PLANT PHENOLS

Very wide group of compounds, which cannot be defined in simple way.

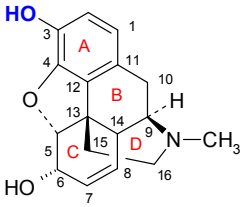
Basic structural characteristic is a presence of at least one aromatic ring substituted at least one hydroxyl group (free or bonded – representing other functionality (for example ether, ester. Or glycoside).

Based on this definition, this group of compound can include substances structurally very different and much more variable from the biological activity and phytochemical classification point of view, for example:

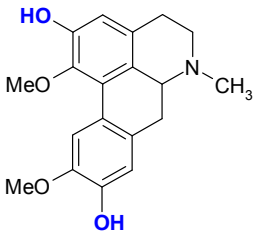
- alkaloids: morphine, boldine,
- terpenoids: thymol, gossypol, carnosol,
- tannins

Therefore, it is necessary to know biosynthesis, precursors, and to well determine borders of unique phytochemical groups.

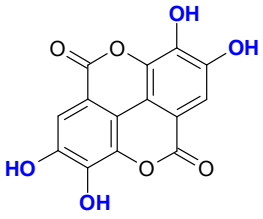
PLANT PHENOLS



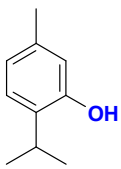
Morphine



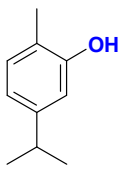
Boldine



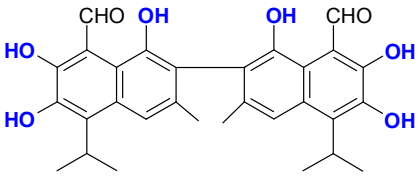
Ellagic acid



Thymol



Carvacrol



Gossypol

PLANT PHENOLS

Plants and microorganism only* are able to biosynthetise aromatic core. Animals are almost ever dependent on:

- intake of aromatic compounds via nutrition
- symbiosis, which brings possibility to produce necessary metabolites containing aromatic structural features (amino acids, vitamins, pigments, toxins)

* Several exceptions exist, for example biosynthesis of estrogene

PLANT PHENOLS

Structural difference of plant phenols is based on two different biosynthetic pathways

- **shikimate**
- **acetate**

Structural difference is increased by common combination of **shikimic acid** and **acetate** pathway, for example flavonoids, stilbenes, pyrones, and xanthones.

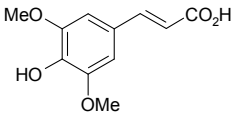
Sometimes the third synthone enters biosynthesis – a **mevalonate**

- **shikimate + mevalonate**: furanocoumarins, pyranocoumarins, some quinones
- **acetate + mevalonate**: cannabinoids, hop bitter acids

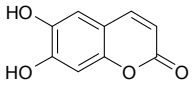
Sometimes all three precursors share one biosynthetic product: prenylflavonoids, rotenoids

PHENOLS FORMATED *VIA* SHIKIMIC AND ACETATE PATHWAYS

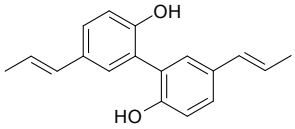
Shikimates



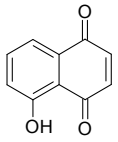
sinapic acid
phenylpropanoic acid



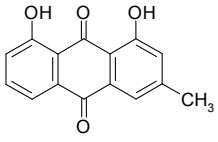
aesculetine
coumarine



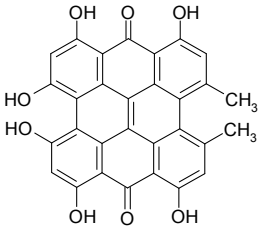
magnoliol
neolignane



juglone
naphtoquinone



chrysophanol
anthraquinone

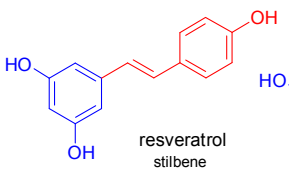


hypericine
naphtodianthrone

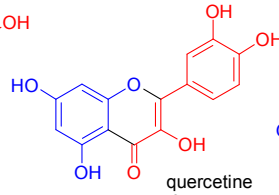
Acetates

PHENOLS FORMED VIA COMBINATION OF METABOLIC PATHWAYS

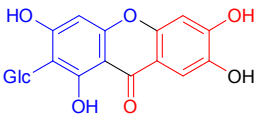
Shikimates + Acetates



resveratrol
stilbene

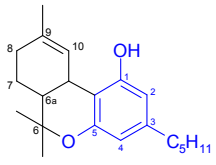


quercetine
flavonol



mangiferine
xanthone

Acetate + Mevalonate



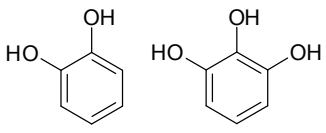
THC

NATURAL MEDICINES DERIVED FROM SHIKIMIC ACID

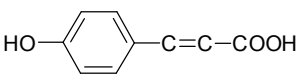
- Shikimic acid is precursor of majority of compounds possessing aromatic ring
  - Substantially lower amount of aromatics is formed via acetate pathways
- Origin of aromate - according to the position of hydroxyl groups:
  - Shikimic acid derived aromatic compounds – OH at position 1,2 (*ortho*, catechol), or 1,2,3 (pyrogallol). If there is one phenolic hydroxyl only, it is at *para* position.
  - Acetate derived aromatic compounds – OH directed into meta- position, for example derivatives of resorcinol and phloroglucine

