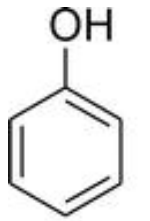
# Phenolic compounds. Classification, methods of analysis. Medicinal plants and raw materials containing simple phenols.

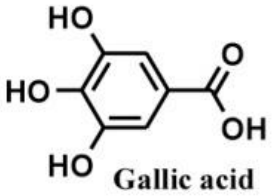
**Phenolic compounds** are secondary metabolites, which are produced in the shikimic acid of plants and pentose phosphate through phenylpropanoid metabolization. They contain benzene rings, with one or more hydroxyl substituents, and range from simple phenolic molecules to highly polymerized compounds.

Also they can be described as compounds that contain a phenol moiety. Phenol itself is a benzene ring that is substituted with a hydroxyl group. Thus, its systematic name is hydroxybenzene.

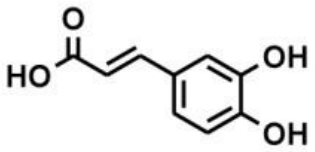



phenol

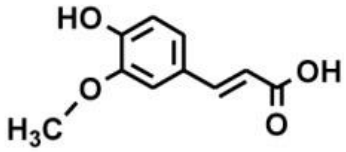
Phenolics are the most pronounced secondary metabolites found in plants, and their distribution is shown throughout the entire metabolic process. These phenolic substances, or polyphenols, contain numerous varieties of compounds: simple flavonoids, phenolic acids, complex flavonoids and colored anthocyanins. These phenolic compounds are usually related to defense responses in the plant. However, phenolic metabolites play an important part in other processes, for instance incorporating attractive substances to accelerate pollination, coloring for camouflage and defense against herbivores, as well as antibacterial and antifungal activities.



