ANTHOCYANINS

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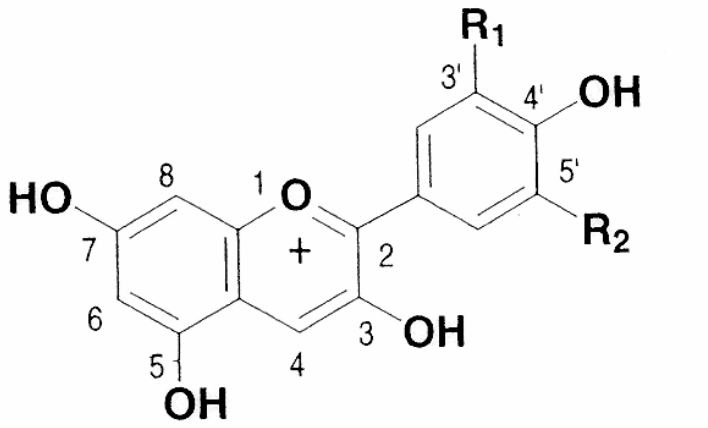
Anthocyanins

- Anthocyanins = antocyan glycosides, Anthocyanidins = aglycons

Aglycons

- Anthocyanidins occur in acidic medium as cations.
- They are always hydroxylated at C-3 and, most often, penta(3,5,7,3',4') or hexasubstituted (3,5,7,3',4',5') by hydroxyl groups, or methoxyl groups, or both.
- The most common aglycones (they are virtually ubiquitous) are pelargonidin (scarlet), cyanidin (crimson), and deiphinidin (purple).



Structures of the chief anthocyanidins

$R_1 = R_2 = H$: *Pelargonidin*

$R_1 = OH$, $R_2 = H$: *Cyanidin*

$R_1 = OCH_3$, $R_2 = H$: *Peonidin*

$R_1 = R_2 = OH$: *Delphinidin*

$R_1 = OCH_3$, $R_2 = OH$: *Petunidin*

$R_1 = R_2 = CH_3$: *Malvidin*

Anthocyanins

Glycosides

•At **least one hydroxyl group** at C-5, C-7, or C-4' **must remain free** to allow the formation of the colored quinonoid structures.

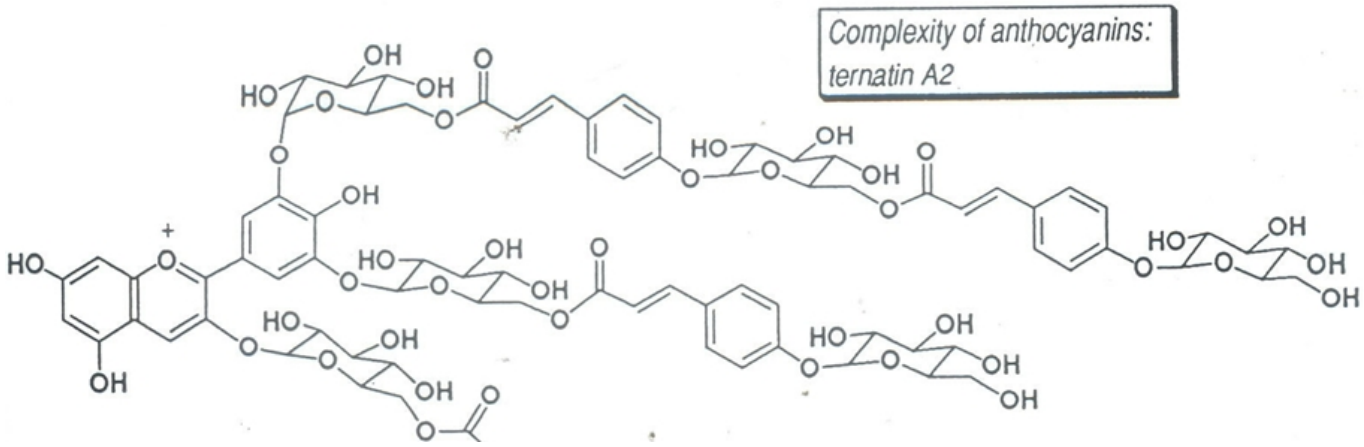
•(In contrast, anthocyanidins are unstable because their 3-hydroxylgroup makes the flavylium ion very reactive.)

•In fact, the **3-hydroxyl group is always linked to a sugar** (very often glucose) to form a stable and water soluble anthocyanin.

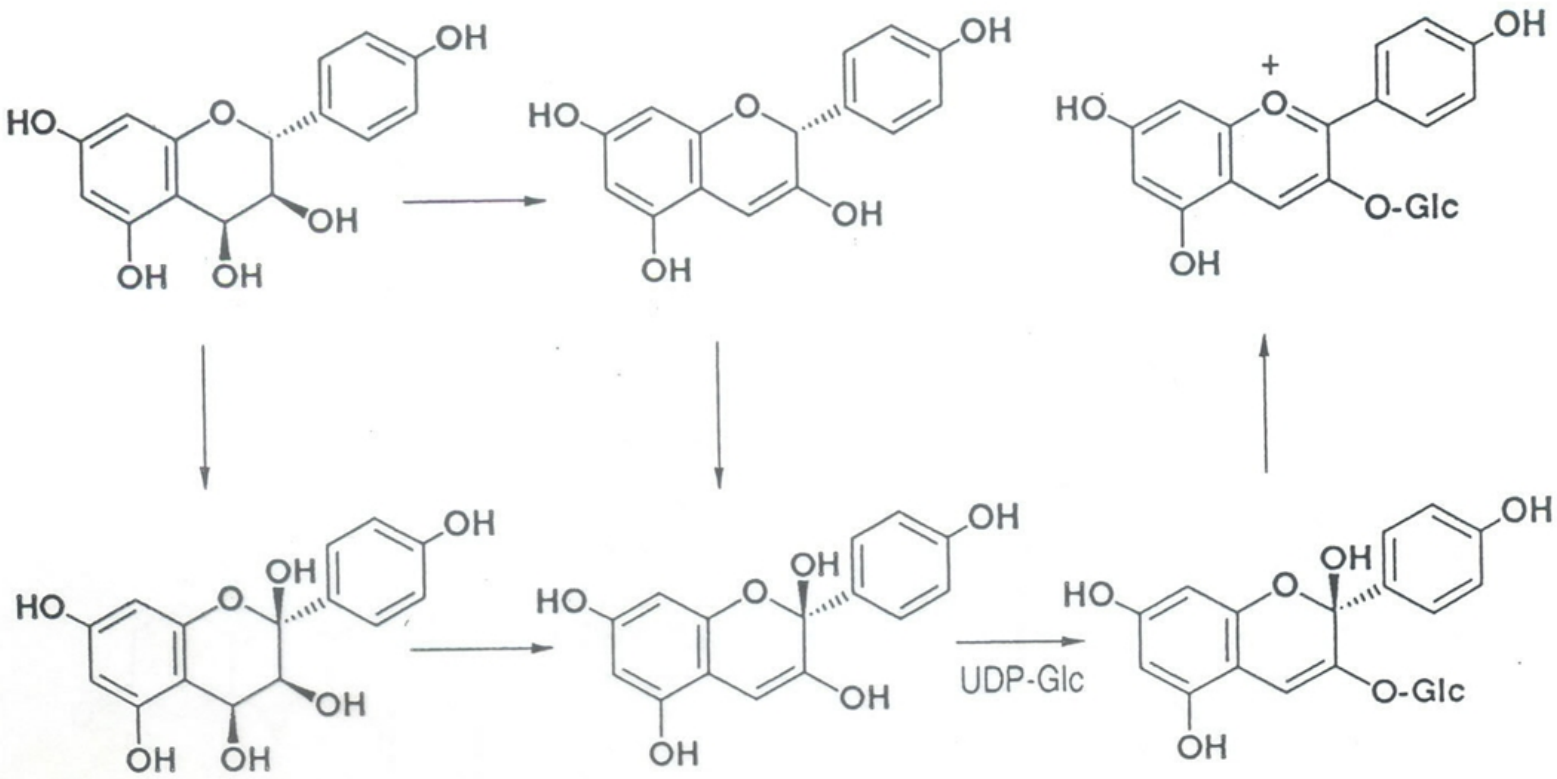
•The most common anthocyanins are 3- **monosides** and 3,5-**diglycosides**, Also known are 3,7-diglycosides and **triglycosides** (for example 3,5,3'-triglycosides).