LOCALIZATION OF HYDROXYL GROUPS AT PHENOLICS

- SHIKIMIC ACID ORIGIN

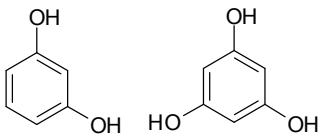


catechol pyrogallol



p-coumaric acid

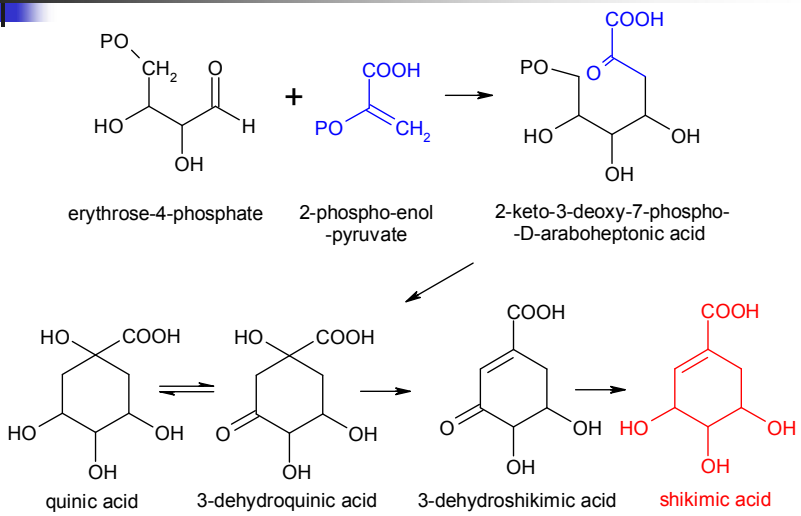
- ACETATE ORIGIN



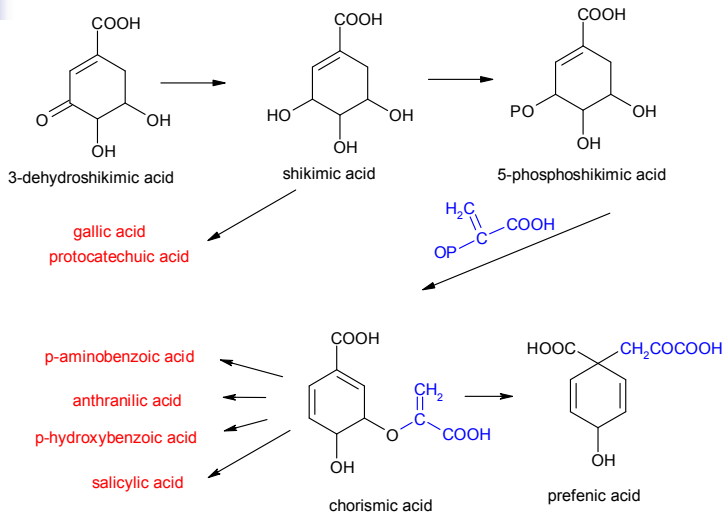
resorcinol phloroglucinol

.....$CH_2COCH_2COCH_2CO$.....

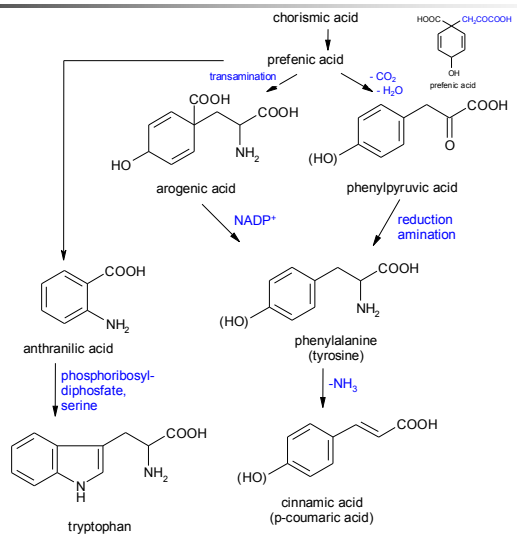
FORMATION OF SHIKIMIC ACID



SHIKIMATE DERIVATIVES

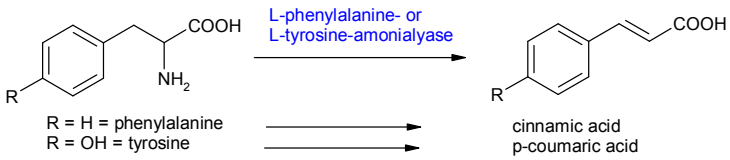


SHIKIMATE DERIVATIVES



FORMATION OF CINNAMIC ACID FROM PHENYLALANINE

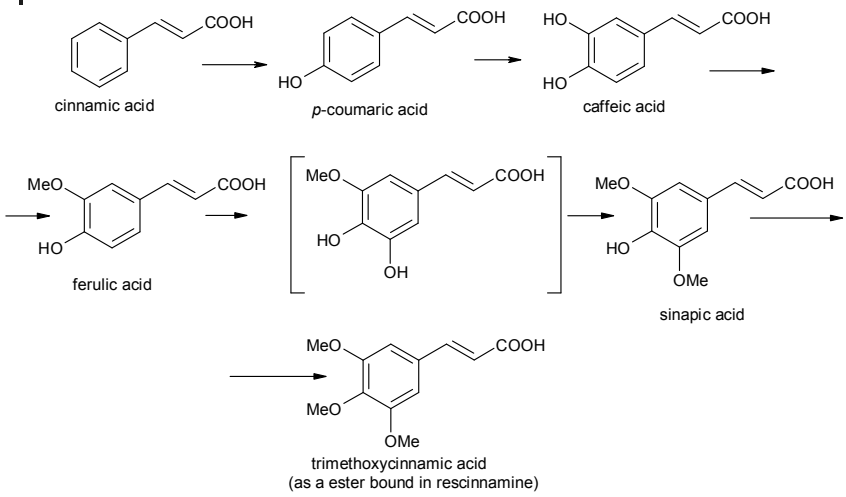
Phenylalanine → proteins
alkaloids
cinnamic acid and its derivatives