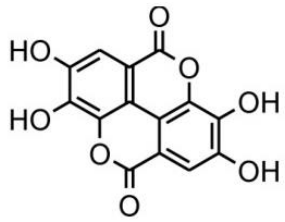
Gallic acid



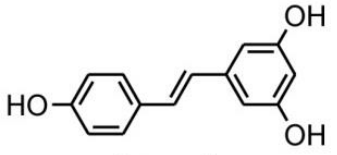
Caffeic acid



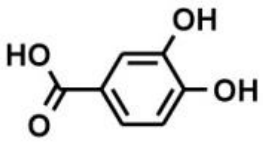
Ferulic acid



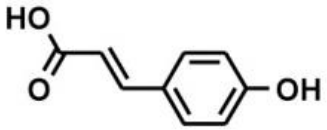
Ellagic acid



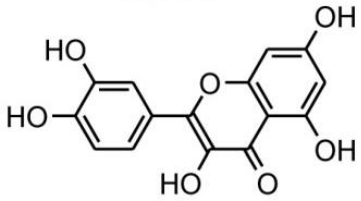
Resveratrol



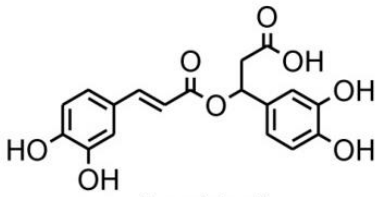
Protocatechuic acid



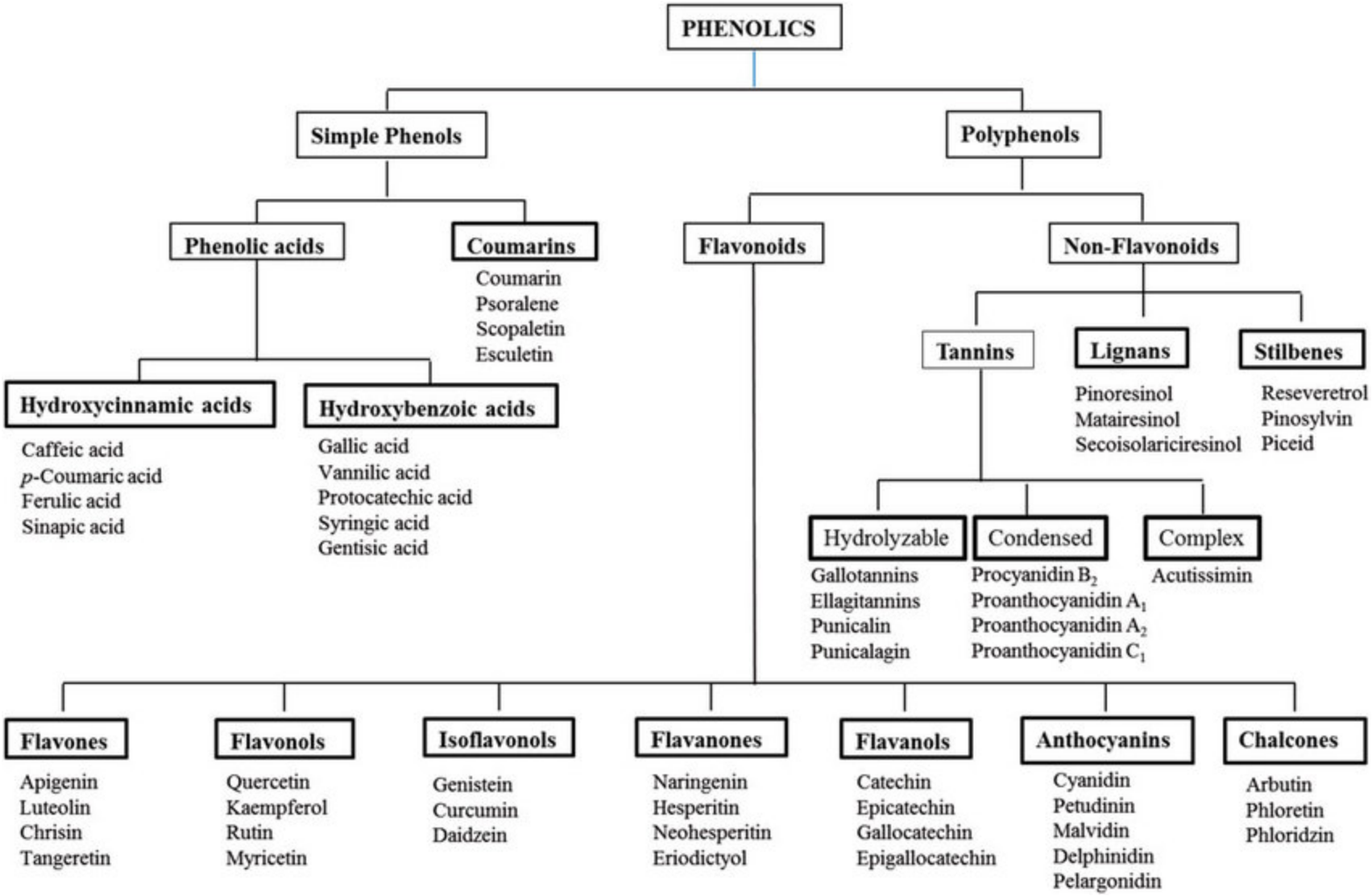
Coumaric acid

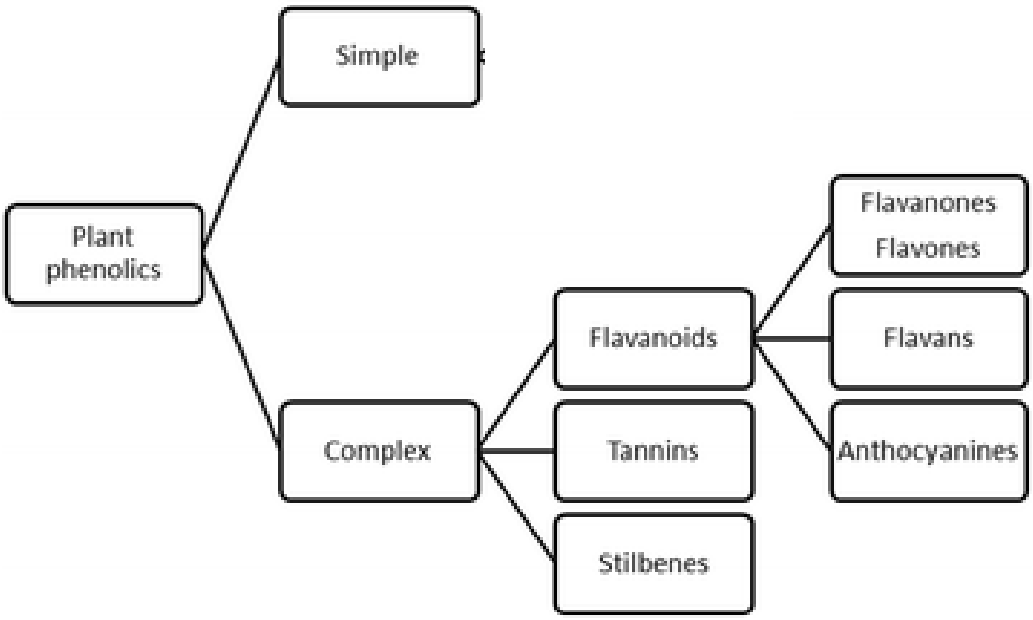


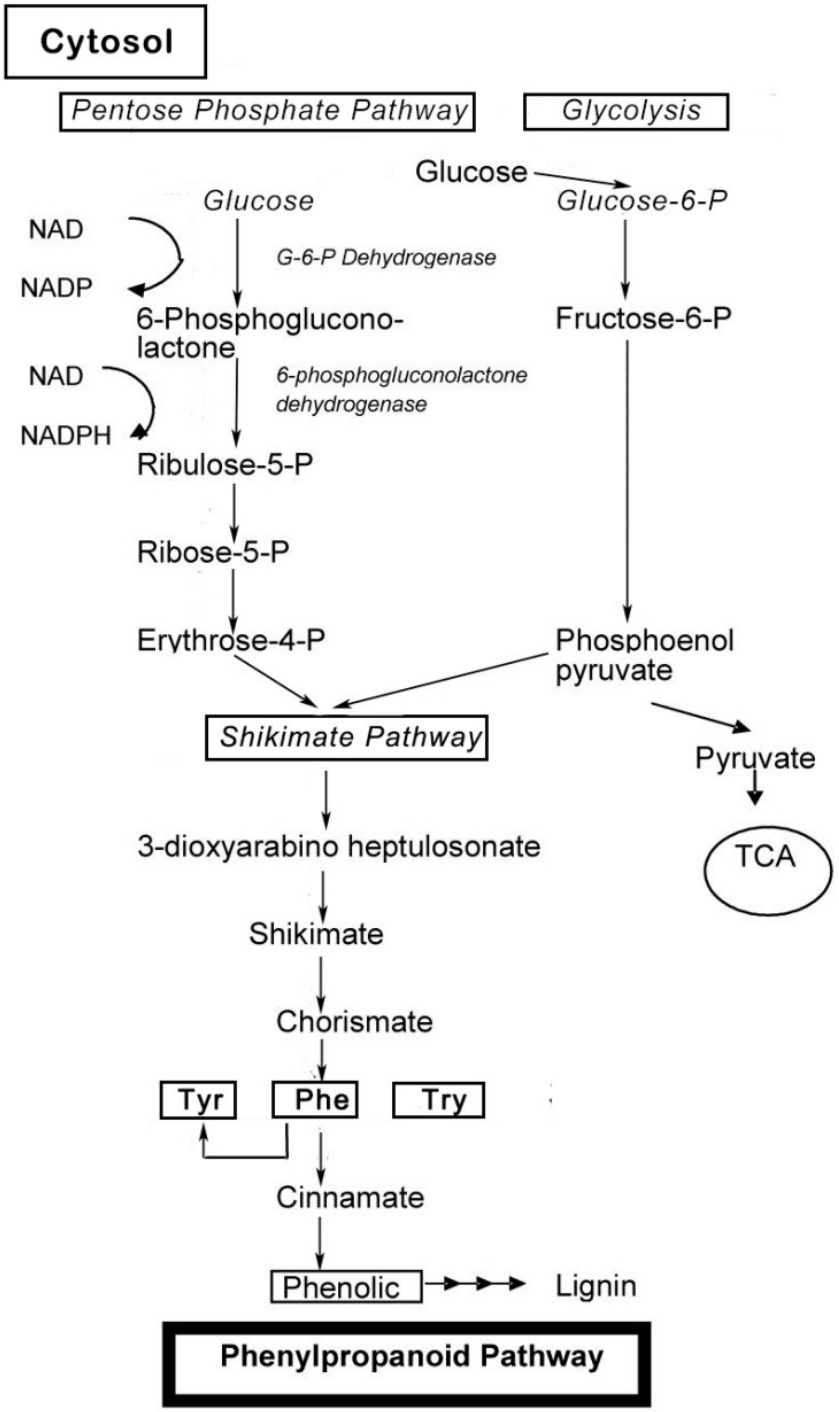
Quercetin



Rosmarinic acid