•**Sugar residue:** can be a monosaccharide (e.g., glucoside, galactoside, rhamnoside), a disaccharide (e.g., rutinoside, xylosylglucoside), or, less often, a trisaccharide.

•Acylation: frequent, by phenyipropanoic acids (e.g., p-coumaric, caffeic, ferulic,sinapic acids) or benzoic acids (gallic acid), generally at C-6". ; Also known by dicarboxylic aliphatic acids (e.g., malonic, malic, oxalic, succinic acids).

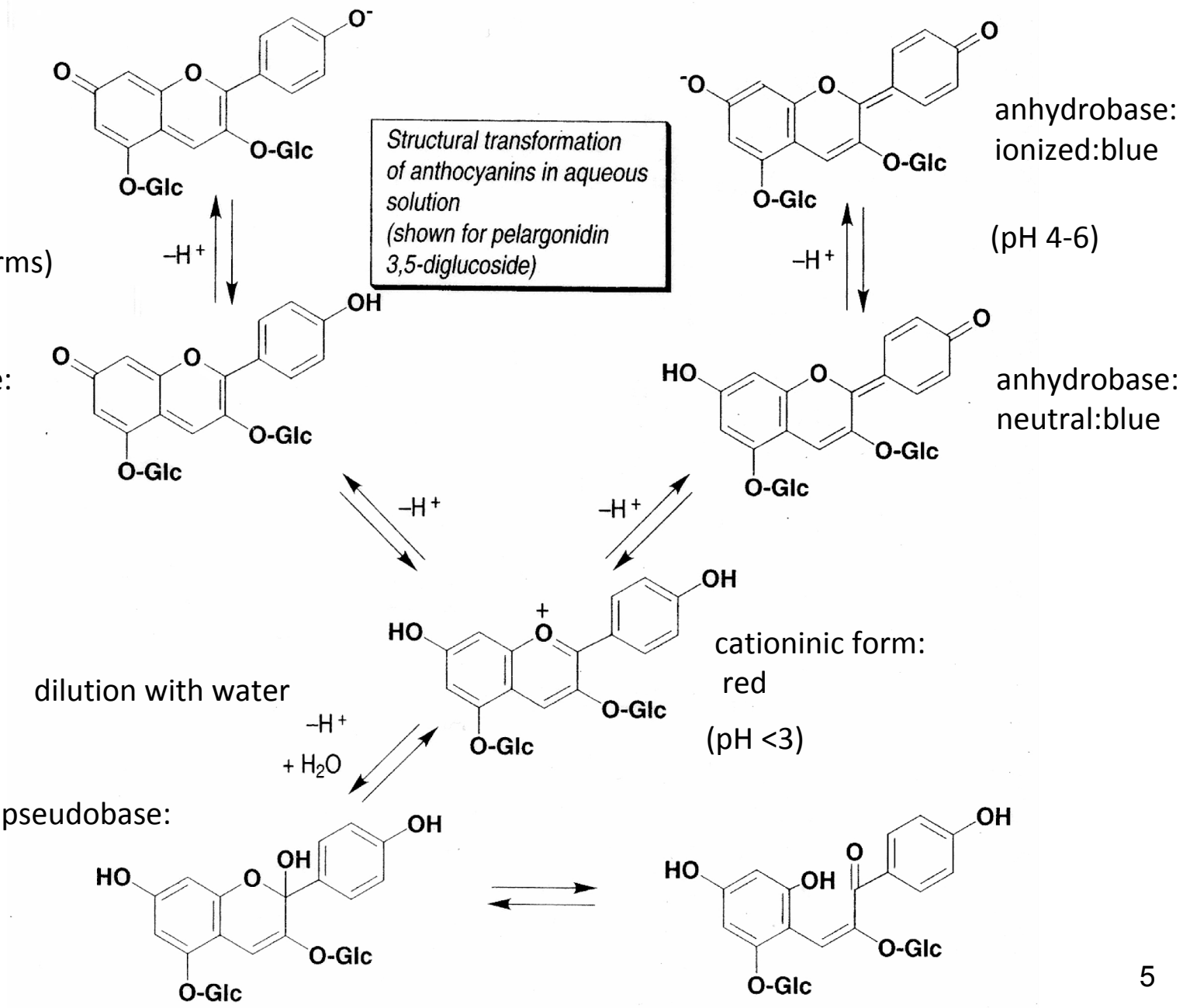


Biosynthetic Origin → general metabolism of flavonoids →precursors: 2,3- trans-dihydro-3,4-cis-dihydroxyflavonols → the diols undergo a hydroxylation (at C-2) and a double dehydration→ glucosylation (UDP-glucose) probably occurs late