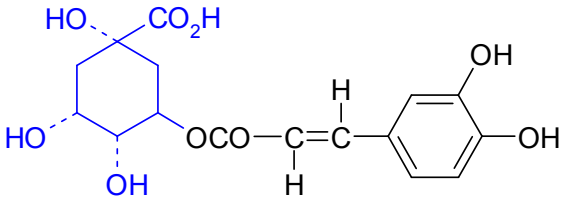
L-phenylalanine-amonia-lyase generally widespread
L-tyrosine-amonia-lyase exclusivelly in grass (Graminae)

stereospecific deamination of natural L-acids

CINNAMIC ACID AND ITS DERIVATIVES



CAFFEIC ACID ESTERS

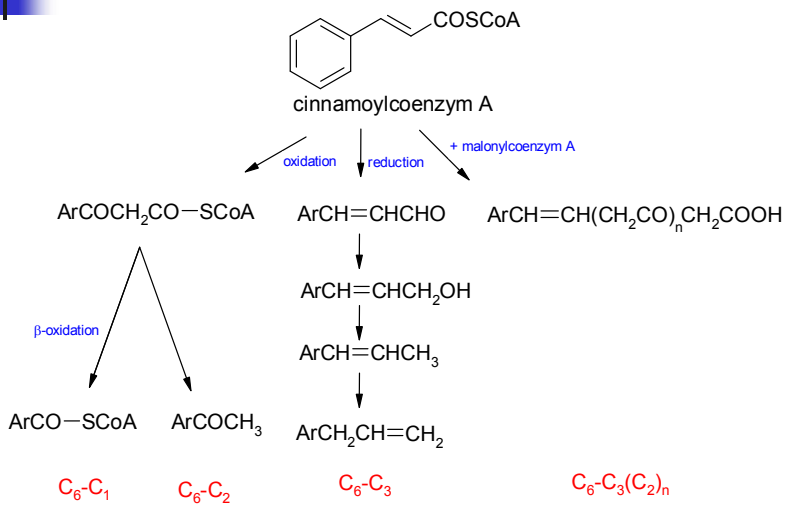


chlorogenic acid

3-O-caffeoylquinic acid

baktericidal effects, cumulation in the place of wound of plant

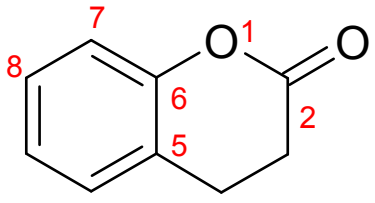
TRANSFORMATION OF CINNAMIC ACID



COUMARINS AND FURANOCOUMARINS

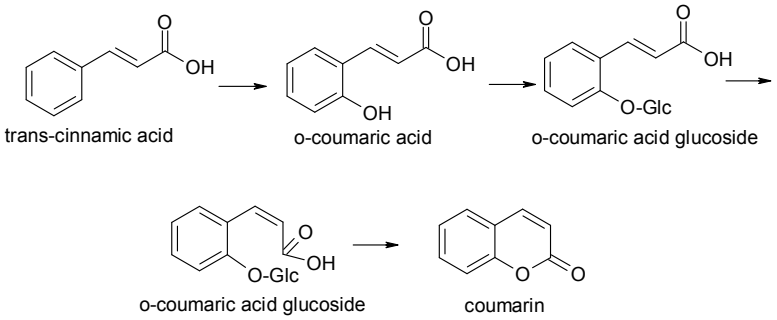
Derivatives of 5,6-benzo-2-pyrone (α-chromone)

- different in substituents at benzene ring (OH, OCH_3, CH_3)

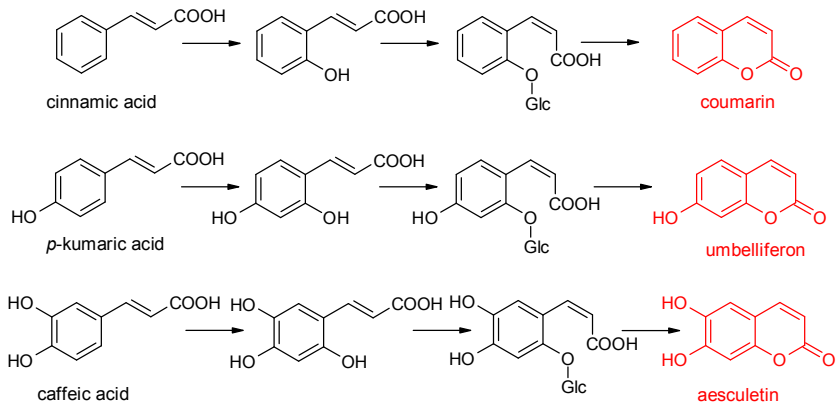


5,6-benzo-2-pyrone

COUMARINS AND FURANOCOUMARINS
Biosynthsis



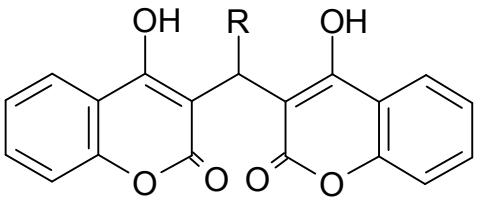
COUMARINS
Lactones of o-hydroxycinnamic acid, 2-benzopyrone derivatives (Fabaceae, Poaceae); characteristic odour)



DICOUMAROL

zapaření sena, microorganisms → compound with anticoagulant effect

Melilotus officinalis



R = H = dicoumarol

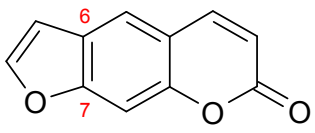
R = $COOC_2H_5$ = pelentan

FURANOCOUMARINS

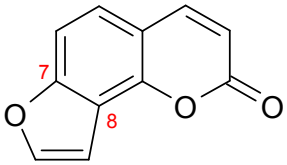
Furanocoumarins contain additional furane ring, which is derived from metabolism of 3-methyl-3-butenyldiphosphate.

