.



54

Biosynthesis

55

Biosynthesis

Coumarins arise from the metabolism of phenylalanine via cinnamic acid, p-coumaric acid.



The specificity of the process resides in:

the 2'-hydroxylation,

Photocatalyzed
isomerization of the double
bond

spontaneous lactonization.

56



Properties, Extraction & Characterization

- Coumarins in the **free state**
- **Soluble** in **alcohols and in organic solvents** such as ether and chlorinated solvents, with which they can be extracted.
- Their **glycosides** are more or less soluble in water.
- Coumarins have a **characteristic UV** spectrum which is heavily influenced by the nature and position of substituents, and by alkalization KOH, NaOCH₃.
- When examined under UV light, TLC spots from coumarin containing drugs have colors which are **enhanced in the presence of ammonia** and range from **blue to yellow and purple**.

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Pharmacological Properties

- Anticoagulant to inhibit formation of blood clots, and so is a therapy for deep vein thrombosis and pulmonary embolism.
- **Vitamin "P" factor**
- Anti-inflammatory, antioxidant, antihyperglycemic, antiadipogenic, antibacterial, and anticancer properties.
- **UTI**
- **Psoriasis**
- **vitiligo**

60

Coumarin Containing Drugs



61

Horse Chestnut

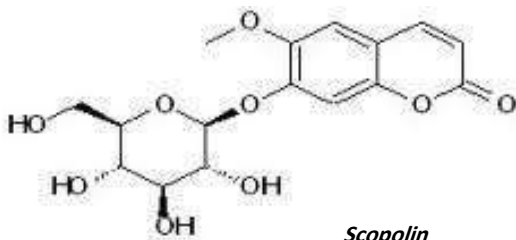
- Scientific name: *Aesculus hippocastanum*
- **Family:** Sapindaceae
- **Horse chestnut** leaves have been used by herbalists as a cough remedy and to reduce fevers. The leaves were also believed to reduce pain and inflammation of arthritis and rheumatism.
- In **traditional herbal medicine**, poultices of the seeds have been used topically to treat skin ulcers and skin cancer.



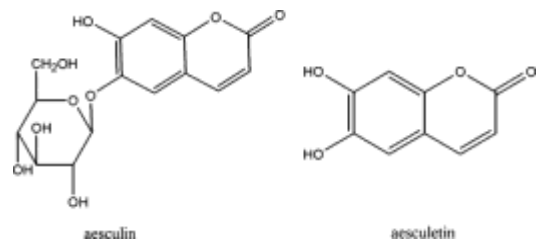
62

Phytochemicals

Hydroxycoumarins



Scopolin



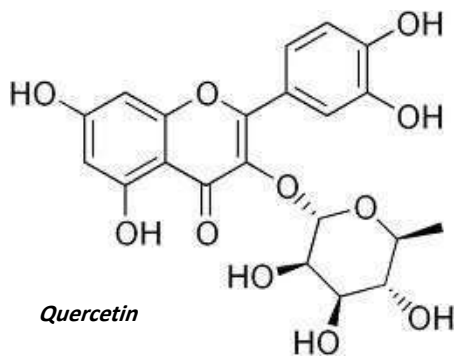
aesculin

aesculetin

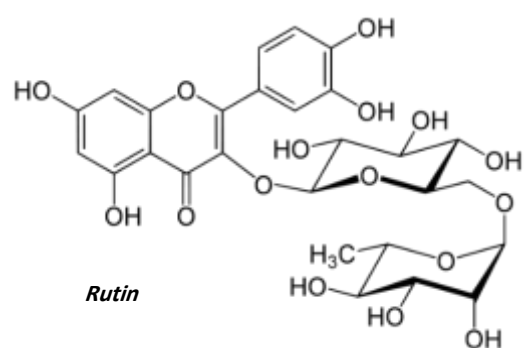
63

Phytochemicals

Flavonoids



Quercetin



Rutin

64

Phytochemicals

Tannins

Triterpene
saponine

65



Biological Properties

- Effects:
 - Improve Vein Health and Flexibility
 - Improve Fertility
 - Improve Circulation
 - Neuron Protection
 - Minimizes Leg Cramping
 - Stop Diarrhea
 - Provide Hemorrhoid Relief
 - Prevent Inflammation
 - Cancer Fighting Properties

66

INDICATIONS / Target Patients



Chronic Venous Insufficiency

67

DRUG INTERACTIONS

- Warfarin, salicylates & other drugs with anti-coagulant properties

68



Khella

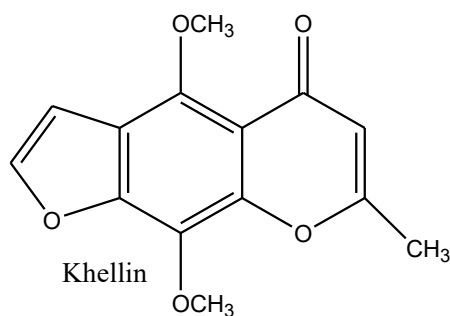
- **Scientific name:** *Ammi Visnaga*
- **Family:** *Apiaceae*
- **Traditional Medicine:**
- **Khella** has traditionally been used for the management of vitiligo, psoriasis, kidney and urinary stones, diabetes, asthma, and urinary tract infections.
- It is also a potent coronary vasodilator with antispasmodic effects, making it useful in treating angina.

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Phytochemicals

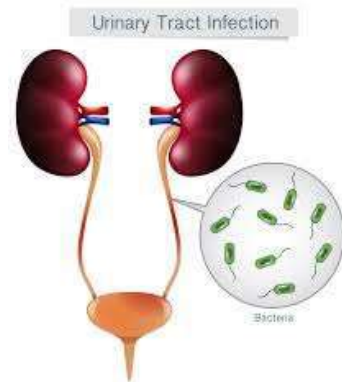
- **Furochromones:** particularly khellin, visnagin, khellol and khellol glucoside
- **Pyranocoumarins:** particularly visnadin and samidin
- **Flavonoids:** Quercetin
- **Volatile oil**
- **Fatty oil.**



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Biological Properties- Effects-

- **Khella shows promise in the prevention of kidney stones**
- **Relieve bladder and urinary tract constriction and spasms.**
- **It is said to help treat asthma, bronchitis, spastic coughs, and emphysema**
- **To prevent atherosclerosis**
- **Health of the gallbladder and bile duct.**
- **Vitiligo**
- **Visnagin is another substance that is isolated from Khella, and, like khellin, it has been shown to have a relaxing effect on the coronary artery only 5-10 times stronger.**



71

Side Effects and Warnings

- **Decreased visual acuity,**
- **Nausea, and vomiting**
- **Headache,**
- **Vertigo,**
- **Insomnia,**
- **Anorexia,**
- **An elevation in liver function test**
- **Constipation,**
- **Itching, and**
- **Weak phototoxic activity.**



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Dong Quai

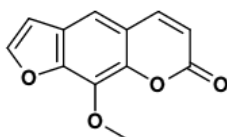
- Scientific name: **Angelica archangelica**
- **Family:** Apiaceae
- **Angelica archangelica** is a perennial herb **used in** alternative medicine to treat a wide range of conditions ranging from heartburn to insomnia. According to folklore.



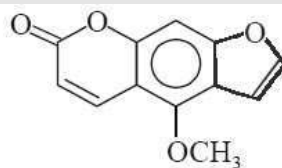
73

PHYTOCHEMICALS

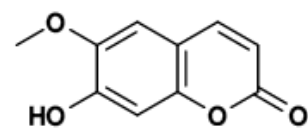
- **Furanocoumarins:** including bergaptene, xanthotoxin, scopoletin, umbelliferone
- **Caffeic acid derivatives:** including chlorogenic acid
- **Ferulic acid**
- **β -sitosterol**
- **Polysaccharide**
- **Lignan**
- **Flavonoids**
- **Volatile oil and Vitamin E, B12, Iron**



Xanthotoxin



Bergapten



Scopoletin

74



75

EFFECTS /Health benefits

- Balancing & **reinforcing the female hormone system.**
- Dong Quai **has hormone-like compounds** which help minimize estrogen problems related to the menstrual cycle.
- Antispasmodic, cholagogue and stimulatory for secretion of gastric juices.
- Anti-inflammatory
- Neurodegeneration
- Wound healing
- Cytotoxic and genotoxic effects

Mechanism of Action

- Have **tonic effects on the uterus**, initially causing **contractions followed by relaxation.**
- When **estrogen levels are high**, displays an overall estrogen-decreasing effect, accounting for its use in the treatment of **menstrual discomforts and PMS.**
- During menopause, **declines in estrogen** levels facilitate its action as a mild estrogenic agonist, used in the treatment of **hot flashes and vaginal dryness.**
- **Coumarins** act as **anti-coagulant activity**; they dilate the blood vessels, stimulate the central nervous system, and increase the blood flow throughout the body.

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INDICATION/Target patients

- Painful menstruation (Dysmenorrhea),
- Menopausal difficulties.
- Female infertility
- For uterine health
- For perimenopause, menopause, and premenstrual syndrome (PMS)
- For blood pressure and blood sugar
- For anemia
- For vaginal dryness and hot flashes
- For anti-inflammatory properties
- For blood vessels and blood flow to organs

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CONTRAINDICATION & Precaution

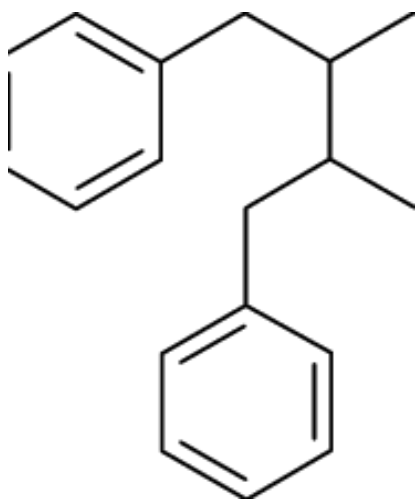


Pregnancy



The blood-thinning properties of Dong Quai (Angelica) may cause menstrual bleeding to increase.

78

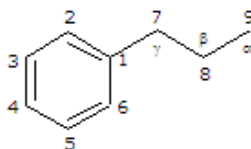


Chapter 4

Lignans, Neolignans

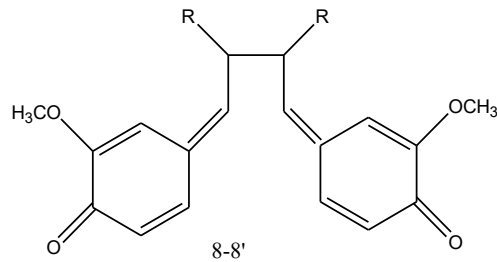
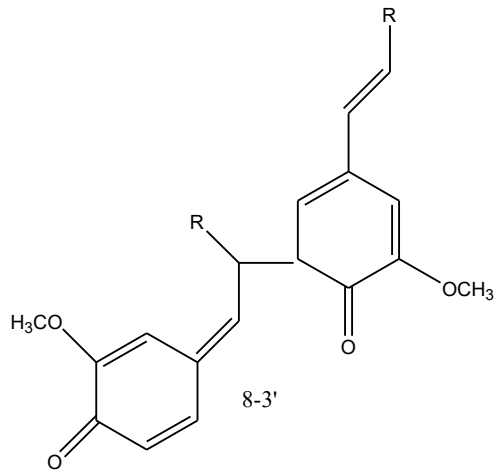
79

Lignans

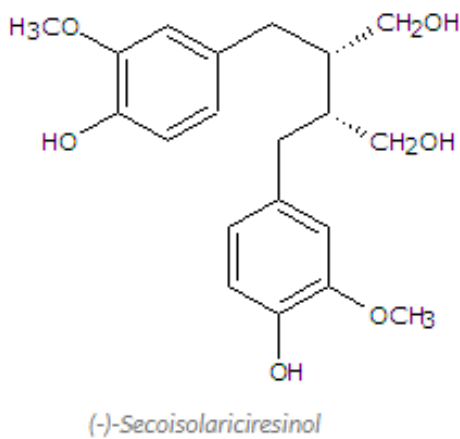


- Lignans are macromolecules, **polymers of basic units of C6-C3** n-propylbenzene, **derived from 1-phenylpropane** which are linked by the β carbon by their side chains (C3).
- Their basic chemical **structure** consists of **two phenylpropane units linked by a C-C bond between the central atoms of the respective side chains (position 8 or β), also called β - β' bond.**
- **Lignans** are a subgroup of **non-flavonoid polyphenols**.
- **Neolignans** are also **condensation products of phenylpropanoids units**.
- In humans, epidemiological and physiological studies have shown that they can exert positive effects in the prevention of lifestyle-related diseases, such as diabetes and cancer.

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Food sources

- The richest dietary source is **flaxseed (linseed)**, that contains mainly **secoisolariciresinol**, but also lariciresinol, pinoresinol and matairesinol in good quantity (for a total amount of more than 3.7 mg/100 g dry weight).
- They are also found in sesame seeds.

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Food sources

- Another important source is **whole grains**. They are also present in other foods, but in concentrations from one hundred to one thousand times lower than those of **flaxseed**. Examples are:
- **Beverages**, generally more abundant in **grapes**, followed in descending order by **black tea**, **soy milk** and **coffee**; **fruits**, such as **apricots**, **pears**, **peaches**, **strawberries**;
- Among **vegetables**, **Brassicaceae**, **garlic**, **asparagus** and **carrots**; **lentils** and **beans**.