PHENOLICS
Simple Phenols
Polyphenols
Phenolic acids
Coumarins
Coumarin
Psoralene
Scopaletin
Esculetin
Flavonoids
Non-Flavonoids
Tannins
Lignans
Stilbenes
Pinoresinol
Matairesinol
Secoisolariciresinol
Reseveretrol
Pinosylvin
Piceid
Hydroxycinnamic acids
Caffeic acid
p-Coumaric acid
Ferulic acid
Sinapic acid
Hydroxybenzoic acids
Gallic acid
Vannilic acid
Protocatechic acid
Syringic acid
Gentisic acid
Hydrolyzable
Condensed
Complex
Gallotannins
Ellagitannins
Punicalin
Punicalagin
Procyanidin B2
Proanthocyanidin A1
Proanthocyanidin A2
Proanthocyanidin C1
Acutissimin
Flavones
Apigenin
Luteolin
Chrisin
Tangeretin
Flavonols
Quercetin
Kaempferol
Rutin
Myricetin
Isoflavonols
Genistein
Curcumin
Daidzein
Flavanones
Naringenin
Hesperitin
Neohesperitin
Eriodictyol
Flavanols
Catechin
Epicatechin
Gallocatechin
Epigallocatechin
Anthocyanins
Cyanidin
Petudinin
Malvidin
Delphinidin
Pelargonidin
Chalcones
Arbutin
Phloretin
Phloridzin


Plant phenolics
Simple
Complex
Flavanoids
Tannins
Stilbenes
Flavanones
Flavones
Flavans
Anthocyanines