Furanocoumarins linear – psoralen (furane ring connected at position 6 and 7)

angular – angelicin (furane ring connected at position 7 and 8)



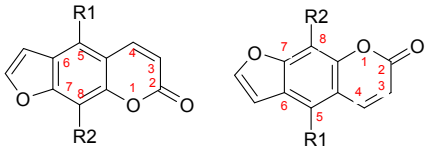
psoralen



angelicin

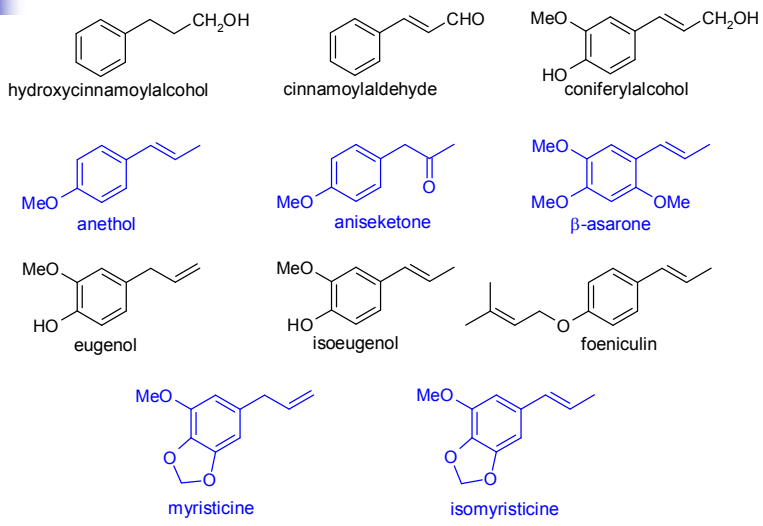
PSORALENES

Occurrence
Rutaceae: *Citrus bergamia*
Apiaceae: *Apium graveolens*, *Ammi majus*
Fabaceae: *Psoralea corylifolia*
Moraceae: *Ficus*
Utilization: photochemotherapy of vitiligo (pigmentation disorder), psoriasis

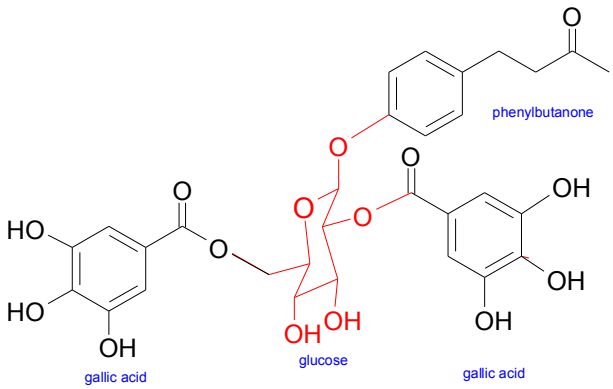


	R1	R2
Psoralene	H	H
Bergaptene	OCH_3	H
Xanthotoxin	H	OCH_3
Imperatorin	H	$=CH_2\text{-}CH=(CH_3)_2$

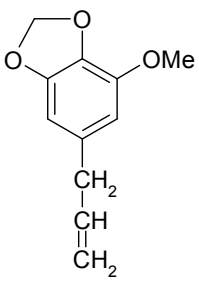
PHENYLPROPANOIDS
different degree of oxidation of three carbon side chain