83

Pharmacological Properties

- **Cytotoxic and antimutagenic** properties
- Reduced risks of prostate cancer, ovarian cancer, breast cancer, **osteoporosis**, and **cardiovascular disease**.

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Drugs Containing Lignans

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Flaxseed

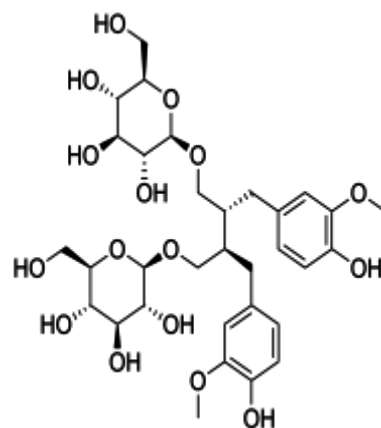
- Scientific name:
Linum usitatissimum
- Family: **Lineaceae**
- Traditional name:
Flaxseed, بذر الكتان



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Phytochemicals

- Lignans: **secoisolariciresinol-diglucoside**: is an antioxidant **phytoestrogen** present in flax, sunflower, sesame, and pumpkin seeds.
- Flaxseeds are the richest dietary source of lignan precursors.
- When ingested, lignan precursors are converted to the **enterolignans, enterodiols and enterolactone**, by bacteria that normally colonize the human intestine.
- The principal lignan precursor found in flaxseed is **secoisolariciresinol diglucoside**

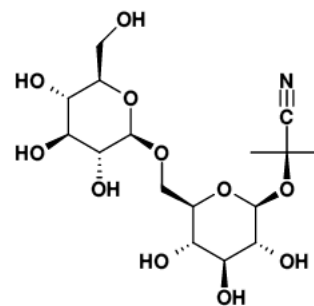
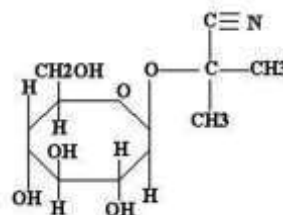


secoisolariciresinol-diglucoside

87

Phytochemicals

- Phenolic acids: ferulic acid, chlorogenic acid & 4-hydroxybenzoic acid
- Polyunsaturated fatty acids (PUFA) **omega-3** (22813mg) vs omega 6 (5911mg)/100g flaxseed.
- **Soluble dietary fibers** (27.3g)
- **Vitamins**: Folate (87.0mg), B₆ (0.5mg) & B₁ (1.6mg)
- **Minerals**: Calcium (255mg), Mg (392mg), P (642mg), K (813mg) Na (30mg), Cu 1.2mg), Mn (2.5mg) and Se (25.4mg)
- **Cyanogenic** compounds: flaxseed contains 264-354 mg of cyanogenic compounds per 100 g of seed, being 10-11.8 mg of linamarin/100 g, 136-162 mg of linustatin/100 g, and 105-183 mg of neolinustatin/100 g of flaxseed.
- Flaxseed grain and flaxseed paste contain about 21% and 34% **protein**



Linustatin

88

Biological Activity

89

Effect

- **Secoisolariciresinol Diglucoside** (SDG) are reported to have as **antioxidant** properties.
- After ingestion, SDG is **converted to enterolignans** (enterodiol and enterolactone) **by the intestinal microflora**; then these metabolites (phytoestrogens) are absorbed and can provide health benefits.
- SDG **decreased the systolic, diastolic** and mean arterial pressure. Data suggested that SDG reduced the angiotensin I-induced rise in the arterial pressures and hence SDG was a potent ACE inhibitor
- Utilization of flaxseed for **glycemic control may also be associated to the decrease in risk of obesity and dyslipidemia and resistance to insulin.**

90

Effect

- Lignans may **protect against certain cancers**, particularly hormone-sensitive cancers such as those of the breast, endometrium and prostate, by interfering with sex hormone metabolism.
- Lignans may **reduce the level of free circulating testosterone** and when bonded together are excreted in the bile, **potentially reducing the risk of polycystic ovary syndrome** in susceptible women, **since this syndrome is associated to high levels of androgens.**
- Reduce the severity of **osteoporosis**.
- A highly significant **reduction in total cholesterol, triglycerides**, low density lipoprotein-cholesterol (LDL-C) and low-density lipoprotein-cholesterol (VLDL-C) levels were observed.

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Effect

Cyanogenic glucosides causes chronic effects, manifested in the nervous system and are observed in populations that ingest high quantities of cyanate in foods.

However, these compounds present instability **when subjected to thermal** and mechanical processes, including cooking in microwaves, autoclaving, and boiling

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Indication/target patients

Postmenopausal women

Osteoporosis

Ovarian polycystic

Reduction of triglycerides

Reduction of cholesterol

Improve digestion

93

Side effects of flaxseed



ALLERGIC
REACTIONS.



INTESTINAL
OBSTRUCTION.



BLOATING.



STOMACH-
ACHE.



CONSTIPATION.



FLATULENCE

94

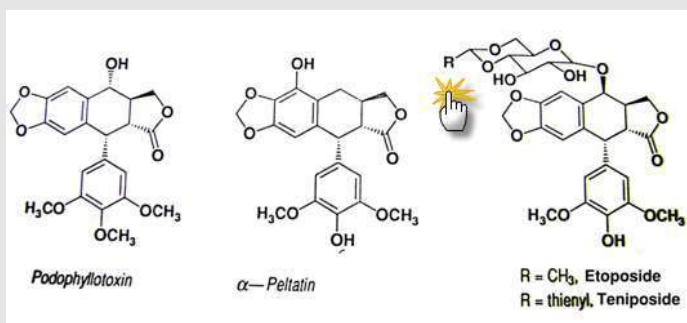


May Apple

- **Scientific name:** *Podophyllum peltatum*
- **Family:** Berberidaceae
- **Parts used:** Dried rhizome & the resin extracted from it.
- **Traditional Medicine:** **Podophyllum** is applied directly to the skin for removal of warts, including plantar warts and sexually transmitted (venereal) warts.

95

Phytochemicals



- Podophyllum resin contains at least 16 active compounds

• Lignans:

- **podophyllotoxin** (20%),
- α -peltatin (5%),
- β -peltatin (10%),
- Quercetin and kampherol

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Biological properties

- Effect
 - A variety of pharmacologically active lignans are present in podophyllum.
 - These lignans (podophyllotoxin being the best known) act as **antimitotic agents**, with the greatest effects in tissues undergoing rapid cell division.
 - Podophyllotoxin binds to tubulin, the protein subunit of the spindle microtubules, blocking cell division in metaphase.
 - Activity of **cytochrome oxidase** and **succin-oxidase in the mitochondria also is reduced**, and **DNA synthesis is blocked**.
 - Podophyllum is **highly lipid soluble** and is absorbed readily from the GI tract.
 - Podophyllotoxin is **eliminated in the bile** with a half-life of 48 hours.

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Contraindication

- The use of podophyllum is contraindicated in **pregnancy**.
- Avoid use in **nursing** patients

98

Indication

Antitumor:

- Several components of podophyllum, including α - and β -peltatins, podophyllotoxin, and its derivatives, have tumor-inhibiting properties. The severe toxicity of podophyllotoxin limits its use as a cytostatic;

Wart eradication:

- Topical application of 20% to 25% podophyllum resin in ethanol or benzoin tincture is a well-established, affordable, and effective remedy for genital warts

Cathartic (Purgative)

- Podophyllum resin is a drastic cathartic. It has a marked purging action, is highly irritant to the intestinal mucosa, and produces violent peristalsis.

Rheumatoid Arthritis (RA)

99

Milk Thistle

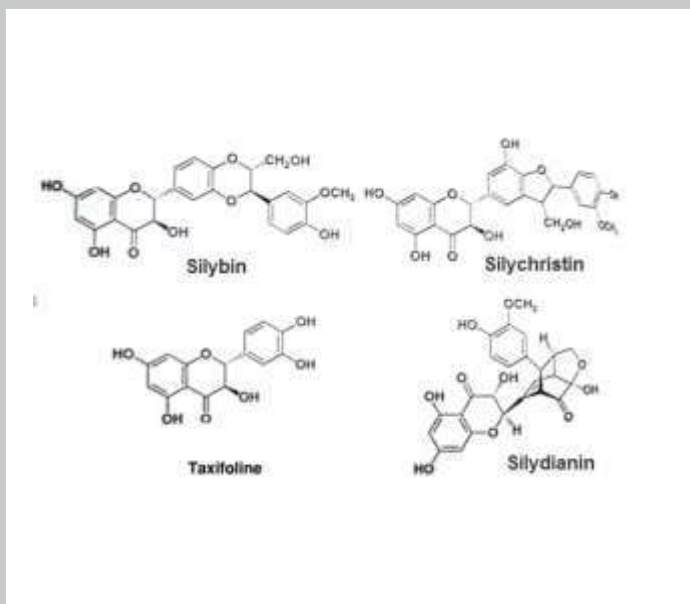


- **Scientific name:** *Silybum marianum L.*
- **Family:** Asteraceae
- **Traditional name:** خف الجمل
- **Part used:** ripe seeds
- **Traditional Uses:** Liver detoxification

100

Phytochemicals:

- **Silymarin** (flavonolignan mixture, 1.5-3%): **chief components silybin A, silybin B** (mixture known as **silibinin**), betaine, isosilibinin, silychristin, silydianin.
- **Flavonoids**: apigenin, chrysoeriol, eriodictyol, naringenin, quercetin, taxifolin
- **Fatty oil** (20-30%)



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Biological Properties

- **Supports liver health**, these liver problems include cirrhosis, jaundice, hepatitis, viral hepatitis and gallbladder disorders.
- **Anti-inflammatory and antioxidant.**
- **Promotes skin health**
- **Reduces cholesterol**
- **Supports weight loss**
- **Reduces insulin resistance**
- **Supports bone health**
- **Boosts the immune system**



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INDICATIONS / Target Patients



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HOW SUPPLIED

- Capsules: 35mg, 70mg, 100mg, 140mg, 150mg, 175mg, 180mg,
- 500mg, 540mg,
- **1000 mg.**



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Broccoli

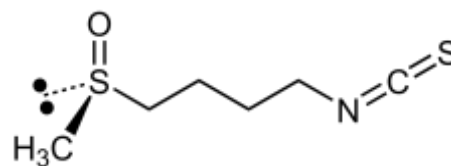
- **Scientific name:** Brassica oleracea var. italica
- **Family:** Brassicaceae
- **Arabic name:** البروكلي
- **Traditional Medicine:** Broccoli is used for high cholesterol,



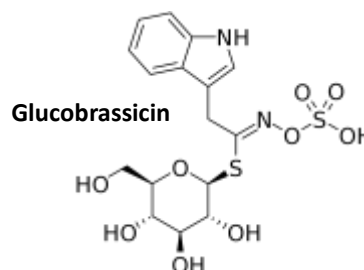
105

Phytochemicals

- Sulforaphane (*Sulforaphane is a compound within the isothiocyanate group of organosulfur compounds. It is obtained from cruciferous vegetables*).
- Glucosinolates, Glucobrassicin
- Sinapic and isochlorogenic acids were predominant phenolics
- Omega 3, Oleic and linoleic acids
- Minerals: Ca, Mg, P, K, Na and Fe
- Vitamin C and vitamins such as A, K, folate & choline
- Carotenoids, such as zeaxanthin and beta-carotene; and kaempferol, a flavonoid.



Sulforaphane



Glucobrassicin

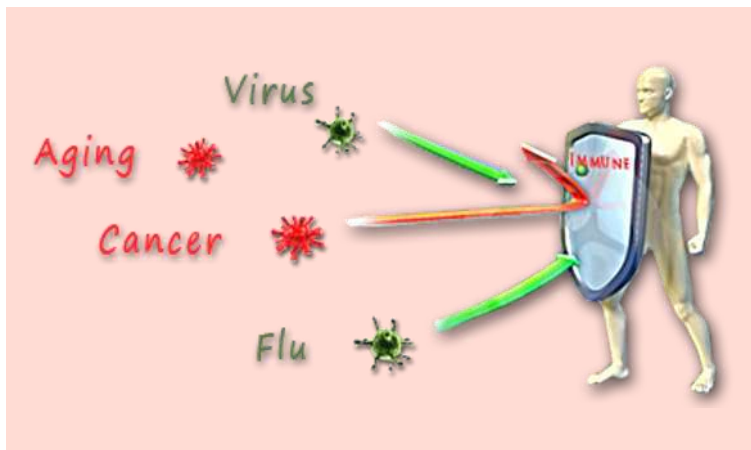
106

Biological activity

- Cancer (bladder, breast, colon, prostate, rectal) (**sulforaphane**)
- Blood sugar control (**sulforaphane**)
- Cholesterol reduction (**soluble fiber**)
- Fibromyalgia (**sulforaphane**)
- Detoxification (**glucobrassicin**)
- Antioxidant (**vitamin C**)

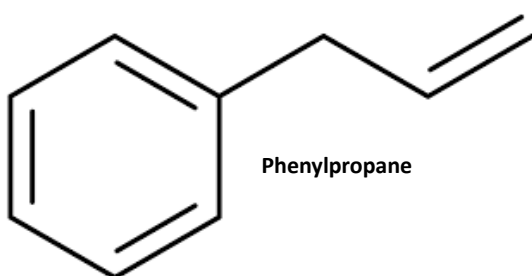
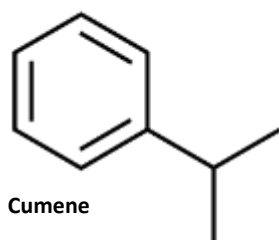
107

Target patients



- **Cancer**
- **Enhance the immune system**

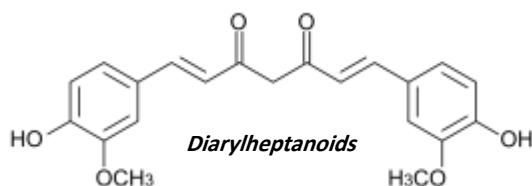
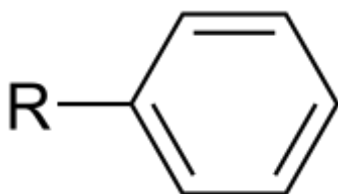
108



Chapter 5

Shikimate: Phenylpropane chain

109



Diarylheptanoids & Aryl alkanes

110

Turmeric

- **Scientific name:** *Curcuma domestica*
- **Family:** Zingiberaceae
- **Traditional name:** الكركم
- **Part used:** Dried Rhizome
- **Traditional Medicine:**
Turmeric is used in Ayurvedic medicine to treat inflammation both inside and out as well as treatment of rheumatoid arthritis and infections.