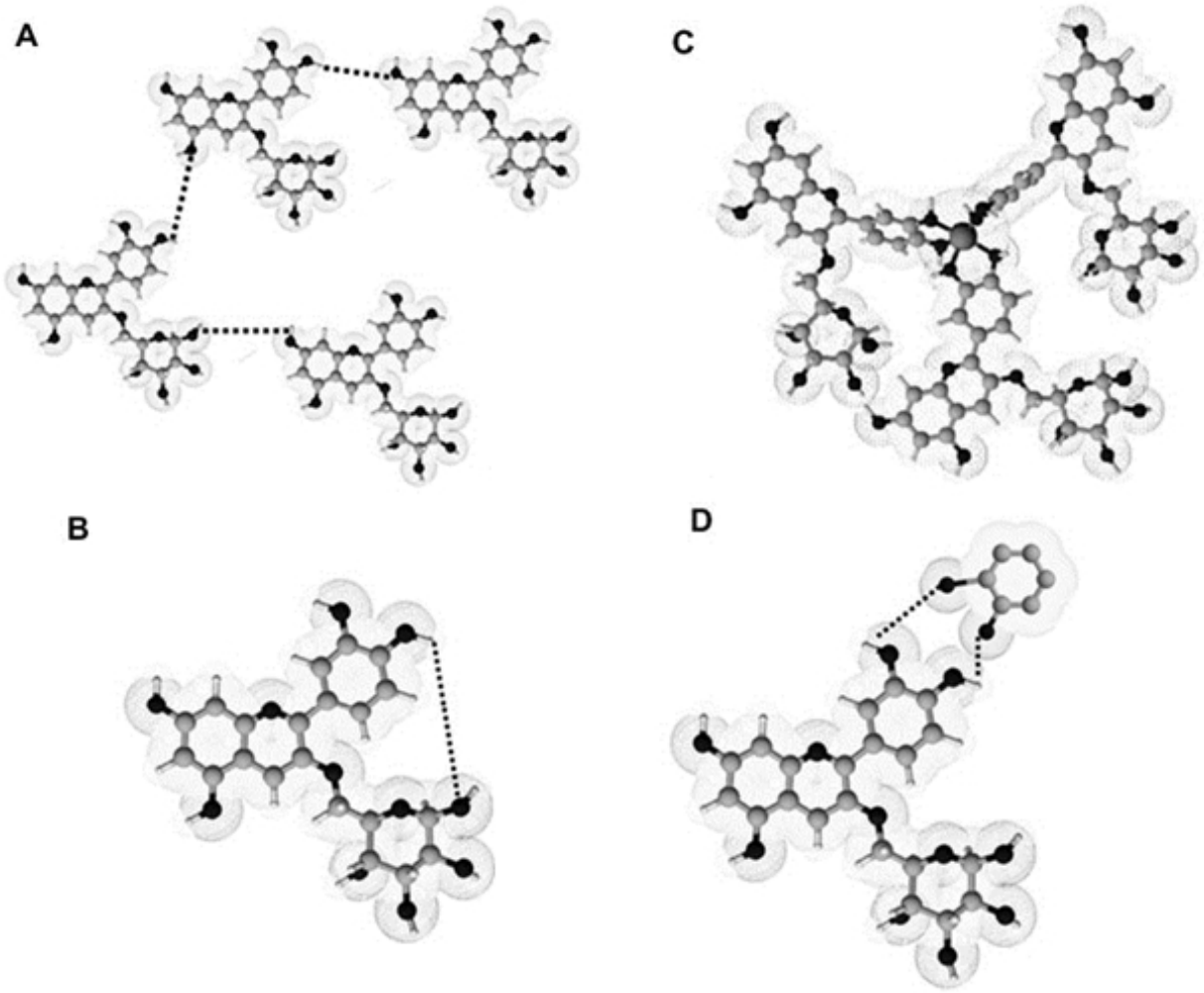


Possible biosynthetic origin of anthocyanins

Properties of 2-phenylbenzopyrylium cation: a weak diacid and a good electrophilic reagent.



Anthocyanins interaction. (A) self-association, (B) intramolecular copigmentation, (C) metal complexation, (D) intermolecular copigmentation (Castañeda-Ovando et al.).



Co-pigmentation is a phenomenon in which the pigments and other colourless organic compounds, or metallic ions, form molecular or complex associations, generating a change or an increment in the colour intensity

Some investigations suggest that the co-pigmentation of anthocyanins with other compounds (co-pigments) is the main mechanism of stabilisation of colour in plants. http://dx.doi.org/10.1016/j.foodchem.2008.09.001,

EXTRACTION AND CHARACTERIZATION

- Anthocyanins are **soluble in** water and alcohols, **insoluble in** apolar organic solvents, and **unstable in** neutral or alkaline medium.
- They are **generally extracted with an alcohol** (methanol, preferrably ethanol if the product is intended for use in food) **in the presence of** a small amount (**0.1-1%**) **of hydrochloric acid**.
- To avoid esterification of the free carboxyl group of acylated anthocyanins by a diacid, and especially **to prevent** their **deacylation**, it is better to use other acids, either **weak acids** (acetic, tartaric, citric) or **volatile acids** (trifluoroacetic), or to work in a **neutral medium** (alcohol mixtures), and to work at **low temperature** (< 30 °C).
- Anthocyanin solutions are very unstable, and they can only be kept under nitrogen, at low temperature, and in the dark.
- **Industrial preparation of anthocyanin extracts**.
  - The oldest procedura is an extraction in aqueous medium in the presence of sulfur dioxide, followed by acidification to regenerate the anthocyanins.
  - More recent procedures: ultrafiltration on cellulose membranes, chromatography on ion-exchange resins.
- **Separation of anthocyanins** is achieved by **chromatographic techniques** (column chromatography on polyamide supports, on polyvinylpyrrolidone supports, or on ion-exchange resins, preparative TLC on cellulose-coated plates, or semipreparative HPLC).

EXTRACTION AND CHARACTERIZATION

HPLC is the method of choice to analyze anthocyanin-containing drugs.

•The **separations** are most often carried out **on reverse phases with acidic water and alcohol gradients**, in which the cationic forms can be **detected at about 500-550 nm**.

•As for flavonoids, **diode array detectors** represent a considerable method enhancement.

•The more complex methods (**LC-MS, MS-MS**) are only available in specialized research laboratories.

As a general rule, **anthocyanin quantitation** is performed by spectrophotometry.