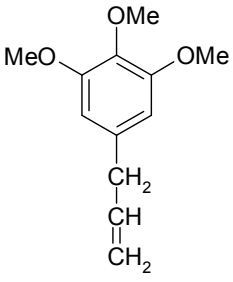
LINDLEIYN



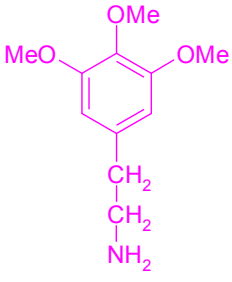
Myristicae semen – content compounds



Myristicine

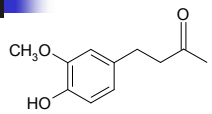


Elemicine

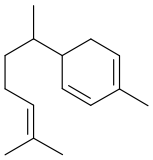


Meskaline, *Anhalonium*

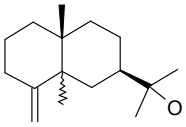
Zingiberis rhizoma – content compounds



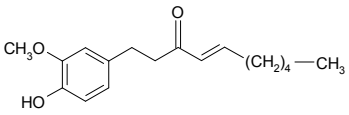
zingerone



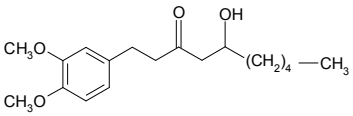
Zingiberene



Zingiberol

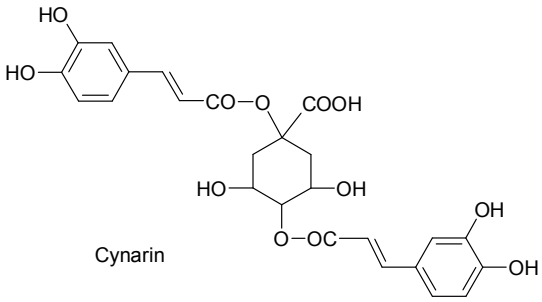


shogaol

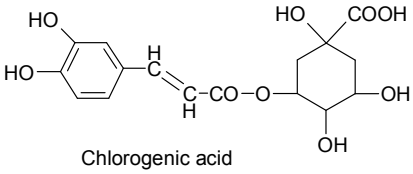


methylgingerol

Cynarae radix, folium – content compounds

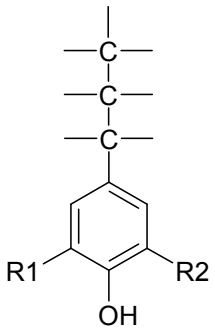


Cynarin



Chlorogenic acid

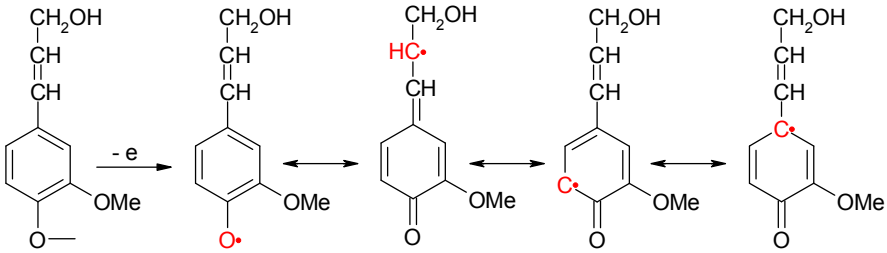
LIGNINE AND LIGNANS



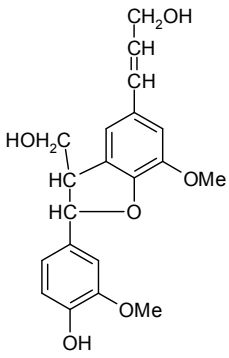
R1 = R2 -H, -OH, -OCH_3

- Wide spread phenylpropanopids
- Lignin – the most widespread polymeric phenolic compound of plant origin
- Formed by oxidative dimerisation o polymerisation of C6-C3 units
- Basic monomers show always *p*-hydroxyphenylpropanoid structure
  - *p*-coumarylalcohol
  - Coniferylalcohol
  - sinapylalcohol

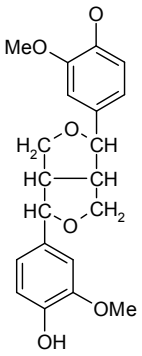
POLYMERISATION OF CONIFERYLALCOHOL
RADICAL MECHANISM – FORMATION OF MESOMERIC RADICALS



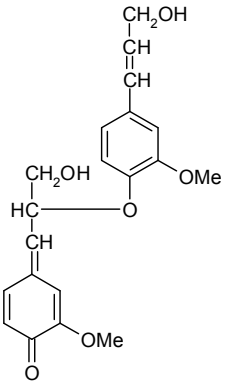
FORMATION OF DILIGNOLS FROM MESOMERIC RADICALS



dehydrodiconyferylalcohol
Rb + Rc

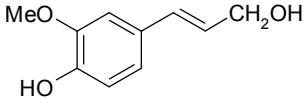


DL-pinoresinol
Rb + Rb

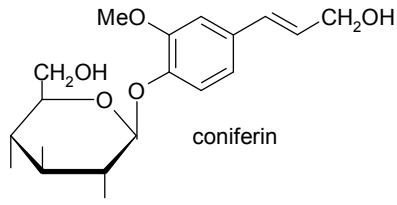


quinonmetide
Ra + Rb

CONIFERYLALCOHOL – CONIFERINE



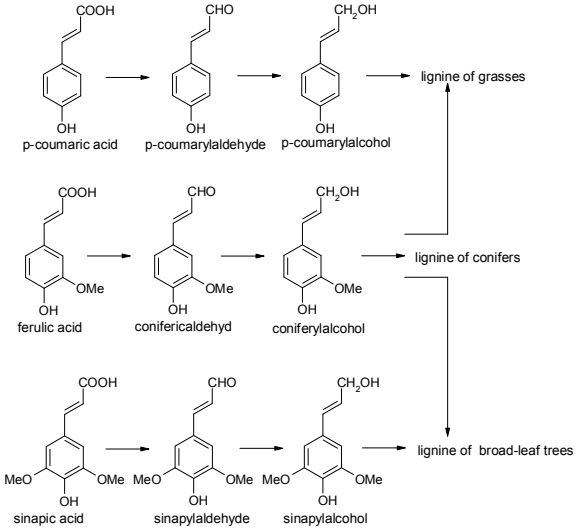
coniferylalcohol



coniferin

(β-D-glucopyranosyl)

LIGNIN AND ITS TYPES

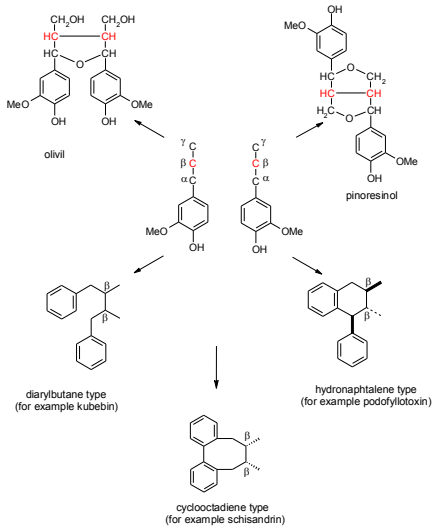


UTILIZATION OF LIGNINE

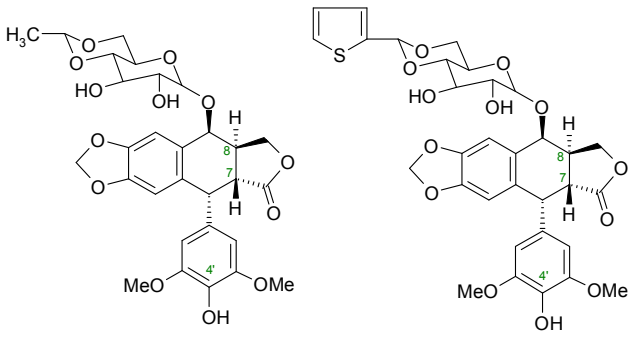
- listed in group of fibers, but is not used as dietary fiber individually
- material for synthesis of vanillin and syringaldehyde
- filler for phenolic plastics
- stiffening (especially of rubber for outsoles)
- additive for greases
- stabilizer of asphalt emulsions
- for precipitation of proteins