111

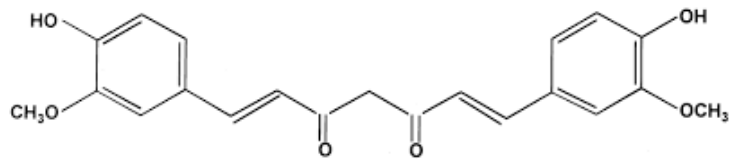
Curcuma domestica vs *Carthamus tinctorius*



112

Phytochemicals

- **Curcuminoids (3-5%), (coloring principles):** including **curcumin**, demethoxy curcumin, bidehydroxy curcumin
- **Volatile oil (3-5%):** alpha- and beta-tumerone (aroma source) & zingib
- **Starch (30-40%):** (arabino-galactan)



CURCUMIN

113

Biological Activity



114

EFFECTS

- **Curcumin** is the main active ingredient in turmeric. It has powerful **anti-inflammatory** effects. **Curcumin** can suppress many molecules known to play major roles in inflammation. **It blocks NF-kB**, a molecule that travels into the nuclei of cells. NF-kB is believed to **play a major role in many chronic diseases**.
- **Curcumin** has powerful **antioxidant** effects.
- **Curcumin boosts levels of the brain** hormone BDNF, which increases the growth of new neurons and fights various degenerative processes in your brain.

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EFFECTS

- **Curcumin** can cross the blood-brain barrier and has been shown to lead to various improvements in the pathological process of **Alzheimer's disease**.
- **Curcumin** has beneficial effects on several factors known to play a role in **heart disease**.
- **Curcumin** has shown some promise in treating **depression**.
- **Curcumin** leads to several changes on the molecular level that may help prevent and perhaps even treat **cancer**.

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Pepper extract and curcumin effects

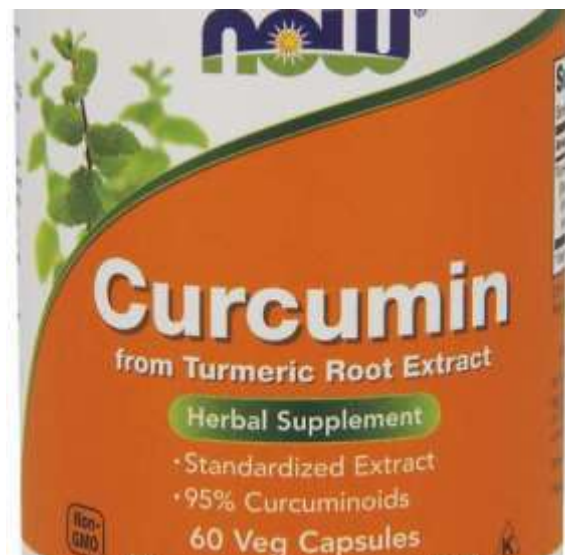
- **Turmeric** and black **pepper** each have health benefits, due to the compound's **curcumin** and piperine.
- As piperine enhances **curcumin** absorption in the body by up to 2,000%, combining the spices magnifies their **effects**.
- They may reduce inflammation and improve digestion, particularly in **supplement** form.



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Indication/Target patients

- Dyspeptic complaints
- Loss of appetite
- Hepatitis
- Immune enhancer
- Skin cancer
- Antidepressant



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Ginger

- **Scientific name:** *Zingiber officinales*
- **Family:** Zingiberaceae
- **Part used:** Dried rhizome
- **Traditional name:** الزنجبيل
- **Traditional Medicine:** It has been used to help digestion, reduce nausea and help fight the flu and common cold, to name a few. Ginger can be used fresh, dried.

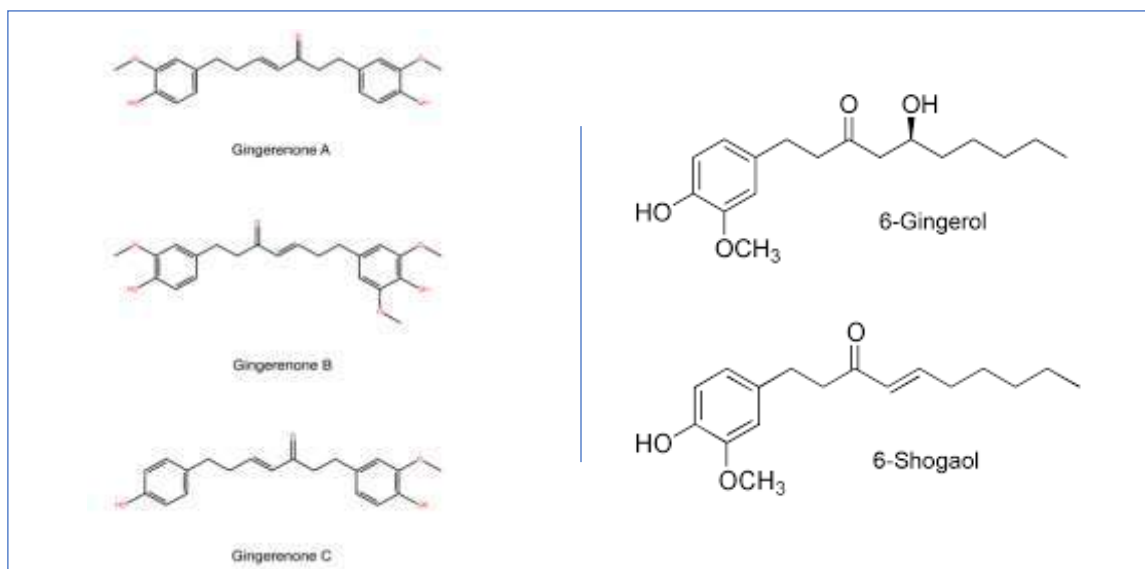


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Phytochemicals:

- ***Aryl alkanes***
 - *Gingerols* (pungent substances)
 - *Shogaols* (pungent substances), formed during storage. arising from the gingerols.
- ***Gingerdiols***
 - *Diarylheptanoids*: gingerenone A, B & C
- ***Volatile oil***
 - (-)-zingiberene and arcurcumene, beta-bisabolene and ar-curcumene, neral and geranial, D-camphor, beta-phellandrene

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Biological Properties

- Ginger is a popular spice. It is high in gingerol, a substance with powerful anti-inflammatory and antioxidant properties.
- Ginger can help prevent various types of nausea.
- Ginger appears to be effective at reducing the day-to-day progression of muscle pain.
- Ginger to be effective at reducing symptoms of osteoarthritis.
- Ginger has been shown to lower blood sugar levels and improve various heart disease risk factors in patients with diabetes.
- Ginger extract can inhibit the growth of many different types of bacteria

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Biological Properties

- Ginger appears to speed up emptying of the stomach, which can be beneficial for people with indigestion and related stomach discomfort.
- Ginger appears to be very effective against menstrual pain when taken at the beginning of the menstrual period.
- Ginger can lead to significant reductions in LDL cholesterol and blood triglyceride levels.
- Ginger contains a substance called 6-gingerol, which may have protective effects against cancer.
- Ginger can protect against age-related damage to the brain. It can also improve brain function in elderly women.

123



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Indication / Target patients



Indigestion (Loss of appetite)



Morning Sickness



Cancer patients undergoing
chemotherapy.



Osteoarthritis

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CONTRAINDICATIONS

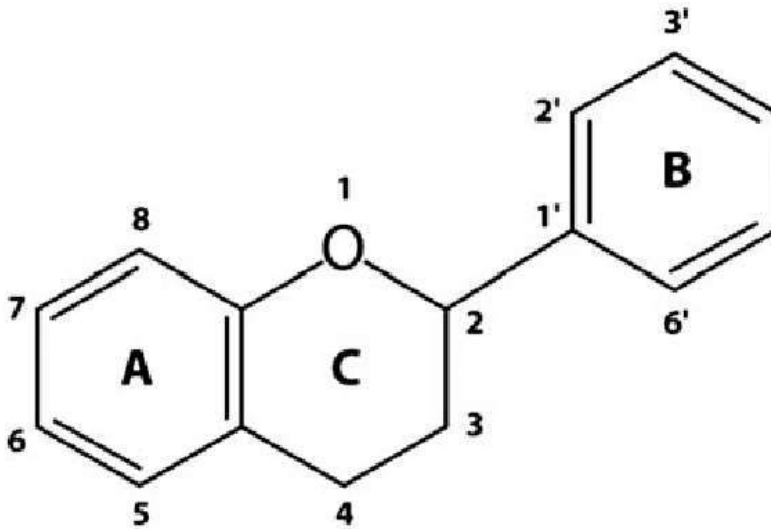
- Because of its cholagogue effect, the drug should not be taken in the **presence of gallstone conditions**.
- Ginger has been found to inhibit thromboxane synthesis; therefore it should not be used by patients who are at **risk for hemorrhage**.



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Chapter 6

Flavonoids



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What Are Flavonoids?

- Flavonoids are a diverse group of phytonutrients (plant chemicals) found in almost all fruits and vegetables. Along with carotenoids, they are responsible for the intense colors in fruits and vegetables.
- Flavonoids are the largest group of phytonutrients, with more than 6,000 types.
- Some of the best-known flavonoids are quercetin and kaempferol.



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General Overview

Occurrence

- Bryophytes, Gymnosperms & Angiosperms

Flavonoids Functions in Plants

- Defense
- Protection from Solar Ultraviolet
- Stress Protection
- Reproduction
- Chemical Messengers
- Heavy Metal Tolerance
- Antioxidant

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Flavonoids types:

Flavones:

- Luteolin and apigenin (celery, parsley, various herbs and hot peppers).

Flavonones:

- Hesperetin, and naringenin. Flavonones are found abundantly in citrus fruits.

Flavonols:

- Quercetin and Kaempferol.

Flavanols:

- There are three primary types of flavanols: **monomers** (more widely known as catechins), **dimers** and **polymers**. Flavanols are found in teas, cocoa, grapes, apples, berries and fava beans.

Isoflavones:

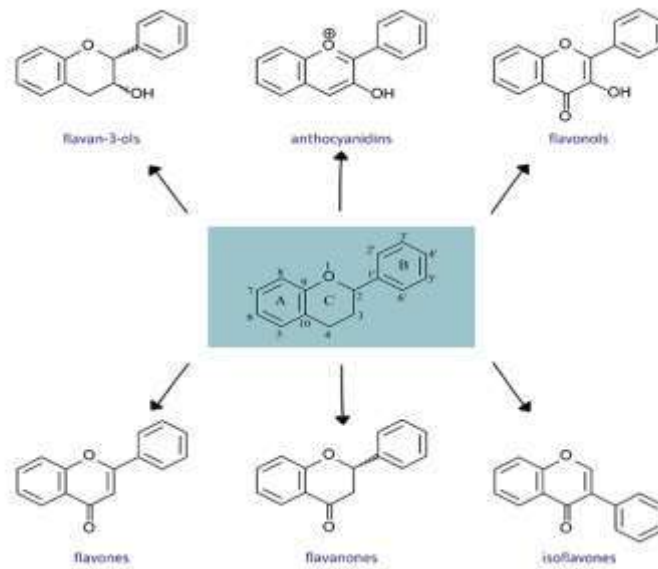
- Genistein, glycitein and daidzein. Isoflavones are highly concentrated in soy products, as well as legumes. They are phytoestrogens.