•At the wavelengths of maximum absorption of these compounds, interferences are exceptional:

•quantitation can be done directly on an acidic solution in alcohol (cationic form) or on an acidified juice.

•To prevent anthocyanin self-association, which would result in a positive deviation from the Beer-Lambert Law, **dilute solutions must be used**.

Quantitative estimates of the constituents of an anthocyanin mixture are now obtained directly by HPLC.

ANTHOCYANINS

PHARMACOLOGICAL ACTIVITY

•**decrease capillary permeability and fragility** (confirmed by biological tests on animals based on the diffusion of dyes)

- participation of the collagen of the vascular wall in the control of the permeability of that wall.
- inhibition of the proteolytic collagen degradation enzymes (elastase, collagenase); (It has been shown in vitro for black currant extracts)

•**antiedema activity**,

•**increase in regeneration of** 'visual purple' or **rhodopsin** (see bilberry

•act like **radical scavengers** in vitro (antioxidant activity).

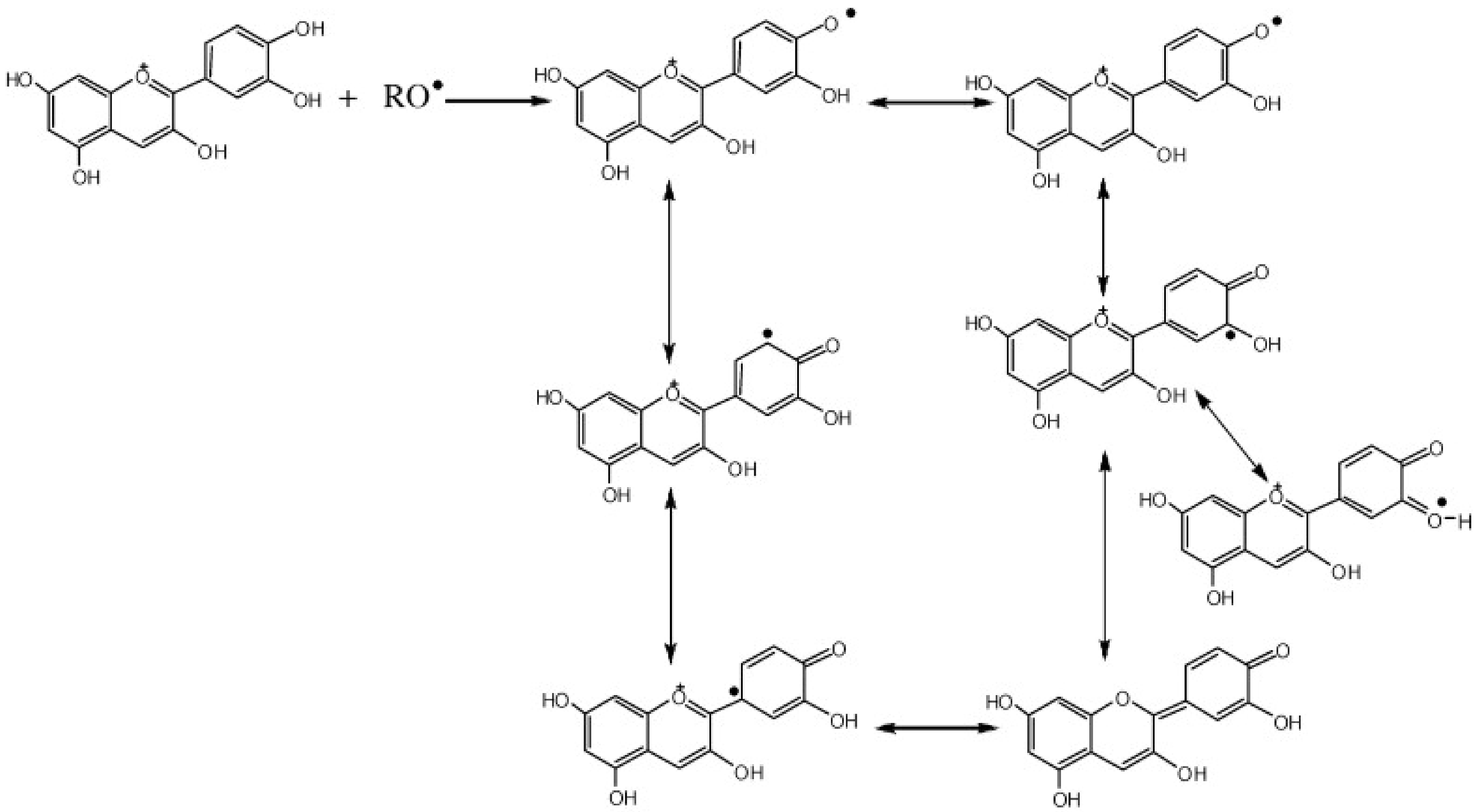
USES

•for the symptomatic treatment of venous and lymphatic insufficiency and capillary fragility (in phiebology, proctology, or gynecology).

•in ophthalmology

- to treat circulatory disorders of the retina or choroid,
- to improve vision at dusk.

Proposed mechanism for the stabilisation of the cyanidine semiquinone radical (resonance) (Castañeda-Ovando et al.).



http://dx.doi.org/10.1016/j.foodchem.2008.09.001, **Chemical studies of anthocyanins: A review,**

ANTHOCYANINS

Other uses

The chief industrial application of anthocyanins is **coloring**

•they are natural pigments for which no animal toxicity has been found, be it acute or chronic.

• Sources:

- **unfermented grape juice**: obtained extracts are either liquids titrated to contain 0.5-1% anthocyanins, or nebulisates titrated to contain 1-5% anthocyanins.
- **elderberry** or **red cabbage** leaves, which are more expensive, but provide a more stable coloring agent.

•Difficulties (restricts the scope of applications):

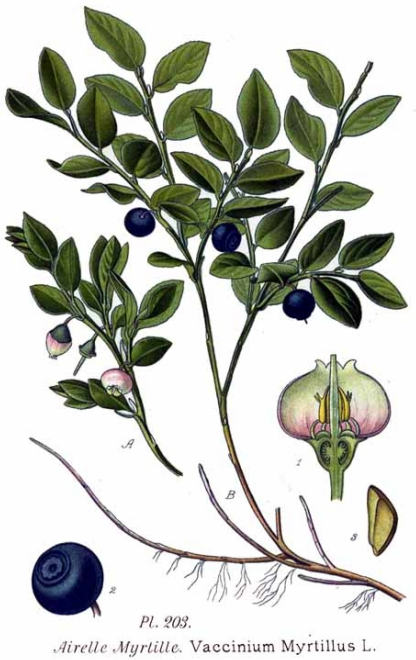
- instability in aqueous media (high): it results in color changes as a function of the pH, and in sensitivity to heat, light, sulfites (often used as preservatives), and metals (food cans).
- The common occurrence of proanthocyanidins and gallotannins in the extracts can also be a problem (for example it makes gelatin precipitate in jams).
- insolubility of anthocyanins in lipids.