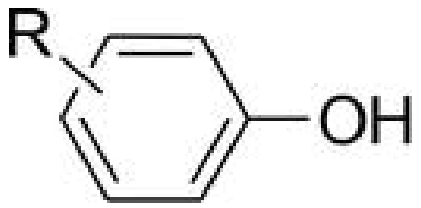


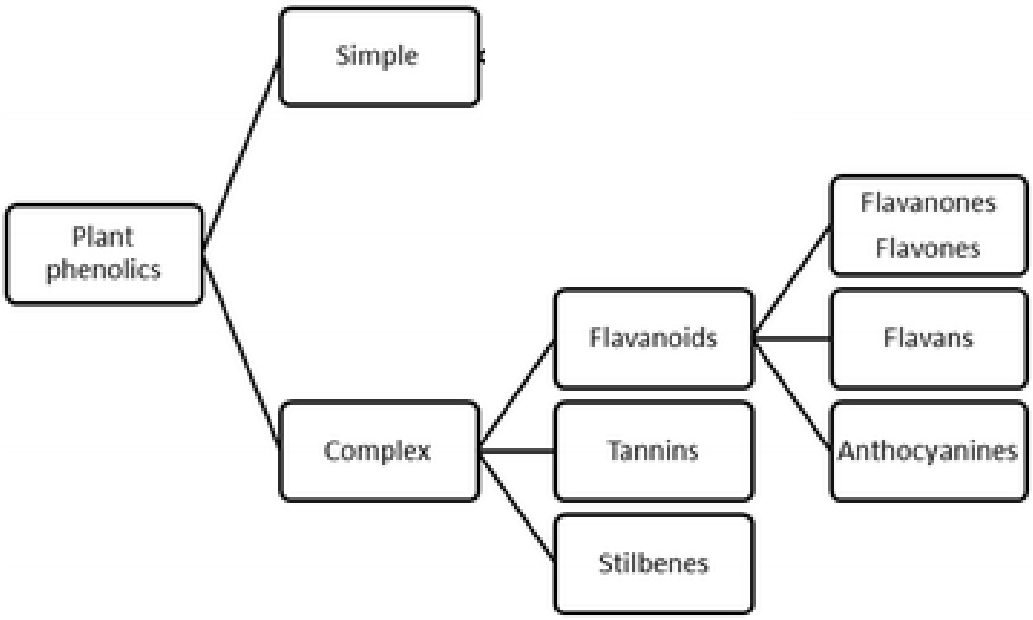

In the synthesis of phenolic compounds, the first procedure is the commitment of glucose to the pentose phosphate pathway (PPP) and transforming glucose-6-phosphate irreversibly to ribulose-5-phosphate. The first committed procedure in the conversion to ribulose-5-phosphate is put into effect by glucose-6-phosphate dehydrogenase (G6PDH). On the one hand, the conversion to ribulose-5-phosphate produces reducing equivalents of nicotinamide adenine dinucleotide phosphate (NADPH) for cellular anabolic reactions. On the other hand, PPP also produces erythrose-4-phosphate along with phosphoenolpyruvate from glycolysis, which is then used through the phenylpropanoid pathway to generate phenolic compounds after being channeled to the shikimic acid pathway to produce phenylalanine.

Phenolic compounds can generally be classified into simple and polyphenolic compounds.

## Simple phenolic compounds

Phenolic compounds that contain one phenol unit (or a derivative of it) are considered "simple". Fundamentally, they are substituted phenol compounds. Simple phenolic compounds have $C_6$ general skeleton representation. The general structure is shown below. The group denoted by "R" (an organic group which could be alkyl, alkenyl, aryl …etc. or hydroxy, alkoxy, amino …etc) which can be in the *ortho* (*o*), *meta* (*m*), or *para* (*p*) positions of the aromatic ring. These descriptors refer, with respect to the position of the hydroxyl group constituting phenol which is given position 1, to 1,2-, 1,3, and 1,4-carbon relationship respectively.

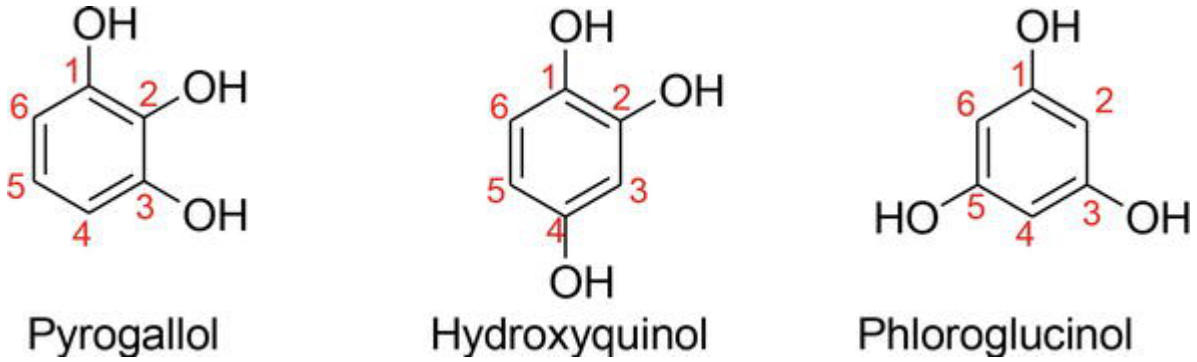



Plant phenolics
Simple
Complex
Flavanoids
Tannins
Stilbenes
Flavanones
Flavones
Flavans
Anthocyanines

Simple substituted phenol compounds can be hydroxyphenols or dihydroxybenzenes. Examples are catechol (1,2-dihydroxybenzene), resorcinol (1,3-dihydroxybenzene), and hydroquinone (1,4-dihydroxybenzene)


The structure of hydroxyl-substituted phenols.