LIGNANS

formed by connection of two C6-C3 compounds (phenylpropanes) via β-carbon atom
(oxidative dimers of coniferylalcohol)



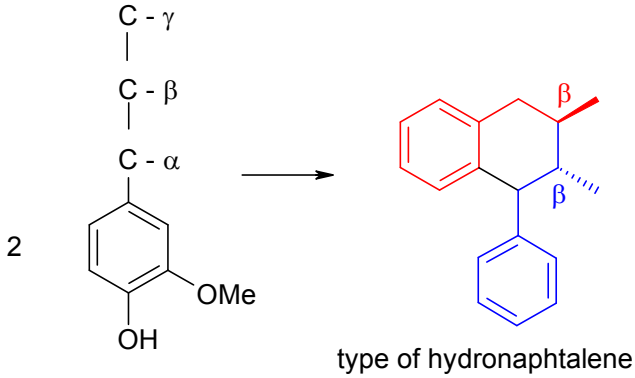
Structure of Etoposide and Teniposide



Etoposide, Vepesid

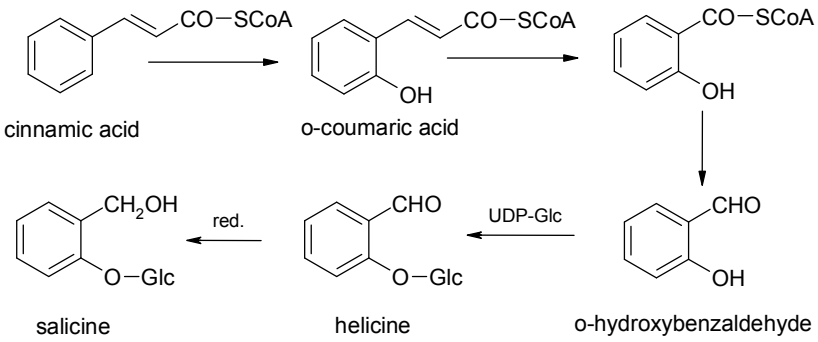
Teniposide

Biosynthesis of podophylline lignans



type of hydronaphtalene

BIOSYNTHESIS OF SALICINE



cinnamic acid

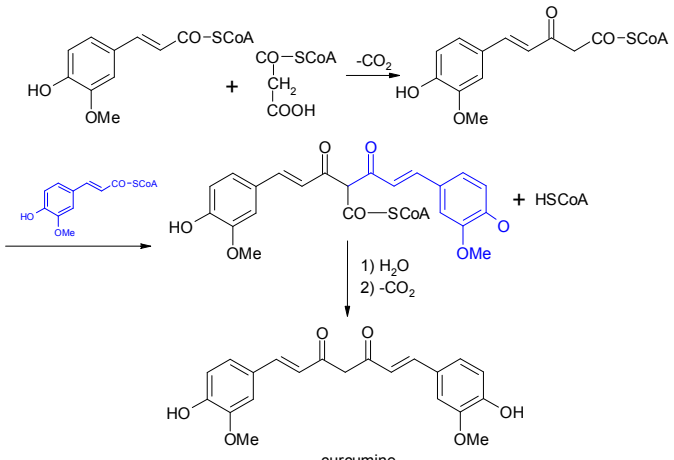
o-coumaric acid

o-hydroxybenzaldehyde

salicine

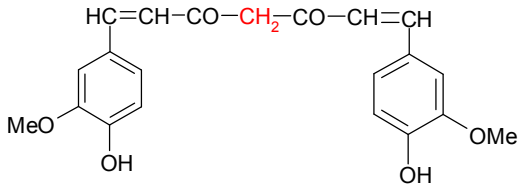
helicine

TEMPORARY FORMATION OF C6-C3-C2 UNIT AT CURCUMINE

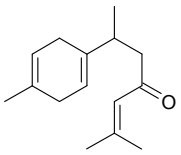


curcumine
Curcuma tinctoria (Zingiberaceae)

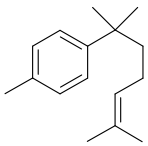
Curcumae xanthorrhizae rhizoma – content compounds