•Anthocyanins are extracted from edible fruits and vegetables and may be used as **food additives** (Eur. id. code E163), for example in beverages (30 mg/L), jams, and confectionery products, to name only a few.

CHIEF ANTHOCYANIN-CONTAINING DRUGS

BILBERRY, *Vaccinium myrtillus* L., Ericaceae

- The bilberry is a subshrub with **coriaceous leaves**.
- The **bell-shaped flowers** grow solitary or in pairs at the base of the leaves.
- The fruit is **a multiseeded** tetra- or pentalocular globose **berry** with a fleshy mesocarp;
- on the flattened top, the remains of the style and the calyx form a **small disc with a dull edge**.



•Blueberries are particularly abundant in the woods that grow on siliceous soils in the mountains of the northern hemisphere.

•The French market is largely dominated by imports (from Poland).

• Other species (e.g., V. corymbosum, cultivated in Germany) are also used in the food industry.

Vaccinium myrtillus, Chemical Composition

Blueberries

•Water (up to 90%), sugars (3 to 7%), and organic acids.

•Phenolic acids, **flavonoids** (hyperin = hyperoside], quercitrin), **proanthocyanidins** (procyanidins B-1 and B-4), and monomeric flavan-3-ols (catechin and epicatechin).

•**Anthocyanins** (in the **fresh fruits**: about 0.5%): C-3 *O*-glucosides, *O*-galactosides, and *O*-arabinosides of cyanidin,peonidin, delphinidin, malvidin , and petunidin.

Bilberry leaf

•Phenolic acids, **flavonoids** (rhamnoglucosyl-, arabinosyl-, and glucuronylquercetin).

•Traces of quinolizidine alkaloids (myrtine, epimyrtine).

•**Proanthocyanidins** and catechin (up to 10 %).

Uses

•**Water –soluble bilberry powder** titrated to contain 70 % anthocyanins. Ingredient of drugs used to treat

- the functional symptomes of **venous and limphatyc vessel insufficiency** ,
- cutaneous **capillary fragility**, and
- mesopic and scotopic **vision** (nyctalopia, myopia).

Vaccinium myrtillus, Uses, Indications

In France

•**Bilberry fruit, fresh or dried**, and **bilberry leaf**: traditionally used to treat the subjective symptoms of **venous insufficiency**, such as fullness in the legs, and to relieve the **symptoms of piles**.

•**The fruit, fresh or dried**: is traditionally used for the adjunctive therapy of the painful component of **functional dyspepsia**.

•**Only the fresh fruit:** for the symptomatic treatment of the functional symptoms of **capillary fragility**,

•B**ilberry leaf or dried fruit**: for the symptomatic treatment of **mild diarrhea**.

In Germany, Commission E:

Bilberry fruit:

as an **adstringent**, in case of **diarrhae**;

as a topical **anti-inflammatory** in case of **irritation** of the **mucous membranes** of the mouth and throat.

CRANBERRY, *Vaccinium macrocarpon* Aiton, Ericaceae

- Cranberry grows wild in eastern North America, from the Carolinas to Canada.
- Cultivated in the United States since the beginning of the nineteenth century,
- It produces small dark red fruits
- widely consumed as such (fresh or frozen) and as cranberry juice (pure or as a cocktail sweetened with corn syrup), cranberry sauce, and so on
- The **fresh fruit** is very rich in **acids** (citric. quinic. benzoic);
- it also contains **anthocyanins** (3-O-galactosides and 3-O-arabinosides of cyanidin and peonidin),
- **catechin**, and **flavonoids**.

Vaccinium macrocarpon

- The beneficial—**bacteriostatic**-—-**effect** of cranberry juice in the treatment of urinary infections is confirmed by secular use.
- It is now postulated that the activity is due to the **inhibition of bacterial adhesion onto mucous membranes.**
- This has been demonstrated in the case of *E. coli* adhesion onto urinary tract epithelial cells, using cranberry juice as well as the urine of mice or humans collected after administration of cranberries.
- The active constituent (possibly a procyanidine) inhibiting the adhesins specific to the pathogenic strains of E. coli has since been isolated from cranberry juice—and also from bilberry (blueberry) juice.
- More recently, a placebo-controlled, double- blind clinical trial showed that
- the **daily consumption of 300 mL of** a commercially- available **cranberry juice induced**, in elderly women (average age 78.5 years), a very **significant decrease in the frequency of urinary bacterial contamination**, after 4-8 weeks of treatment, a delay which may correspond to an initial action on the intestinal bacterial flora.
- In the United States, the recommended use of cranberries is as a dilute juice; dried juice capsules are also available.

BLACK CURRANT, *Ribes nigrum* L., Grossulariaceae

- This bushy shrub is cultivated for its edible fruits (in the Burgundy region of France and in central Europe).
- The black currant leaf as well as the fruit are used in pharmacy (Fr. Ph., 10th Ed.).

- Tri- to pentalobate leaves, the underside of which are pale, pubescent, and scattered with yellow secretory glands.
- Flowers : reddish, grouped in dangling racemes, a pubescent calyx which is longer than the corolla.
- Fruit : a fragrant black berry on top of which the remains of the calyx can be seen.

Constituents

•**Fruit**: sugars (10-15%); organic acids; flavonol glycosides ; anthocyanins : cyanidin and deiphinidin glycosides.

•**Leaves:** a small amount of essential oil; flavonoids: hyperin, astragalin, rhamnoglucosides and glucoxylosides of quercetin and kaempferol; dimeric and trimeric prodelphinidins.

BLACK CURRANT,

Uses

- **Fruit**
  - **t**o prepare extracts enriched in anthocyanins
  - With therapeutic indications identical to those of the bilberry

- **Leaves** (in phytopharmaceuticals, traditionally)
  - to facilitate urinary and digestive elimination functions,
  - to enhance the renal excretion of water, and
  - as an adjunct in weight loss programs.
  - orally and topically, for the symptomatic treatment of minor painful symptoms of the joints.

Contemporary phytotherapy prescribes the preparations based on the **buds** in the same fashion.