Anthocyanidins:

- Malvidin and cyanidin. Good sources of anthocyanidins include red, purple and blue berries; pomegranates, plums & Malvea

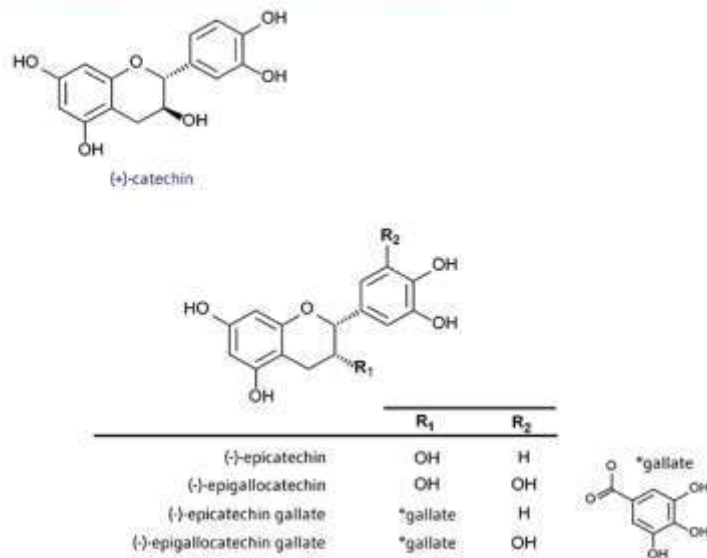
130

Figure 1. Basic Structures of Flavonoid Subclasses



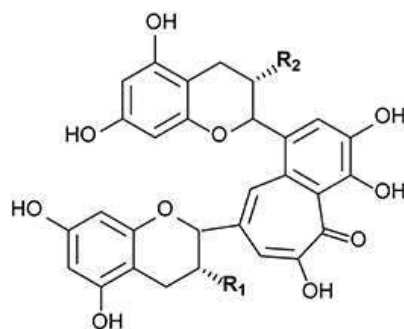
131

Figure 2. Chemical Structures of Some Flavan-3-ol Monomers (Catechins)



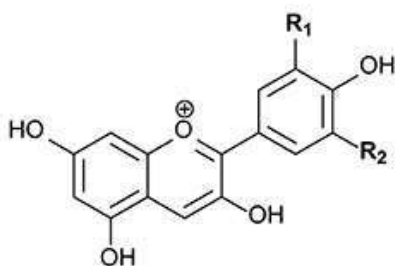
132

Figure 3. Chemical Structures of Theaflavins



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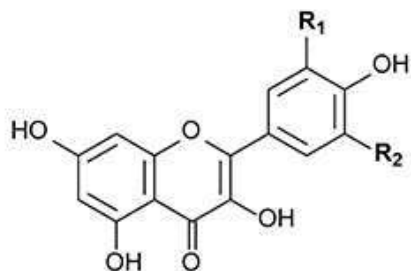
Figure 4. Chemical Structures of Anthocyanidins



	R ₁	R ₂
Cyanidin	OH	H
Delphinidin	OH	OH
Malvidin	OCH ₃	OCH ₃
Pelargonidin	H	H
Peonidin	OCH ₃	H
Petunidin	OCH ₃	OH

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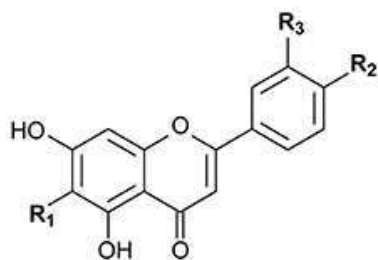
Figure 5. Chemical Structures of Flavonols



	R ₁	R ₂
Isorhamnetin	OCH ₃	H
Kaempferol	H	H
Myricetin	OH	OH
Quercetin	OH	H

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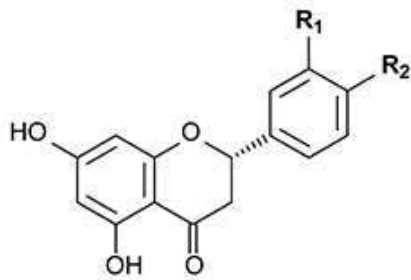
Figure 6. Chemical Structures of Flavones



	R ₁	R ₂	R ₃
Apigenin	H	OH	H
Luteolin	H	OH	OH
Baicalein	OH	H	H
Chrysin	H	H	H

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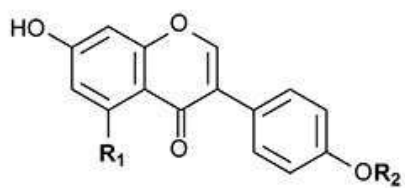
Figure 7. Chemical Structures of Flavanones



	R ₁	R ₂
Eriodictyol	OH	OH
Hesperetin	OH	OCH ₃
Naringenin	H	OH

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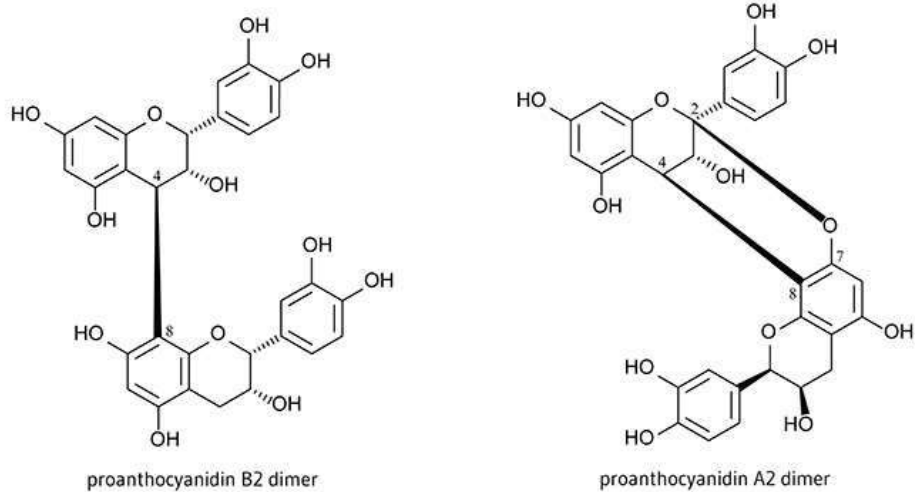
Figure 8. Chemical Structures of Isoflavones



	R ₁	R ₂
Daidzein	H	H
Genistein	OH	H
Glycitein	OCH ₃	H
Biochanin A	OH	CH ₃
Formononetin	H	CH ₃

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Figure 9. Chemical Structures of Proanthocyanidin Dimers

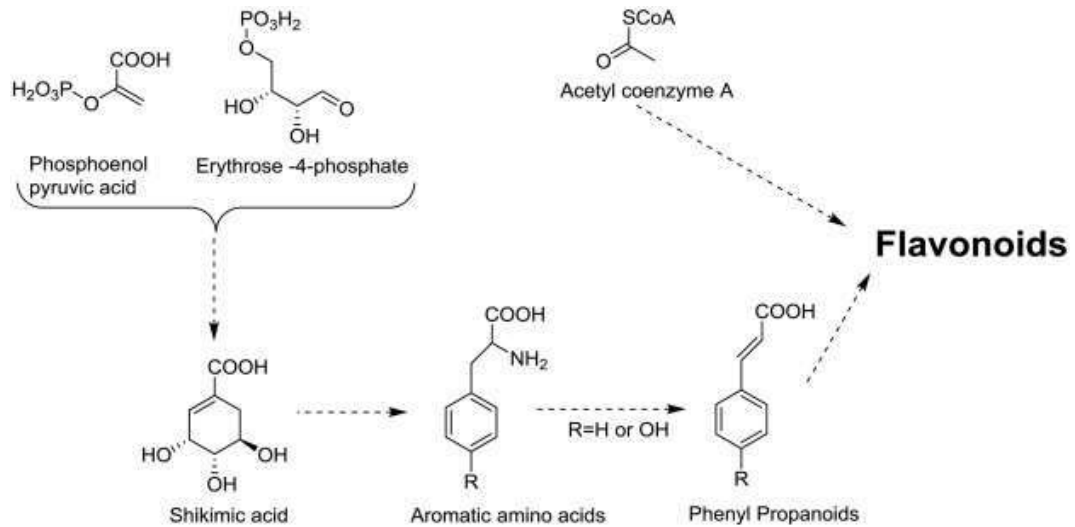


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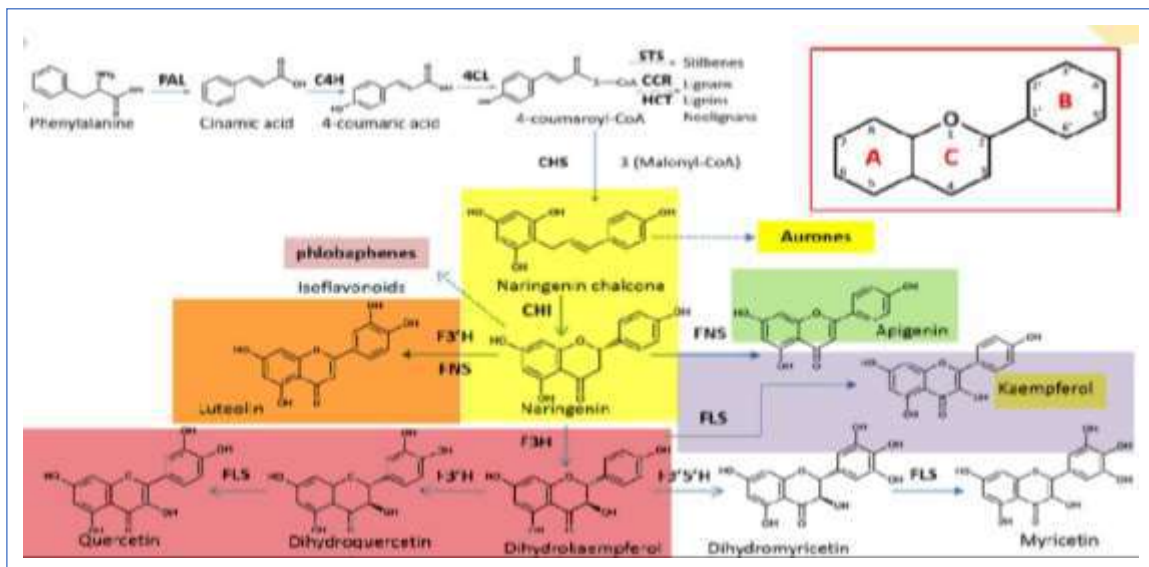
Flavonoid Biosynthesis

140

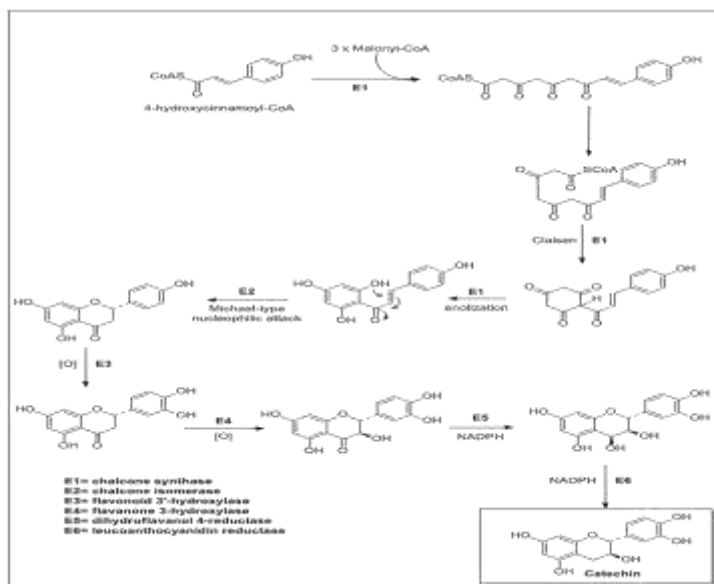
- The flavonoid pathway is part of the larger phenylpropanoids pathway



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Physical & Chemical Properties

- Flavonoids are **water soluble and soluble in alcohols**, aglycones, for the most part, **soluble in polar organic solvents**, when they have at least one free phenolic group, they **dissolve in alkaline** hydroxide solutions.
- **Lipophilic flavonoids can wash with hexane and then extracted by solvents of medium polarity.**
- The glycosides (Flavonosides) can be extracted by acetone or by alcohols mixed with water.

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Separation & Extraction

- The separation and purification of the different flavonoids is based on the usual chromatographic techniques (Paper (PC), HPLC).
- **Extraction:** the solvent is chosen as a function of the type of flavonoid required.
- **Polarity** is an important consideration here.
 - **Less polar flavonoids** (e.g., isoflavones, flavanones, methylated flavones, and flavonols) are **extracted with chloroform**, dichloromethane, diethyl ether, or ethyl acetate, while flavonoid glycosides and
 - **More polar** aglycones are **extracted with alcohols** or alcohol–water mixtures.
- **Glycosides have increased water solubility and aqueous alcoholic solutions are suitable.**
- **Flavan-3-ols extracted directly with water.**
- **Anthocyanins are extracted with cold acidified methanol.**

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Biological Properties

- **Flavonoids:** Factor “P”, diuretic, anti-inflammatory and they inhibit the development of infection.
 - **Apigenin:** has an anxiolytic effect and can regulate the level of neurotransmitters & hepatoprotector.
 - **Quercetin** has antiviral properties. It is also important to know that flavonoids in general strengthen the immune system.
- **Anthocyanins:** improve vision by stimulating ocular microcirculation and improving visual acuity at dusk.
- **Isoflavones:** have an estrogenic effect and complement estrogen deficiency, so they can relieve menopausal symptoms.