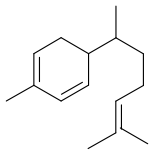
Curcumine



Turmerone

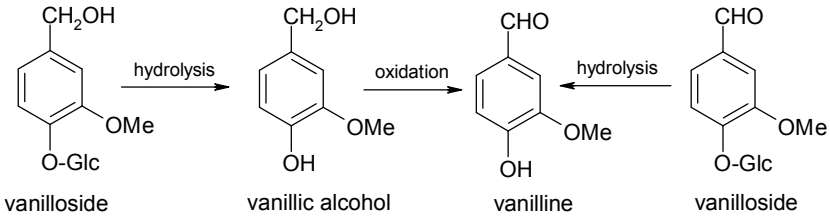


Curcumene

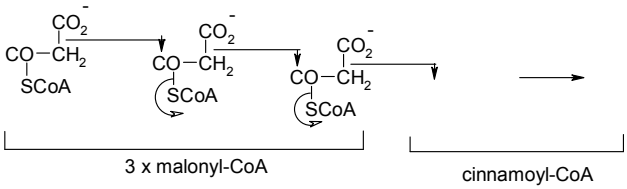


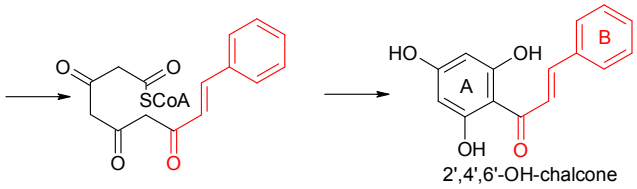
Zingiberene

VANILLAE FRUCTUS

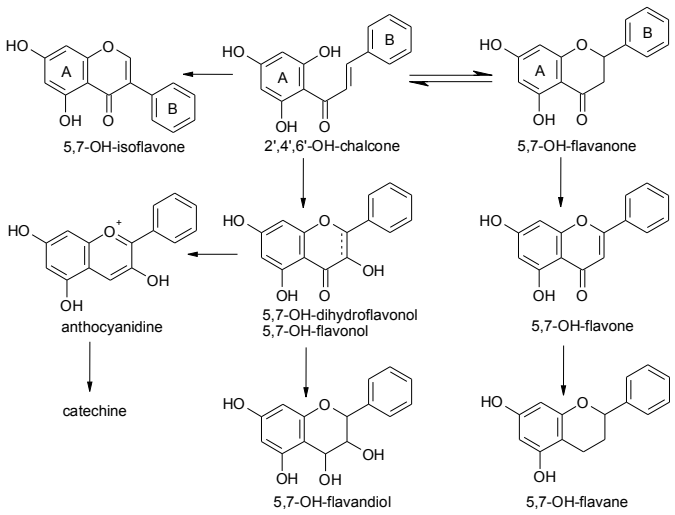


FLAVONOIDS
1st level – formation of chalcone





FLAVONOIDS



VENOPHARMACS – DRUGS FOR TREATMENT OF VENOUS DISEASES

RUTOSIDE

SOPHORAE FLOS

Sophora japonica L. – Chinese Scholar Tree or Japanese Pagoda Tree (Fabaceae).

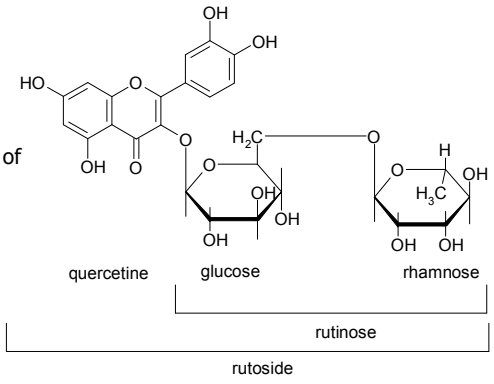
Producents: China, Japan

Drug – not-untrolled flower buds with content of up to 20 % rutoside

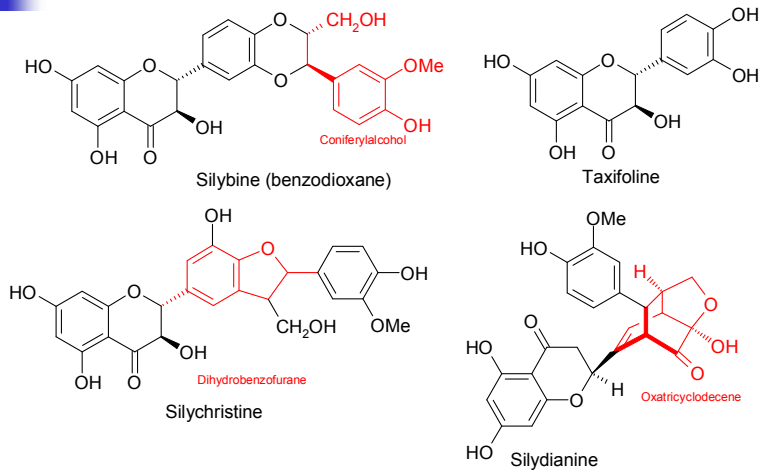
Semi-synthetic derivate tris-β-hydroxy-ethyl = troxerutine, CILKANOL

FAGOPYRI HERBA

Fagopyrum – buckwheat (Polygonaceae)
Drug contains 1-2 % of rutoside, isolation difficult



Silybi mariani fructus – content compounds
Silybum marianum – milk thistle



TANNINS

Characterization

- Heterogeneous organic polyphenols of high molecular weight
- Amorphous compounds formatting in water colloid acid solutions of astringent taste
- With protein format insoluble substances → limiting therapeutic usage; leather manufacturing industry – tan the furs (skin) to leathers
- Almost insoluble substances formatting with heavy metals and alklaoids (with exception of morphine, atropine, cocaine), with salts of iron produce inks
- Ability ot agglutinate erythrocytes
- Oxidation, condensation and polymerization to non-effective phlobaphenes
- On the certain stage of development plant defense against microorganisms

Occurrence:

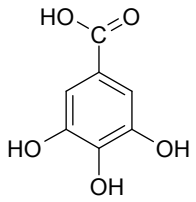
Dicotyledonous plant with exception of Papaveraceae and Brassicaceae
Rarely monocotyledonous plants

CLASSIFICATION OF TANNINS ACCORDING TO THE STRUCTURE

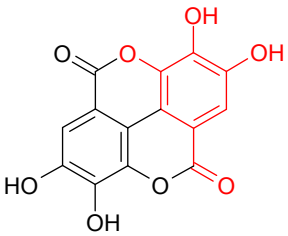
TANNINS

- HYDROLYZABLE (glycosidal)
  - GALLOTANINS — Gallic acid + sugar
  - ELLAGITANINS — Ellagic acid + sugar
- CONDENSED
  - CATECHINS — hydrogenated flavonols resp. catechins