- These are rich in diterpenoid acids (hardwickiic acid), and are
- prized for their essential oil, which is used in food technology.
- The composition of this essential oil varies with cultivars, but the chief constituents are almost always hydrocarbons (A3- carene, sabinene, phellandrenes, and limonene).

VINE, *Vitis vinifera* L. (tinctoria varieties), Vitaceae

- The term “vine” designates cultivars with black grapes, red pulp, and leaves that turn red in the fall, partially or completely .

- The dried vine leaf was the subject of a monograph in the 10th edition of the French Pharmacopoeia.
- The pharmaceutical industry also uses grape seeds.

Constituents

- Anthocyanins (up to 0.3%): 3-O-glycosides of cyanidin and peonidin;
- monocaffeoyltartaric acid, phenylpropanoic acids,
- flavonol glucosides,
- hydrolyzable tannins (esters of glucose and of gallic and dehydrohexahydroxydiphenic acids),
- proanthocyanidins.

VINE

Uses

Vine leaf-based phytopharmaceuticals are traditionally used (orally and topically) to treat

- the functional symptoms of capillary fragility such as ecchymosis and petechiae,
- the subjective symptoms of venous insufficiency such as fullness in the legs, and
- the symptoms of hemorrhoids.
- Topically, they are traditionally used for eye irritation or discomfort of various etiologies (e.g., eye strain, seawater or swimming pooi water, or smoky atmospheres).

EUROPEAN ELDER, *Sambucus nigra* L., Caprifoliaceae

- The flower—it is the subject of a monograph in the European Pharmacopoeia .
- The fruit, a source of extracts used as food coloring.

- The European elder is a shrub widespread in western Europe.
- Its bark has small cracks and
- its leaves are imparipinnate.
- Large (20 cm) inflorescences of strong-smelling flowers,
- black berries with their purplish-red juice and three seeds.
- The flower is fairly easy to identify.

- However, to verify the absence, in the drug, of flowers of dwarf elder (*S. ebulus* L)—with red instead of yellow anthers—the French Pharmacopoeia requires a TLC analysis of the flavonoid content of a methanol extract.
- It contains sambunigrin

cyanogenic glycosides .

S. ebulus L

EUROPEAN ELDER

Flowers

Constituents

- Flavonoids (>0.8%, Ph. Eur.): rutin, isoquercitrin,
- Derivatives of caffeic acid, free and esterified.
- Triterpenes
- Essential oil
  - smells like muscat grapes, has a pasty consistency,
  - contains fatty acids, 3,7-dimethyl-1,3,7-octatrien-3-ol, linalol, cis-hexenol, and rose oxides, among others.

Uses

Elder flower

- **In France** it is traditionally used
  - to enhance the urinary and digestive elimination functions,
  - as an adjunct in weight loss programs, and
  - to enhance the renal elimination of water
- **In Germany**, Comission E indications
  - As a sudorific, causing an increasein bronchial secretion
  - Colds and coughs

EUROPEAN ELDER

Fruits

- **Constituents**
  - Cyanidin glycosides: 3-*O*-glucosyl-, 3-*O*-sambubiosyl-, 3,5-diglucosyl-, and 3-saqmbubiosyl-5-glucosyl-cyanidins.
  - Flavonoids, acids (citric, malic), saccharides, 0.1 mL/kg essential oil.
  - The seed contain cyanogenic glycosides .
- The ripe fruit, edible fresh or as a jam , is the source of an extract used as food coloring (e.g., to color cherry or pomegranate syrup)
- Traditionally used – in France – for medicinal purposes, for the same indications as the leaf.

Phenoloids in Zingiberaceae family (diarylheptanoids and arylalkanones)

TURMERIC, *Curcuma domestica* Val. = *C. longa* L., Zingiberaceae

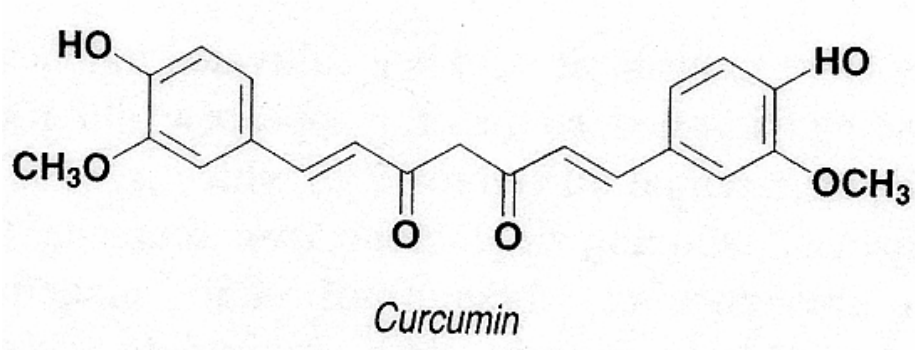
- **Perennial** by a rhizome,
- turmeric has **large sheathing leaves** with an elliptic blade and pinnate veins.
- The **flowers** are **yellow**, **gathered into a spike** with bracts, and
- have an **irregular corolla** with a developed **posterior petal**,
- an androecium reduced to one fertile stamen and staminodes forming a petaloid label, and
- a gynoecium with three carpels.

- **Several cultivars** grown in India, Sri Lanka, Indonesia, China, and Jamaica. For the most part (80%) the world production comes from India.
- Commercial turmeric commonly consists of the ovate primary rhizomes (“bulb” or “round” turmeric), the cylindrical secondary rhizomes (“fingers”), or a mixture of both.
- Fingers: gray and grooved surface and a diameter of about 1 cm.
- Break with a clean fracture, reddish-yellow inside; odor aromatic, taste warm,somewhat bitter.

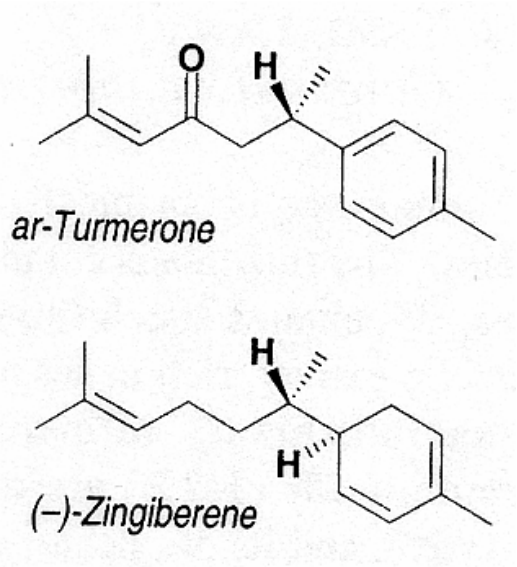
TURMERIC

Chemical Composition

- Starch (45-55%); arabinogalactans (ukonans)
- **Essential oil** (2.5 to 6%) rich in monocyclic sesquiterpenes :
  - hydrocarbons: **zingiberene,** - and 6-curcumene ; their oxygenated derivatives : **turmerone**, *S*-(+)-ar-turmerone, curlone, α- and γ-atlantone;
- **Curcuminoids** (can reach 8 %):
  - The coloring principles in the drug, structurally related to a diarylheptane,
  - **curcumin** (50 to 60%), desmethoxycurcumin, bisdesmethoxycurcumin, dihydrocurcumin .