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Dietary Sources of Flavonoids

- **Quercetin (Flavonols):** Vegetables, fruits and beverages, spices, soups, fruit juices
- **Kaempferol (Flavonols):** Apples, grapes, tomatoes, green tea, potatoes, onions, broccoli, Brussels sprouts, squash, cucumbers, lettuce, green beans, peaches, blackberries, raspberries, spinach
- **Rutin (Flavonols):** Green tea, grape seeds, red pepper, apple, citrus fruits, berries, peaches
- **Naringenin (Flavanone):** Grapes
- **Hesperidin (Flavanone):** Bitter orange, petit grain, orange, orange juice, lemon, lime
- **Theaflavin (Catechins):** Tea leaves, black tea, oolong tea
- **Epicatechin (Flavan-3-ols):** Milk, chocolate
- **Luteolin (Flavones):** Celery, broccoli, green pepper, parsley, thyme, dandelion, perilla, chamomile tea, carrots, olive oil, peppermint, rosemary, navel oranges, oregano

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Flavonoids Containing Drugs



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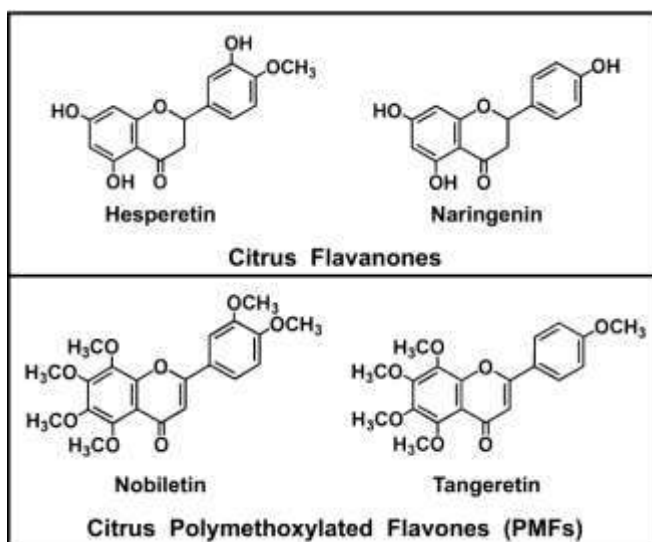
Citrus flavonoids



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Citrus flavonoids

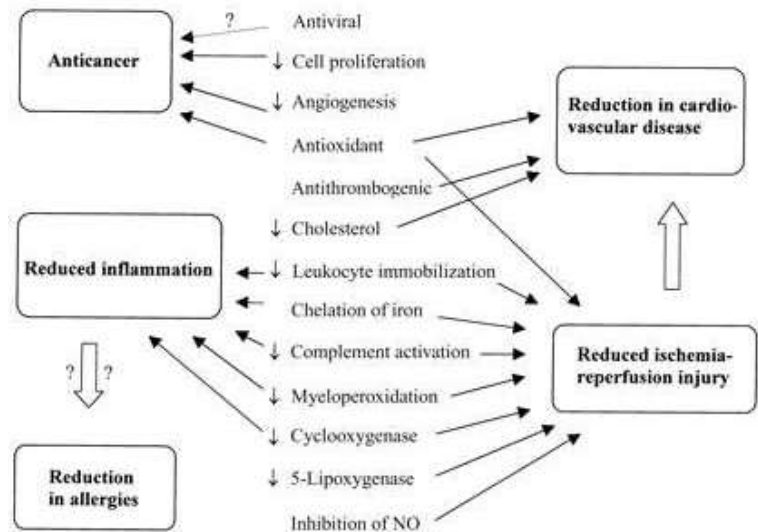
- Rutaceae family
- These are very abundant in pericarp and are mainly flavanone glycosides.



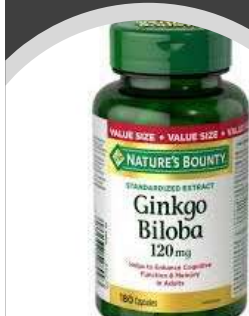
150

Clinical Effects

- Factor "P"
- Anti-inflammatory effects
- Antiviral effects (**Quercetin**)
- Antiatherosclerosis effects
- Antitumor effects
- Antithrombogenic effects
- Antiosteoporotic effects



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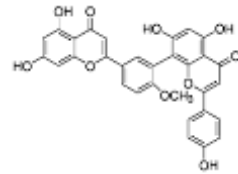
Ginkgo

- **Scientific name:** *Ginkgo biloba*
- **Family:** Ginkgoaceae
- **Traditional Medicine:** maidenhair tree

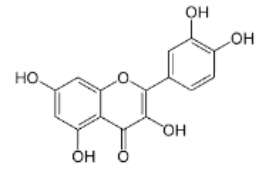
152

Phytochemicals

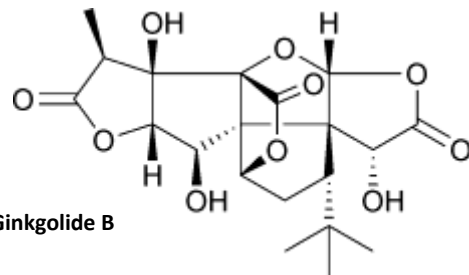
- **Flavonols:** Quercetin
- **Ginkgolide:** Ginkgolide A, B, C
- **Bioflavonoids:** Ginkgetin



Bilobetin



Quercetin



Ginkgolide B

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Biological Activity

- **Dementia:** There isn't enough evidence to support the use of ginkgo to prevent dementia or treat people with mild cognitive impairment.
- **Claudication:** A review of the research suggests that taking ginkgo has no significant benefits for people with this condition.



Side Effects



- Ginkgo can cause:
 - Headache
 - Dizziness
 - Heart palpitations
 - Upset stomach
 - Constipation
 - Allergic skin reactions



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Interactions

- Alprazolam (Xanax).
- Anticoagulants and anti-platelet drugs, herbs and supplements.
- Anticonvulsants and seizure threshold lowering drugs, herbs and supplements.
- Antidepressants
- Statins
- Ibuprofen
- Antidiabetics



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Passion flower

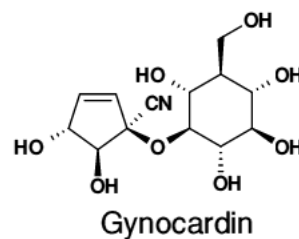
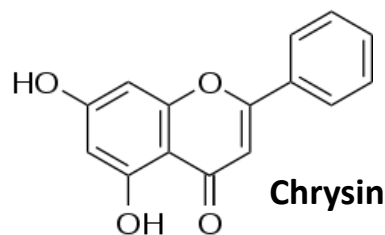
- **Scientific name:** *Passiflora incarnate*
- **Family:** Passifloraceae
- **Traditional Medicine:**

Wounds, earaches, and liver problems.

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PHYTOCHEMICALS

- **Flavonoids:** Chrysin, (found also in propolis)
- **Alkaloids:** beta-carboline harmala
- **Cyanogenic glycosides:** gynocardin
- **Volatile oils**
- **Minerals:** phosphorus, magnesium sulfur and potassium



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Biological Effects

- Passion flower might help with anxiety.
- Help treat stomach problems.
- Help relieve insomnia
- Attention deficit-hyperactivity disorder (ADHD),
- Reducing pain,
- Reliving fibromyalgia,
- Relieving opioid withdrawal symptoms,
- Reducing **nervousness** before surgery.

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Thyme

- **Scientific name:** *Thymus vulgaris*
- **Genus:** Origanum
- **Family:** Lamiaceae
- **Traditional name:** الزعتر البري
- **Traditional Medicine:**

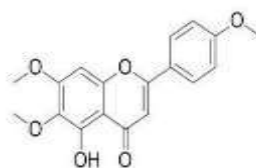
Diarrhea, stomachache, arthritis, and sore throat.



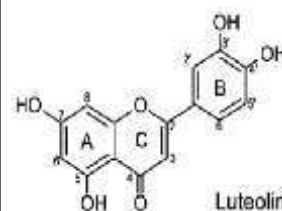
160

Phytochemicals

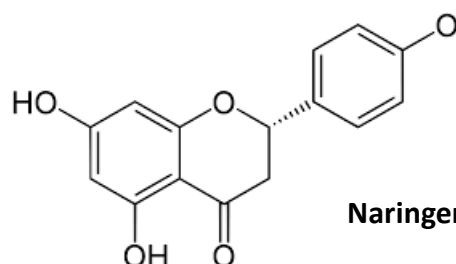
- **Flavonoids:** luteolin, apigenin, naringenin, salvigenin, & thymine
- **Volatile oil :** thymol (20-55%)
- **Caffeic acid derivatives:** Rosmarinic acid
- **Triterpenes:** ursolic acid & oleanolic acid
- Richer in potassium, calcium, and iron
- **Richer in vitamins A and C.**



Salvigenin



Luteolin

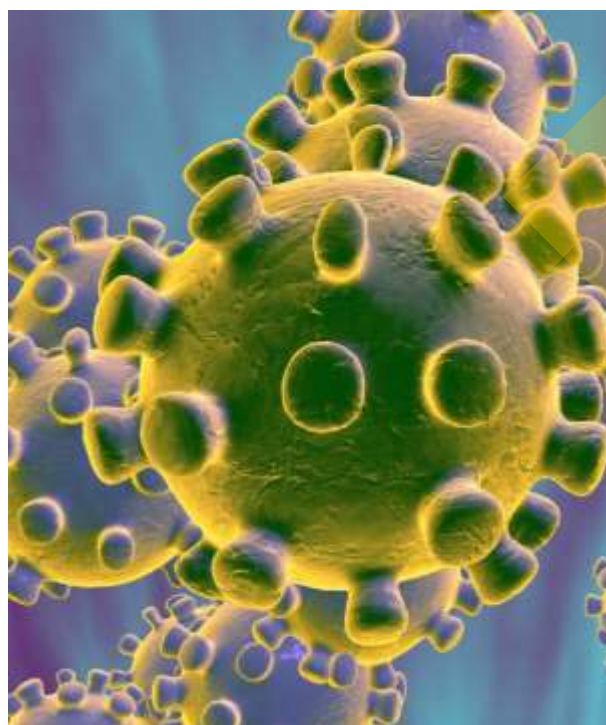


Naringenin

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Biological activity

- Natural antiseptic & disinfectant
- Boost the immunity
- Supports Respiratory Health
- Mood Booster
- ability to support skin health
- Powerful Antioxidant
- Promotes Oral Health



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Apium

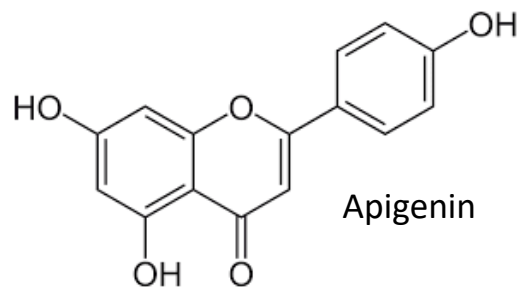
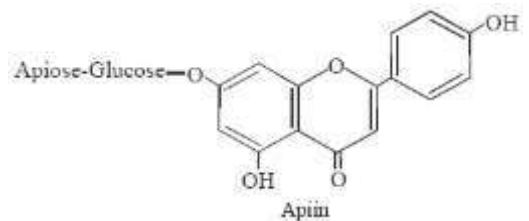
- Scientific name: *Apium graveolens*
- Family: Umbelliferae
- Traditional name: Celery-
الكرفس



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Phytochemicals

- **Celery** contains phenolic acid, which is an antioxidant.
- Apiin and apigenin
- Vitamin C, B vitamins, calcium, magnesium, and manganese.



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Biological activity

- Boosts Immune System
- Antioxidant
- Nerve Tonic
- Lowers Arthritis Pain
- Celery supports digestive health
- Lowers Cholesterol Level
- Reduces Blood Pressure
- Prevents Urinary Tract Infections
- Weight Loss
- Anticancer Properties

Healthy Collection



CELERY

NUTRITIONAL FACTS PER 100G

PRINCIPLE		VITAMINS		MINERALS	
		Percentage of RDA*			
Energy	17.6 Kcal	Vitamin K	40%	Manganese	6%
Carbohydrates	3.8 g	Vitamin A	10%	Potassium	8%
Protein	0.8 g	Vitamin C	6%	Calcium	4%
Total Fat	0.2 g	Folate	10%	Sodium	4%

*Recommended Dietary Allowances

*Recommended Dietary Allowances

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Chapter 7

Anthocyanins



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Introduction

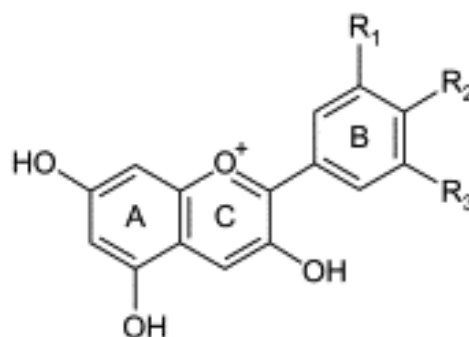
- **Antho (flower) cyanin (dark blue)**
- Anthocyanins are water-soluble vacuolar pigments that, depending on their pH, may appear red, purple, blue or black.
- Food plants rich in anthocyanins include the blueberry, raspberry, black rice, and black soybean, among many others that are red, blue, purple, or black.
- Some of the colors of autumn leaves are derived from anthocyanins
- Anthocyanins belong to a parent class of molecules flavonoids synthesized via the phenylpropanoid pathway.