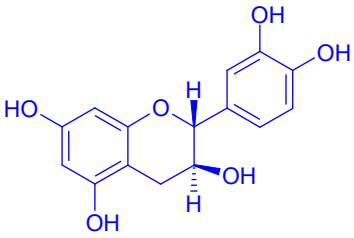
BASIC BUILDING BLOCKS OF TANNINS



Gallic acid



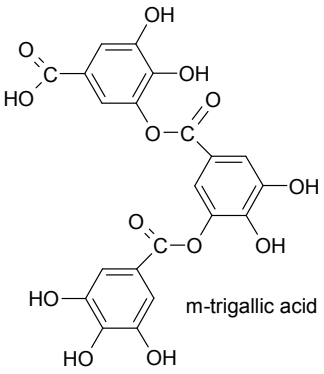
Ellagic acid



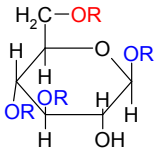
Catechine

EXAMPLE OF DEPSIDIC BOND

ESTER BOND BETWEEN CARBOXYL GROUP OF ONE MOLECULE AND HYDROXYL OF THE SECOND MOLECULE OF THE SAME SUBSTANCE



m-trigallic acid

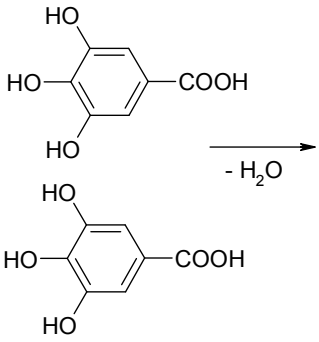


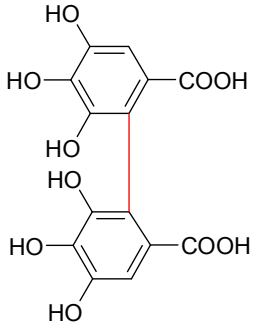
Tannine

R = gallic acid

R = m-trigallic acid

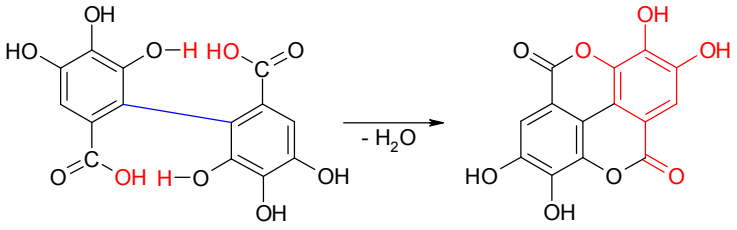
CONNECTION OF GALLIC ACID MOLECULES WITH C-C BOND





Hexahydroxydiphenic acid
(dimer of gallic acid)

FORMATION OF ELLAGIC ACID



Hexahydroxydiphenic acid

Ellagic acid

CONDENSED TANNINS (CATECHINS)

Basic building block is catechine and its isomers, further blocks are hydroxyflavandiols (leucoanthocyanidins), hydroxyderivatives of cinnamic acid.

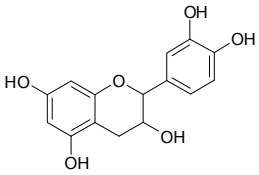
Majority of condensed tannins is poduced by „postmortal" condensation with influence of enzymes.

Catechins condense in weakly acidic environment of cytosol into true in water soluble amorphous tannins. This is observed during the postmortal procedures when wood is stored. Condensation can proceed into dark in water insoluble phlobaphenes.

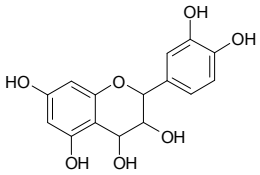
Enzymatic transformation of catechins by polyphenoloxidases (for example red pigmentation of cacao beans).

Some catechine tannins are in form of esters of catechine with gallic acid (for example epicatechine-3-gallate in *Theae folium*).

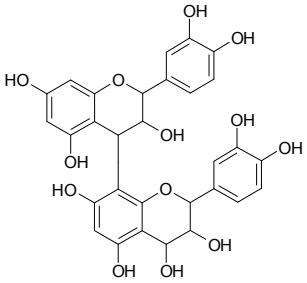
CONDENSED TANNINS (CATECHINS)



Catechine (3-flavanol)



Leucoanthocyanidins (3,4-flavandiol)



Dimeric condensation product
as the first step of tannins formation
from flavandiol and catechine

DRUGS WITH CONTENT OF TANNINS

Tanninum – Tannine ČL 2005 Quercus infectoria, gall oak (Fagaceae)

Hamamelidis folium – Vilínový list ČL 2005 Hamamelis virginiana, witch hazel (Hamamelidaceae)

Quercus cortex – Dubová kůra ČL 2005 Quercus robur, English oak, Q. petraea, sessile oak (Fagaceae)

Agrimoniae herba – Řepíková nať ČL 2005 Agrimonia eupatoria, agrimony (Rosaceae)

Myrtilli fructus recens – fresh blueberry ČL 2005

Myrtilli fructus siccus – dried blueberry ČL 2005 Vaccinium myrtillus, (Vacciniaceae)

Tormentillae rhizoma – ČL 2005 Potentilla erecta (P. tormentilla), tormentil (Rosaceae)

FURTHER DRUGS WITH TANNIN CONTENT

Juglandis folium – *Juglans regia*, hasel nut (Juglandaceae)

Bistortae rhizoma – *Polygonum bistorta*, bistort (Polygonaceae)

Rubi fruticosi folium – *Rubus fruticosus*, blackberry (Rosaceae)

Catechu – Katechu (*Acacia catechu* – mimosa catechu, Mimosaceae)
Solidified extract of wood of Indian/African tree, containing up to 50 % of catechine tannins. Pwerfull astringent.

Kino – Kino (*Pterocarpus marsupium* – indian kino tree, Fabaceae)
Solidified juice flowing from stem after wounding, tree of eastern India and Sri Lanka, containing up to 85 % of catechine tannins.