Curcumin



ar-Turmerone

(–)-Zingiberene

TURMERIC, Pharmacological Properties

Curcumin

•Its **anti-inflammatory activity** has been demonstrated in animal experiments and promoted by observations reported in India in man.

•Is apparently devoid of side effects.

•The mechanism of action remains poorly-understood:

- inhibition of the increase in activity of lysosomal enzymes,
- effect on the synthesis of prostaglandins, or
- interference with the response of granulocytes to stimuli linked to the inflammatory phenomenon.

The drug has a definite action on the

- Hepatic parenchyma: the **hydroalcoholic extract prevents the cytotoxic effects of carbon tetrachloride** in vivo in the mouse and in vitro in cultured rat hepatocytes.
- Stomach: the **ethanolic extract** (0.5 g/kg in the rat) is **active against ulcers** and protects cells .

TURMERIC

Uses

•**Food coloring:** turmeric cultivars with the highest curcumin content (e.g., Allepey, > 6.5%).

•**Curcumin** (>90%):

- It is a **nontoxic authorized color** (Eur. id. code E1oo).
- It is **heat resistant** and scarcely sensitive to changes in pH.
- It is used as the rhizome powder, or the oleoresin, or extracts and curcumin solutions of variable concentration, sometimes adsorbed onto hydrocolloids.

•**Spice:** Madras (3.5% curcumin) and other cultivars . **Turmeric** is, alongside coriander and other spices, **one of the main ingredients** of **curry powders** (these may also contain chili, ginger, clove, fenugreek).

•**Oleoresin** is also used in food technology.

• **In phytopharmaceuticals** : traditionally used

- as a choleretic and cholagogue,
- for functional dyspepsia attributed to a hepatic origin,
- as an appetite stimulant.
- Biliary tract obstruction is a contraindication (Commission E).

TEMU LAWAQ, *Curcuma xanthorrhiza* Roxb., Zingiberaceae

- Temu lawaq is botanically very close to turmeric, and is a cultivated **Indonesian species.**
- **The rhizome** is cut after being harvested, so the drug appears as thin round slices.

Constituents

- Starch (30-40%),
- **Essential oil** (up to 12%): rich in **sesquiterpenes**: **zingiberene**, **ar-curcumene,** (*R*)(—)-xanthorrhizol, turmerones, bisacurones, bisacumol, and bisacurol.
- **Curcuminoids** (1-2%): **curcumin**, its monodemethoxylated derivative, and its di-, hexa-, and octahydrogenated derivatives. Monophenolic and non-phenolic analogs have been isolated from rhizomes collected in Thailand.

Uses

- A traditional folk remedy in southeast Asia: it is used as **cholagogue** and **choleretic.**
- In Germany, Commission E :
  - its use acceptable **for gastrointestinal symptoms**,
  - biliary tract obstruction is a contraindication,
  - prolonged use can cause gastric irritation.

GINGER, *Zingiber officinalis* Roscoe, Zingiberaceae

This **spice**, is used in the oriental traditional medicines, especially for **functional dyspepsia**.

•Originally from India, ginger is cultivated in India, China, and all of southeast Asia (Indonesia, Philippines), and in the tropical regions of Africa (Nigeria).

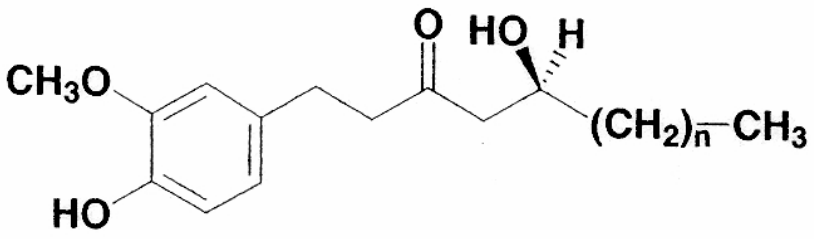
- Large herbaceous perennial plant,
- lanceolate leaves,
- thick inflorescence with overlapping lateral bracts,
- pale green flowers with purple label.

- The rhizome is ramified within one plane.
- Appearance, depending on the mode of preparation: gray with a wrinkled surface (coated or unscraped), white with a smooth surface (uncoated or scraped), or prepared (preserved).
- Fibrous and granular fracture; odor aromatic, taste warm and pungent.

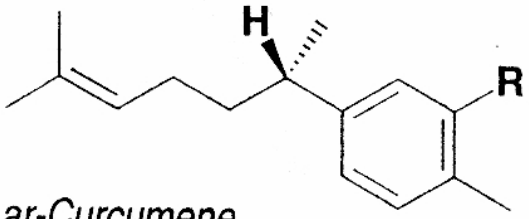
GINGER

Chemical Composition

- Starch (60%), proteins, fats (10%), from 10 to 25 mL/kg essential oil, and a resin.
- **Essential oil** (composition highly depends on geographical origin):
  - **Sesquiterpene hydrocarbons** (30-70%): (—)-**zingiberene**, (+)-**ar-curcumene**, (—)-β-sesquiphellandrene, *E,E*-β-farnesene, β-bisabolene. Monoterpene aldehydes (citrals) and alcohols.
- **Gingerols =** 1 -(3' -methoxy-4' -hydroxyphenyl)-5-hydroxyalkan-3-ones:
  - [3-6]-, [8]-, [10]-, and [12]-**gingerols** bearing a side chain with 7-10, 12, 14, or 16 carbon atoms, respectively;
  - alongside the **corresponding ketones**, and dehydration products (**shogaols**).
- Labdane-type diterpenes, galonolactone and its dialdehyde derivative.