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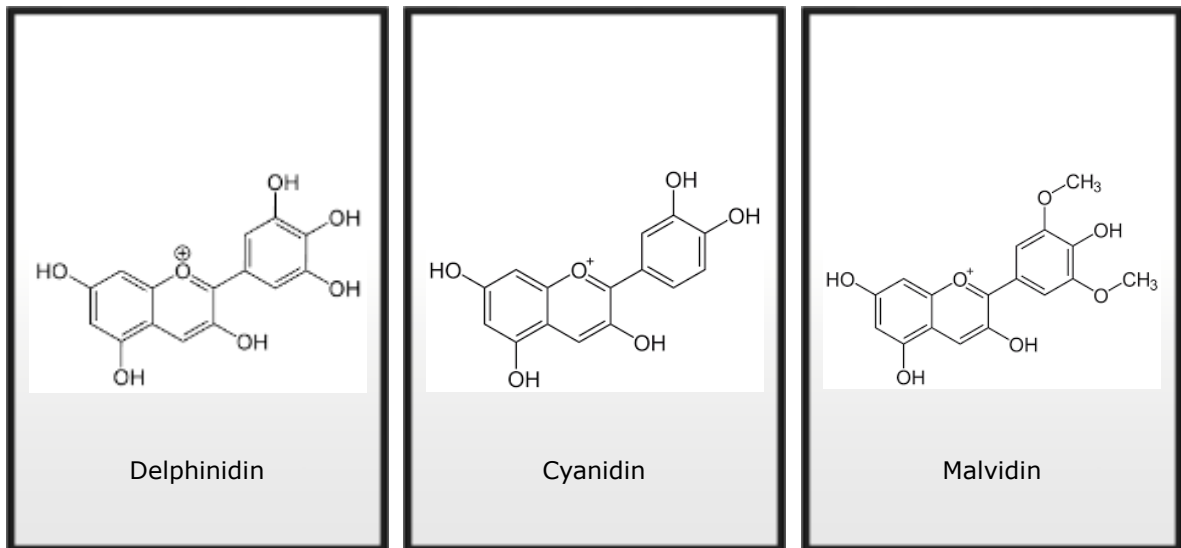
Chemistry of Anthocyanin

- These pigments occur as glycosides (anthocyanins) and their aglycone (anthocyanidin) are derived from the 2-phenylbenzopyrylium (flavylium cation).

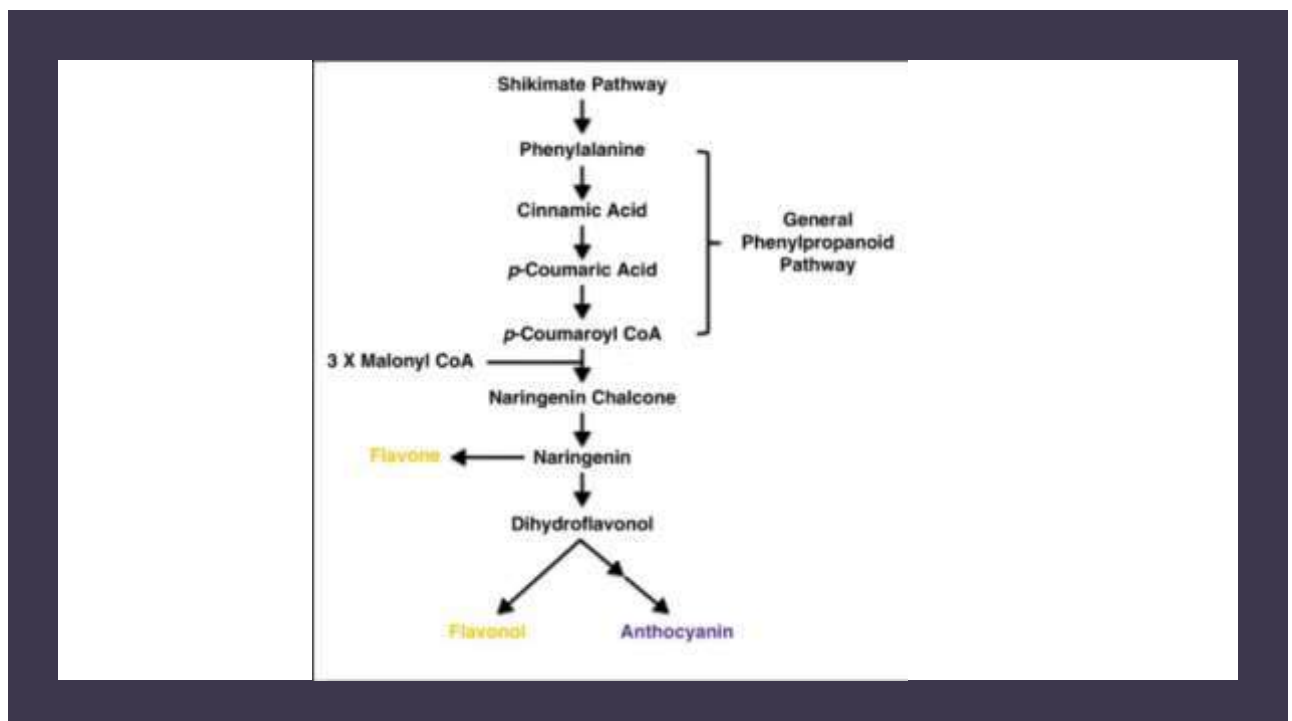


Chemical structure of anthocyanin

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Physico-chemical properties, extraction

- **Anthocyanins are soluble in water and alcohols**, and insoluble in polar organic solvents.
- They are generally **extracted** with an **alcohol** in the presence of **small amount of HCl**,
- In **strong acid medium**, the cation is **red and stable**,
- In **weak acid** medium the cation loss one or two protons and this led to anhydro-base **blue** in color.
- **Hydrating** the molecule (in 2-position) leads to carbinol, which is **colorless**.
- **Anthocyanins solutions are very unstable**,
- they can only be kept under nitrogen at low temperature and in the dark.
- The separation of anthocyanins is achieved by chromatographic techniques (TLC, HPLC).

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Biological Activity

- Anthocyanin acting as antioxidants and fighting free radicals, anthocyanins may offer anti-inflammatory, anti-viral, and anti-cancer benefits.
- Anthocyanins may enhance heart health
- Anthocyanins appear to improve cholesterol levels and blood sugar metabolism, as well as fight oxidative stress.
- Factor "P"

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Anthocyanins Containing Drugs



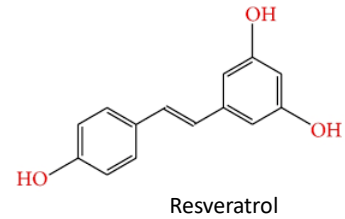
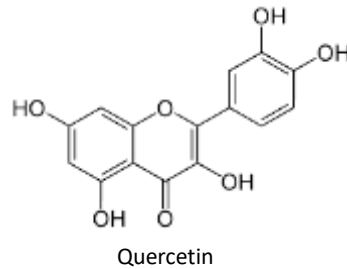
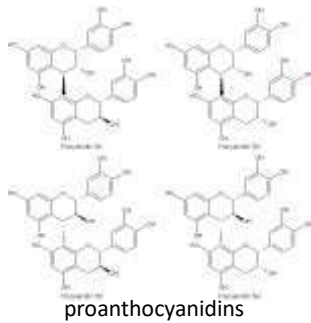
173

Blueberry

- **Scientific name:** *Vaccinium myrtillus*
- **Family:** Ericaceae
- **Genus:** Vaccinium
- **Traditional Medicine:**
 - boost the health of blood vessels
 - treat or prevent high blood pressure & high cholesterol.



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Phytochemistry

- Blueberries are rich in anthocyanins, proanthocyanidins,
- Chlorogenic acid
- Resveratrol,
- Quercetin,
- Tannins,

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NUTRIENT VALUE

- Blueberries have a diverse range of micronutrients, with notably high levels of the essential dietary mineral manganese, vitamin B₆, vitamin C, vitamin K and dietary fiber.

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Effect

- Blueberries have the highest antioxidant capacity of all the popular fruits and vegetables.
- Blueberries and blueberry juice reduce DNA damage, which is a leading driver of aging and cancer.
- Reduce a predominant risk factor for heart disease by preventing oxidative damage to “bad” LDL cholesterol.
- Regular blueberry intake is tied to lower blood pressure in numerous studies.
- Maintain Brain Function and Improve Memory
- Anti-Diabetes Effects
- Fight Urinary Tract Infections
- Reduce Muscle Damage After Persistent Exercise

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Indication (Target patient)

- Memory disorder
- Vein insufficiency
- Hemorrhoids
- Hypertensive
- Elders
- UTI
- Hyperlipidemic patients

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Black Currant

- **Scientific name:** *Ribes nigrum*
- **Family:** Grossulariaceae
- **Parts used:**
Fruits, leaves and seeds
- **Traditional Medicine:** Black currant seed oil is used for lowering high cholesterol. It is also used for high blood pressure, rheumatoid arthritis (RA),

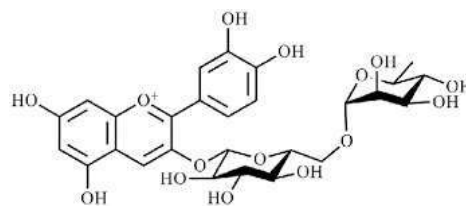


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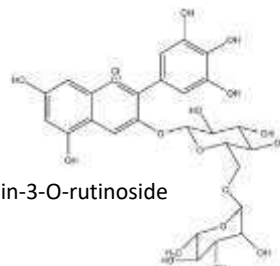
PHYTOCHEMICALS: BLACK CURRANT FRUITS

- **Anthocyanins:** chiefly cyanidin-3-O-rutinoside and delphinidin-3-O-rutinoside.
- **Phenol carboxylic acid derivatives:** caffeoyl-, p-cumaroyl and
 - feruloyl-quinic acids; p-cumaroyl and feruloyl glucoses
- **Flavonoids:** chief components isoquercitrin, myricetin glucoside, rutin
- **Fruit acids (3.5%):** malic acid, citric acid, isocitric acid
- **Rich in vitamins C, A, B1, B5, B6, E**

cyanidin-3-O-rutinoside



delphinidin-3-O-rutinoside



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EFFECTS

Boosts immune system (antiviral)

Reduce joint or muscle pain, stiffness, soreness & damage

Skin soother (psoriasis)

Increased heart blood flow

Improve eye function

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Indication

Chronic Venous Insufficiency



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Chapter 8

Tannins



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Tannins

- **Tannins** are a class of astringent, polyphenolic biomolecules that bind to and precipitate proteins and various other organic compounds including amino acids and alkaloids.
- The term *tannin* refers to the use of oak and other bark in tanning animal hides into leather.
- The tannin compounds are widely distributed in many species of plants, where they play a role in protection from predation (including as pesticides) and might help in regulating plant growth.

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Tannins

- Tannins commonly referred to as tannic acid are water-soluble polyphenols that are present in many plant foods.
- They have been reported to be responsible for decreases in feed intake, growth rate, feed efficiency, net metabolizable energy, and protein digestibility in experimental animals.
- Therefore, foods rich in tannins are considered to be of low nutritional value.

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Types of Tannins

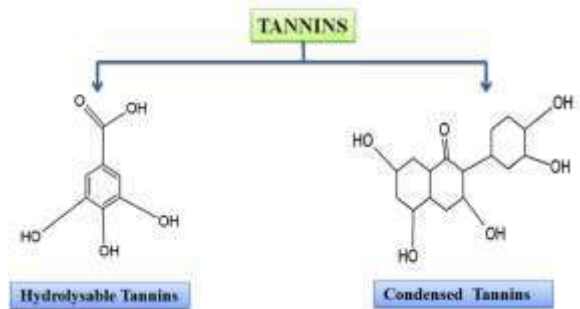
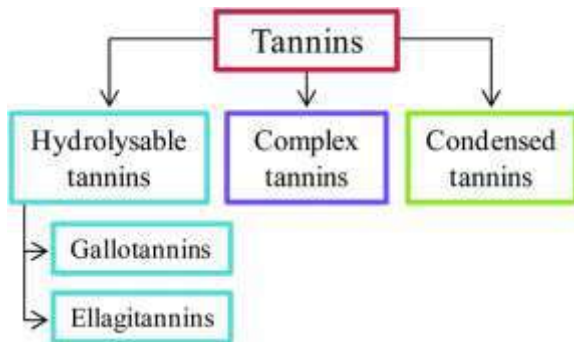
True Tannins

- **hydrolysable tannins:**
 - These may be hydrolyzed by acids or enzymes such as tannase
 - Gallic acid & Ellagic acid
 - Two principal types of hydrolysable tannins are gallitannins and ellagitannins
- **condensed tannins** (proanthocyanidins)
 - They are related to **flavonoid pigments** and **flavan-3-ol**
 - **Catechins** which also occur with the tannins and flavan-3,4-diols (**Lecoanthocyanidins**)
 - On treatment with acids or enzymes condensed tannins are converted into red insoluble compounds known as **Phlobaphenes**.
 - On dry distillation they yield **Catechol**

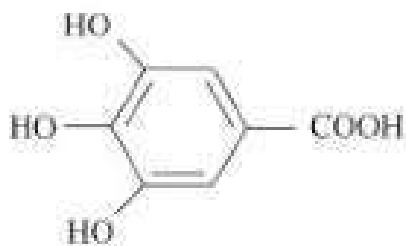
Pseudo- Tannins (polyphenolic compounds of lower molecular weight than true tannins).

186

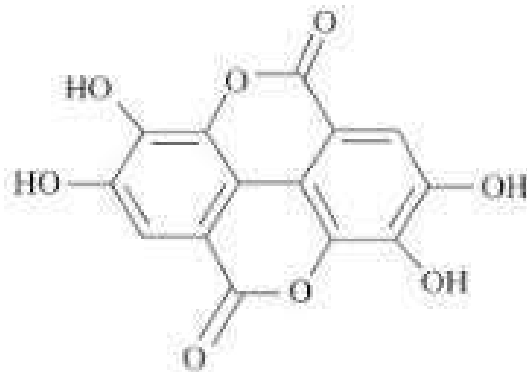
Types of tannins



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Gallic acid



Ellagic acid

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Biological activity of tannins

- Stop hemorrhage
- Treatment of burns
- Antidiarrheals
- Antidote in poisoning by heavy metals
- Antioxidant effect
- Antitumor / Carcinogenic
- Leather industry
- Food industry

189

Tannins Containing Drugs



190

Oak

- **Scientific name:**

Quercus infectoria

- **Family:** Fagaceae

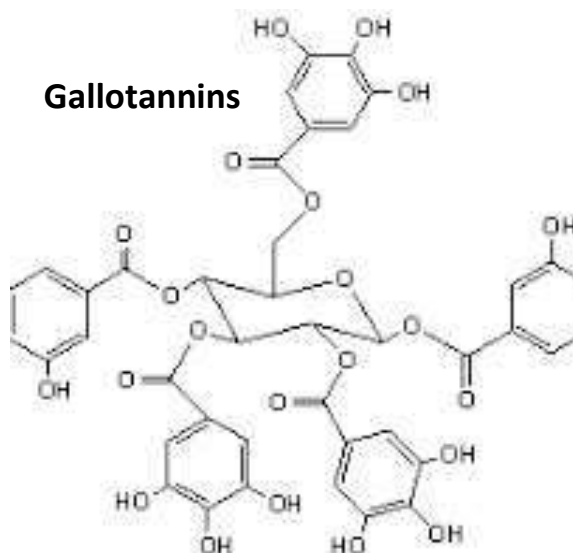
- **Parts used:** Fruits & Leaf



191

PHYTOCHEMICALS

- *Tannins (60 to 70%):* gallotannins, particularly hexa- and heptagalloyl-glucoses.
- *Phenol carboxylic acids:* gallic acid (3%), ellagic acid (2%).



192

Indication

- **Oak bark** is used as a tea for diarrhea, colds, fever, cough, and bronchitis; for stimulating appetite; and for improving digestion.
- **Oak bark** can be prepared as an enema, suppository, or sitz bath to treat **hemorrhoids** or as a douche to treat leukorrhea.
- Powdered, it can be used as a snuff to stop nosebleeds.
- They can be applied topically as a compress in the treatment of **hemorrhoids**

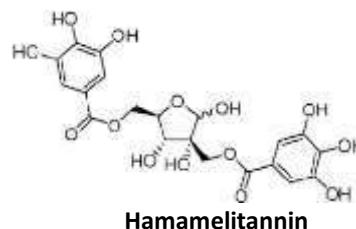
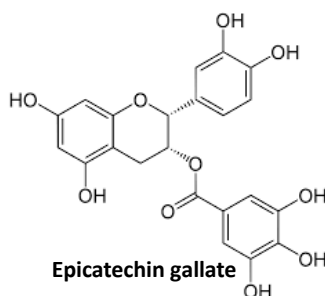
193

Witch Hazel

- **Scientific name:**
Hamamelis virginiana
- **Family:** Hamamelidaceae
- **Parts used:** bark, ; fresh and dried leaves
- **Traditional Medicine:**
astringent and anti-inflammatory remedy.



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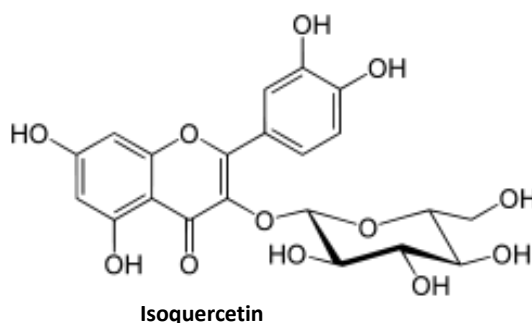
Phytochemicals Bark

- *Tannins (up to 12%)*: including hamamelitannin.
- *Catechins*: including (+) catechin, (+) gallo catechin, (-) epicatechin gallate, (-) epigallocatechin gallate.

195

Phytochemicals leaf

- *Tannins (5%)*: including hamamelitannin.
- *Catechins*: including (+) catechin, (+) gallo catechin, (-) epicatechin gallate, (-) epigallocatechin gallate.
- **Volatile oil (0.01 to 0.5%)**:
- *Flavonoids*: including quercitrin, isoquercetin



196

EFFECTS

- Witch Hazel bark & leaves is astringent, anti-inflammatory and locally hemostatic.

197

INDICATIONS

- Hemorrhoids
- Inflammation of the mouth and pharynx (leaf only)
- Inflammation of the skin
- Venous insufficiency
- Wounds and bumps



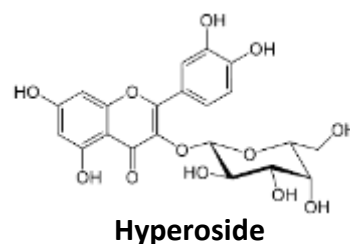
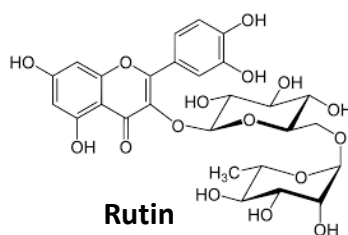
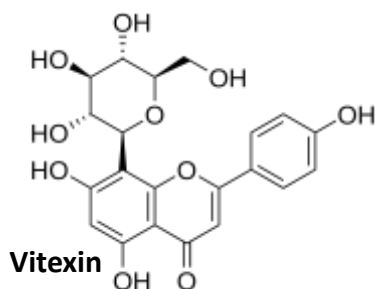
198

Hawthorn

- **Scientific name:** *Crataegus laevigata*
- **Family:** Rosacea
- **Traditional name:** الزعرور
- **Parts used:** white thorn flowers, leaves, fruit
- **Traditional Uses:** Chinese Medicine use of Hawthorne for fat or rich meal digestion and energy medicine for the heart.



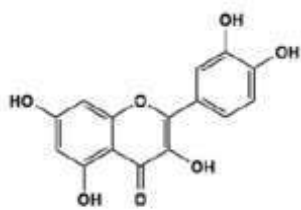
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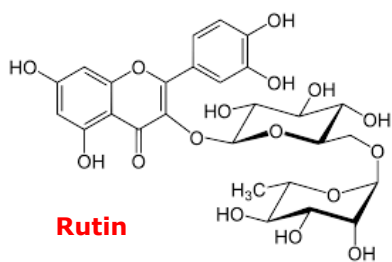
Phytochemicals

- Flavonoids (1.8%): hyperoside, rutin, vitexin
- Oligomeric **proanthocyanidins** (2.4%)
- Biogenic amines, including tyramine
- Triterpenes (0.6%): including oleanolic acid, ursolic acid, 2-alpha-hydroxy oleanolic acid (crataegolic acid)
- Fibers

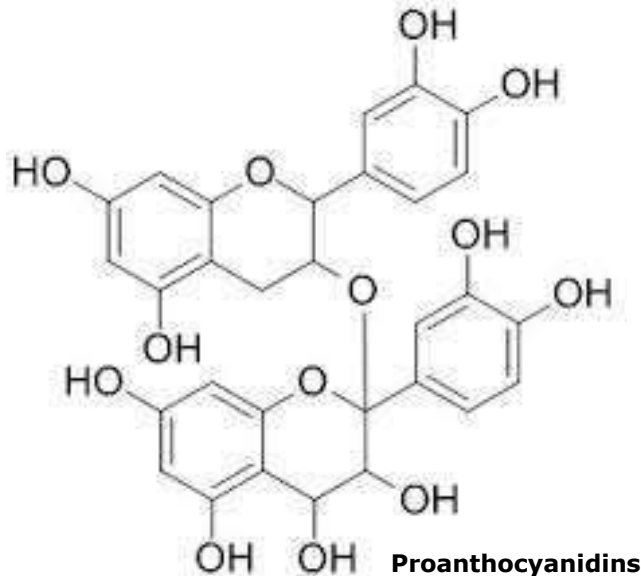
200



Quercetin



Rutin



Proanthocyanidins

201

EFFECT

- Factor “P”;
- Strong antioxidant agent;
- They cause an increase in coronary blood flow due to dilatory effects resulting in an improvement of myocardial blood flow, due to present of proanthocyanidins and flavonoids;
- Hawthorn has a very mild sedative effect, which may help decrease anxiety symptoms;
- Diuretic;
- Decrease blood fats;
- Aid digestion (fiber);
- Prevent hair loss (polyphenols).

202

Indication (Target patients)

Hypertensive

Obese as a
risk factor for
hypertension

Anxious

203

Blackberry

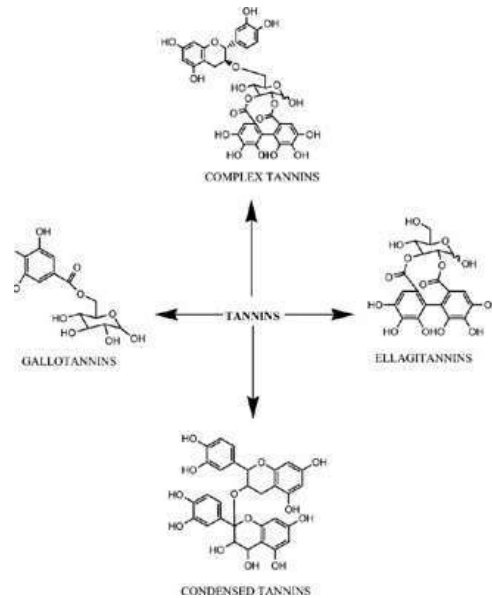
- **Scientific name:**
Rubus fruticosus
- **Family:** Rosacea
- **Parts used:** leaves,
roots and berries.



204

Phytochemicals

- **Tannins:**
Gallotannins & ellagitannins
- **Flavonoids**
- **Fibers**
- **Mineral:** K, Ca, P, Mg, Cu, Mn, Se
- **Vitamins:** A, C, K, Folate, Choline



205

Effects

- Strong anti-inflammatory & antioxidant agent
- Lower Cholesterol
- Prevent Gum Infections
- Support Strong Bones
- Promote Brain Health
- Antiallergic agent

206

Indication

Diarrhea

Itchy skin

Sinus congestion

Memory loss

Nutritive agent

207



208

Quinones-Overview

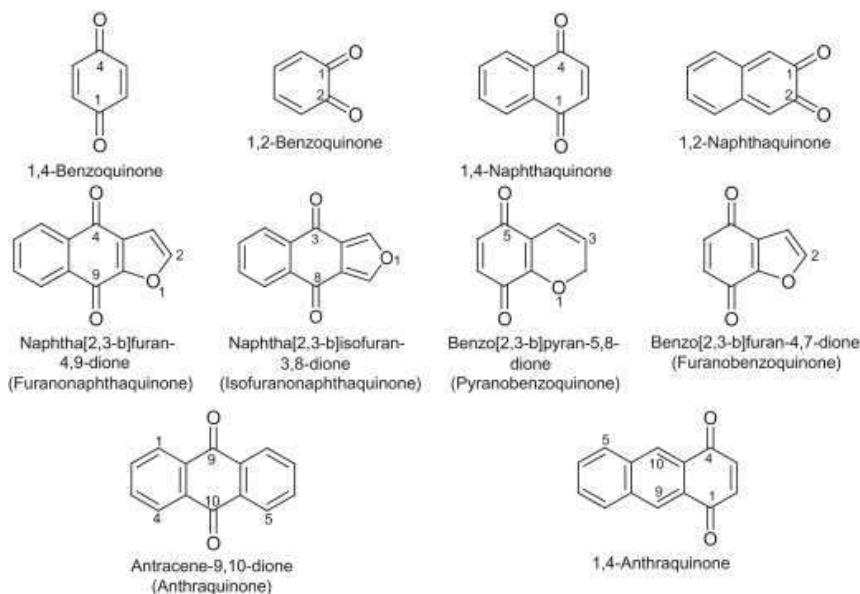
- Quinones are secondary metabolites isolated principally from plants and having an aromatic (hexacyclic saturated) di-one or di-ketone system.
- They are generally derived from the oxidation of hydroquinones.
- Naturally occurring quinones are widely distributed and include benzoquinones, naphthoquinones, anthraquinones, and polyquinones.

209

Types of Quinones

- **Benzoquinones:** These are groups of compounds containing two carbonyl groups on a saturated hexacyclic aromatic ring system (benzene ring), usually at *ortho* or *para* positions (monocyclic).
- **Naphthoquinones:** These occur to some extent in fungi and are extremely common in higher plants; they contain the naphthalene nucleus with two carbonyl groups on one nucleus, usually at the *ortho* or *para* position (bicyclic).
- **Anthraquinones:** These are common fungal metabolites and also occur in higher plants. They are compounds containing the anthracene nucleus with two carbonyl groups, usually on ring B at *para* positions (tricyclic).
- **Polyquinones:** These are dimers of the different types of quinones. Some polyquinones are of mixed origin. Inter- or intramolecular oxidative coupling can occur with formation of carbon-carbon or carbon-oxygen bonds.