Gingerols (n=1-4,6,8,10)



R = H: *ar-Curcumene*
R = OH: *Xanthorrhizol*

GINGER, Pharmacological Properties

- Used since remote times in India and China.
- **Animal experiments** :
  - oleoresin is a **cholesterol lowering** agent (in rodents),
  - [6]-gingerol is a **cholagogue** (in the rat by the intraperitoneal route),
  - [8]-gingerol is a **hepatoprotective** agent (prevents the toxic effects of carbon tetrachloride in rat hepatocytes).
  - the acetone extract and zingiberene have an **antiulcer effect** in the rat
  - The drug has **an anti-inflammatory activity** (possibly acting on prostaglandin and leukotriene production).
- **Human studies** (on antiemetic properties)
  - Most trials reveal an activity superior to that of a placebo for **motion sickness**, **post-operative nausea**, or **morning sickness** (at the usual dose of 1 g per day).
  - These trial results are divergent ; (among the reasons: ginger products used were not standardized).
- **Antiemetic action**: may be the consequence of direct effects on the gastrointestinal tract: in the mouse, the stimulation of gastrointestinal motility by the acetone extract (75 mg/kg), by [61-shogaol (2.5 mg/kg), or by gingerols is comparable to that of metoclopramide (10 mg/kg).
- Other authors, however, noted the lack of effect of ginger powder on the rate of gastric emptying in healthy humans.
- The drug is not toxic and has no side effects.

GINGER

Uses

• Used (especially for functional dispepsia) for over 25 centuries in the formulation of countless traditional Oriental remedies (China, Japan).

•In France: in phytomedicines: traditionally used for motion sickness.

•In Germany: the rhizome powder is used for gastrointestinal distress and to prevent motion sickness (2 g/day).

•Commission E:

- Ginger is a spasmolytic in animals
- in humans, it has antiemetic, positive inotropic, and stimulant effects (intestinal peristalsis, salivary and gastric secretions).
- Ginger must not be used to prevent morning sickness in pregnant women.

KAVA, *Piper methysticum* Forst. f., Piperaceae

- *P. methysticum,* a pepper tree which grows in the islands of western Polynesia (Papua New Guinea, Tonga, Samoa, Fiji, Vanuatu) and as far as Tahiti.

- A perennial dioecious **subshrub** with
- **cordate leaves.**
- **Decaploid** and **sterile**.
- Multiplies by vegetative propagation.

- The term **kava** designates **a beverage** prepared by soaking in water the rhizome or root fragments, after grinding them with a pestle or chewing them.
- It has been consumed for centuries according to a ceremonial described in 1875 by Captain Cook.
- This ritual beverage **induces a sensation of well-being**.
- It continues to play an important role in the culture of that part of the globe.

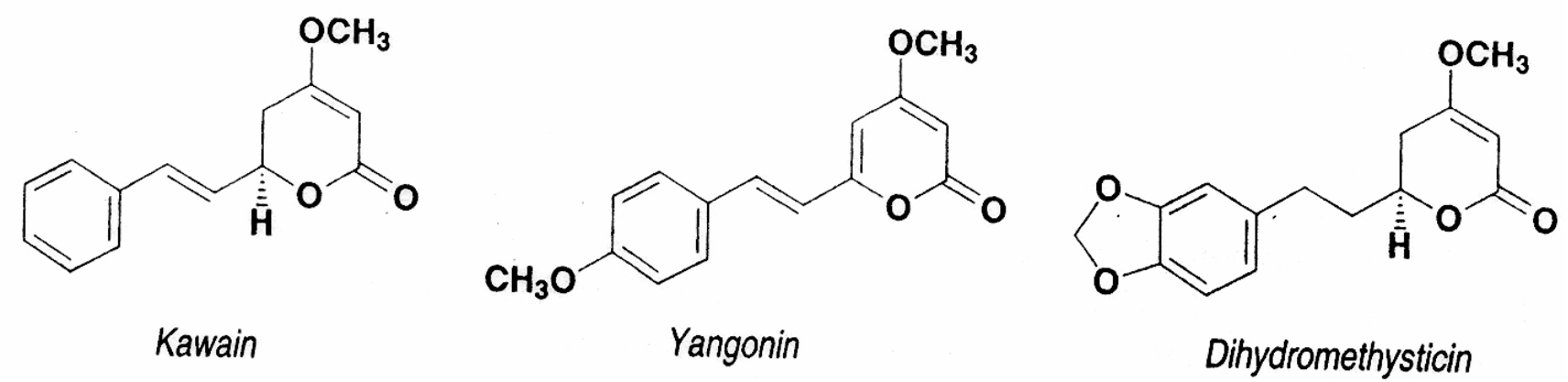
KAVA

Constituents

•Mono- or di-**unsaturated α-pyrones**, substituted by a styryl or phenethyl group, itself substituted (methoxyl, methylenedioxyl) or not.

– They include **yangonin**, (+)-methysticin, (+)-**dihydromethysticin**, (+)-**kawain,** (+)-dihydrokawain**,** demethoxyyangonin, and minor products (e.g., dehydrokawain, 7 ,8-dihydroyangonin, 10- and 11 -methoxyyangonins).

•**Resin** *content* can fluctuate *from 3 to 20%* depending on cultivars and location (rhizome, lateral roots) and its *composition* varies with the *chemotype*.



KAVA, Pharmacological research

- The pyrones
  - **induce sleep** in rodents (per os) and **are sedatives** in rodents, cats, and rabbits.
  - cause muscle relaxation and several are anticonvulsant (strychnine, electroshock).
- The kavapyrones (DHK, DHM) are analgesics and weak local anesthetics.
- The aqueous extract and the lipid-soluble fraction decrease spontaneous movement, but
- the (mild) sedation induced by the aqueous extract is not accompanied by a loss of muscular tone;
- the resin induces sleep, but the aqueous extract does not (mouse, IP).
- **Kava** and **kawain induce sleep** by **acting on the limbic system** (EEG in cats)
- **Klinical trials** indicated that **a kava extract** is more **efficacious** than a placebo in patients who suffer from non-psychotic anxiety.
- In Germany, **pharmaceuticals based on standardized extracts** (i.e., 35-120 mg kavapyrones) were promoted **as sleep disorder and anxiety medicines**.
- **Nowdays their application is contraindicated due to the hepatotoxic adverse reactions** reported in association with the use of all types of kava products in the South Pacific Islands, Australia, Europe, and the US.
- It appears that poor quality of the kava material was responsible for the liver toxicity.
- Therefore, a sophisticated approach to establish kava quality standardizations is needed for safe human use of kava as relaxing traditional beverages, the anxiolytic drugs, and recreational dietary supplements.