210



211

Properties, Extraction, Separation & Characterization

- There are mild **oxidation reagents**, free quinones are practically **insoluble in water**,
- **Extracted by the common organic solvents**,
- Separation requires the common chromatographic techniques.
- **Glycosides extraction is achieved with water or with rather dilute hydro-alcoholic solutions.**
- Various color reactions can be used to characterize quinones. The main one is **Bornträger's reaction, in alkaline aqueous medium**, color which ranges, depending on the structure and the substitutes of the quinone, from orange-red to purplish-violet.

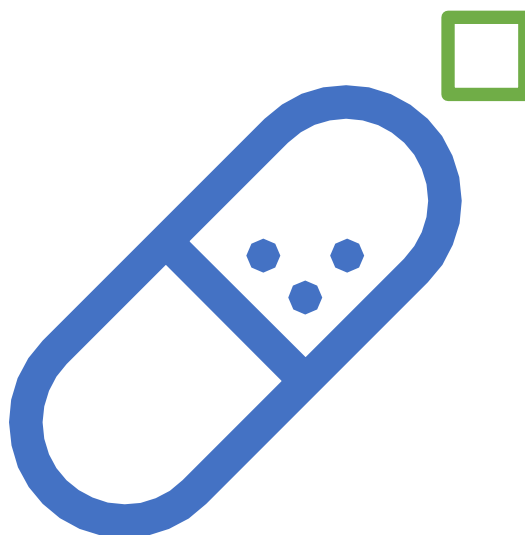
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Biological Properties

- Drugs containing 1,8 dihydroxyanthraquinone derivatives are laxative & purgative
- Strong urinary antiseptic
- Antibacterial and antifungal
- Synthetic hydroquinone has dermatological applications.

213

Quinone Containing Drugs



214

Senna

- **Scientific name:** *Cassia angustifolia*
- **Family:** Caesalpinaceae
- **Traditional name:**
سنا / سنامکا
- **Traditional Medicine:**
Laxative

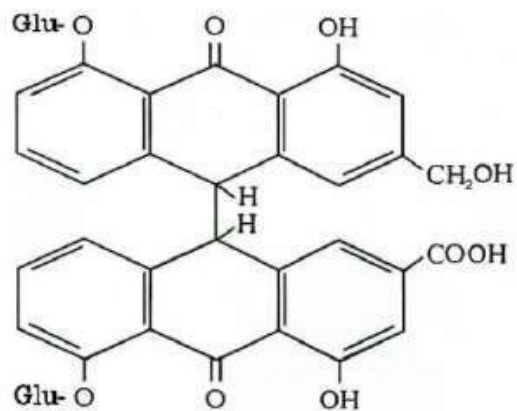
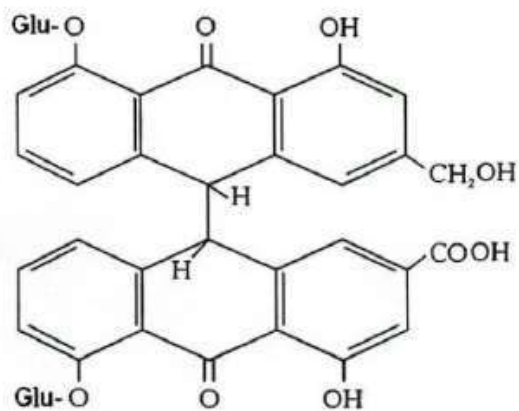


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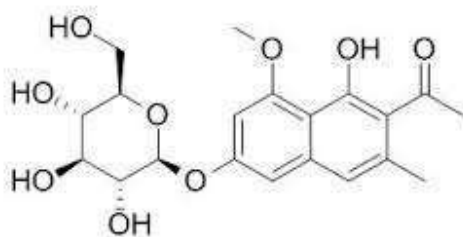
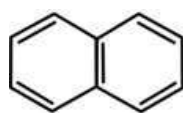
PHYTOCHEMICALS

- **Anthracene derivatives** (2.5-3.5%): chief components sennosides A, Al and B, as well as sennosides C and D.
- **Naphthacene derivatives:**
Tinnevellin-6-glucosides
- **Naphthalene derivatives**
- **Flavonoids**
- Tannins
- Reducing sugars
- Saponin
- Cardiac glycosides
- Steroids
- **Alkaloids**

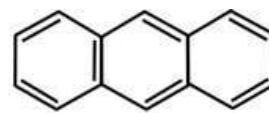
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**Sennoside A****Sennoside B**

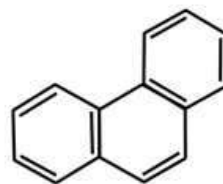
217

**Tinnevellin-6-glucosides**

naphthalene



anthracene



phenanthrene

218

EFFECTS

- The laxative effect is due to the action of sennosides and their active metabolite, rhein anthrone, in the colon. The laxative effect is realized by inhibition of water and electrolyte absorption from the large intestine, which increases the volume and pressure of the intestinal contents. This will stimulate colon motility resulting in propulsive contractions.
- In addition, stimulation of active chloride secretion increases water and electrolyte content of the intestine.

219



Contraindication

- **Weight loss**
- **Children**
- **Geriatrics**
- **Pregnant & nursing woman**
- **Intestinal obstruction,**
- **Acute inflammatory intestinal diseases**
- **Appendicitis**

220

Indication



Acute
constipation



Evacuation of the bowel
prior to diagnostic tests of
the gastrointestinal and
colorectal area.

221

Herb-Drug interaction

Digitalis Glycosides — with prolonged use or abuse of Senna, loss of potassium may potentiate digitalis toxicity.

Estrogen — the serum level of estrogen is decreased when given concomitantly with Senna due to the effect of intestinal transit on the absorption of estrogens.

Indomethacin:
decreases the
therapeutic effect of
the Senna

Nifedipine (calcium channel blocker) — Therapeutic effects induced by rhein anthrone also involve the calcium channel which can be blocked by nifedipine, but not verapamil (calcium channel blocker also).

222

Aloe

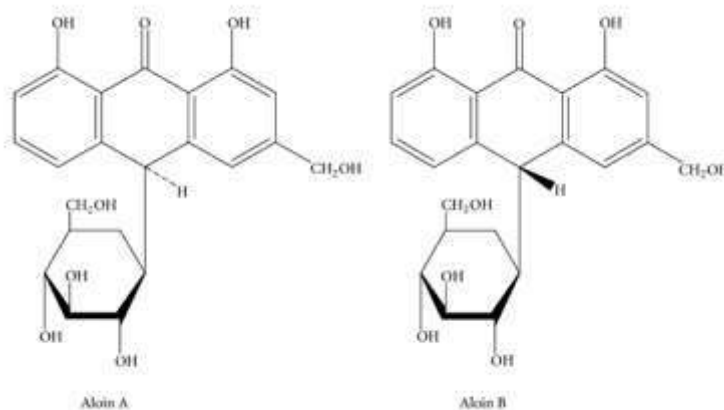
- **Scientific name:**
Aloe vera
- **Family:** Liliaceae
- **Part used:** dried juice of the leaves.
- **Traditional Medicine:**
skin healer



223

Phytochemicals

- Anthraquinone derivatives, which are aloe-emodin-anthrone-10-C-glycosides,
- **Aloin which is a mixture of aloin A and B.**



224

Effect & indication

- Laxative
- Antibacterial
- Antiviral
- Stomach infection
- Skin healing



225

Saint John's Wort

- **Scientific name:**
Hypericum perforatum
- **Family:** Clusiaceae
- **Traditional name:**
حشيشة القديس جون
- **Parts used:**
Buds and flowers

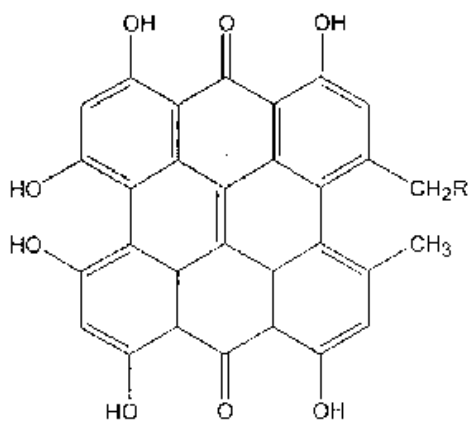


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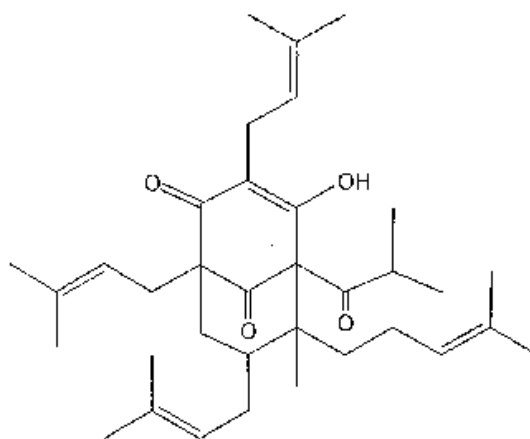
Phytochemicals

- **Acylphloroglucinols:** hyperforin (the active principle) with small quantities of **hyperforin**.
- **Anthracene derivatives:** favoring naphthodianthrone, especially **hypericin**.
- **Xanthenes:** 1, 3, 6, 7-tetrahydroxy-xanthone
- **Procyanidines**
- **Caffeic acid derivatives:** **chlorogenic acid**.
- **Flavonoids:** **Quercetin**
- **Volatile oil**

227



	R
Hypericin	H
Pseudohypericin	OH



Hyperforin

228

Effects / Health benefits

- **Hypericum** has weak effects on catechol-O-methyl transferase, an enzyme that is responsible for the breakdown of chemicals in the brain including serotonin, norepinephrine, and dopamine.
- Helps to fight hot flashes.
- Help to treat premenstrual syndrome (PMS) and fibromyalgia
- Treat anxiety.
- Treats depression.
- Helps to fight off viral and bacterial infections.

229

INDICATIONS / Target patients



Postmenopausal



Anxiety



Swings moods

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Chapter 10

Orcinols & Phloroglucinols



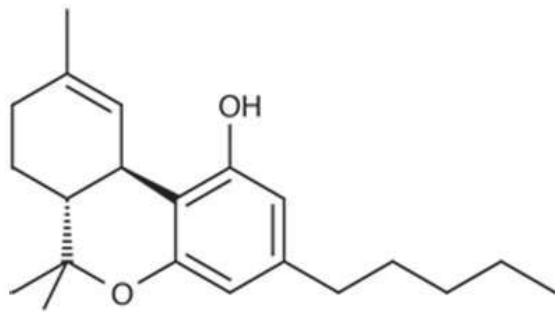
231

Cannabis / hashish / Marijuana

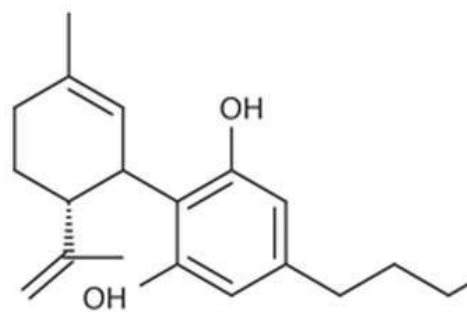
- **Scientific name:**
Cannabis sativa
- **Family:** Cannabaceae
- **Parts used:**
 - Twig tips of the female flowers
 - Leaves
 - Seeds/oil
- **Traditional name:**
الحشيش / ماريجوana



232



Delta-9-tetrahydrocannabinol (THC)



Cannabidiol

Phytochemicals:

- **Cannabinoids:** chief active agent 9-tetrahydrocannabinol (9-THC = 1-THC)
- **Flavonoids:** including canniflavone-1, canniflavone-2.
- **Volatile oil:** beta-caryophyllenes, humules

233

EFFECT

- **Psychotropic action:** The symptoms are mood swings, reduction in drive, inability to think clearly, confusion, lack of concentration, impairment of short-term memory and perception of time.
- Complex tasks become more difficult, the capacity to understand or empathize is impaired. Negative reactions such as anxiety, panic and psychosis can occur.

234

Cannabinoids Receptors

- There are currently two known types of Cannabinoids receptors, **CB1 and CB2**.
- **CB1** receptors are found primarily in the **brain**, CB1 receptors appear to be *responsible for the euphoric and anticonvulsive* effects of cannabis.
- **CB2** receptors are almost exclusively found in the **immune system**, with the greatest density in the spleen.
- **CB2** receptors appear to be **responsible for the anti-inflammatory** and possible other therapeutic effects of cannabis.
- **THC has a greater affinity for the CB1 receptor than for the CB2 receptors. Its effects are perceived to be more cerebral.**

235

Cannabis tolerance

- Tolerance is the capacity to endure continued subjection to a drug without adverse reaction.
- Tolerance at all levels of complexity in the brain involves "learning" in the sense of the acquisition of compensatory adaptations to the consequences of the presence of a drug-produced disturbance in function.
- Cognitive function showed the highest degree of tolerance among the various domains examined by cannabis tolerance studies.

236

LD50

- LD50 the amount of a toxic agent, that is sufficient to kill 50 percent of a population of animals usually within a certain time.
- The intragastric LD50 with the emulsion was 800 mg/kg (female rats) and with the sesame oil formulation, 1270 mg/kg (male rats).
- The I.V LD50 was 36–40 mg/kg, similar to the inhalation dose when the latter was corrected for Δ^9 -THC losses in the rodent nasal passages.

237

Cannabis seed / oil

- Nutritive value:
 - Protein
 - Omega 3
 - Fiber
 - Minerals: Mg, P, K
 - Vitamins: B1, B3, B6, Folate



238



239



240