Other simple substituted phenol compounds can also be dihydroxyphenols or trihydroxybenzenes. Examples are pyrogallol (1,2,3-trihydroxybenzene), hydroxyquinol (1,2,4-trihydroxybenzene), and phloroglucinol (1,3,5-trihydroxybenzene)




The structure of dihydroxyl-substituted phenols.

**Physical properties.**

Simple phenolic compounds are colourless, less often slightly coloured, crystalline substances with a certain melting point, optically active. They have a specific odour, sometimes aromatic (thymol, carvacrol). In plants, they are more often found as glycosides, which are well soluble in water, alcohol, acetone; insoluble in ether, chloroform. Aglycones are weakly soluble in water, but well soluble in ether, benzene, chloroform and ethyl acetate. Simple phenols have characteristic absorption spectra in the UV and visible regions of the spectrum.Phenolic acids are crystalline substances, soluble in alcohol, ethyl acetate, ether, aqueous solutions of sodium hydrocarbonate and acetate.Gossypol is a fine crystalline powder of light yellow to dark yellow colour with a greenish tint, practically insoluble in water, slightly soluble in alcohol, well soluble in lipid phases.

**Chemical properties.**

The chemical properties of simple phenolic compounds are due to the presence of:- aromatic ring, phenolic hydroxyl, carboxylic group;- glycosidic bonding.
Chemical reactions are characteristic of phenolic compounds:

1. *Hydrolysis reaction* (due to the glycosidic bond). Phenolic glycosides are easily hydrolyzed by acids, bases or enzymes to aglycon and sugars.
2. *Oxidation reaction*. Phenolic glycosides are easily oxidised, especially in an alkaline environment (even by air oxygen), forming quinoid compounds.
3. *Salt formation reaction*. Phenolic compounds, having acidic properties, form water-soluble phenolates with alkalis.
4. *Reactions of complexation*. Phenolic compounds form complexes with metal ions (iron, lead, magnesium, aluminium, molybdenum, copper, nickel) in different colours.
5. *Reaction of azo-combination with diazonium salts*. Phenolic compounds with diazonium salts form azo-colours from orange to cherry red.
6. *The reaction of formation of esters* (depsides). The depsides form phenolic acids (digallic, trigallic acids).

**Qualitative and quantitative analysis.**

Qualitative and quantitative analysis of raw materials is based on physical and chemical properties.Qualitative analysis.Phenolic compounds are extracted from plant raw materials with water. The aqueous extracts are purified from the accompanying substances by precipitating them with a solution of lead acetate. Qualitative reactions are carried out with the purified extract. Phenologlycosides with a free phenolic hydroxyl give all reactions characteristic of phenols (with salts of iron, aluminium, molybdenum, etc.).

**Specific reactions**

1. for arbutin (raw material of cowberry and bearberry):

(a) With crystalline ferrous oxide sulphate. The reaction is based on obtaining a complex which changes colour from lilac to dark violet, with further formation of a dark violet precipitate.

(b) With 10% solution of sodium phosphorus molybdenum acid in hydrochloric acid. The reaction is based on the formation of a blue compound.

2. on salidroside (rhodiola rosea raw material): Azo-combination reaction with diazotinated sodium sulphacyl to form a cherry red azo dye.

*Chromatographic examination*:
Different types of chromatography are used (paper chromatography, thin layer chromatography, etc.).

**Qualitative determination**

Spectrophotometric analysis

## Specifics of collecting, drying and storing raw materials containing simple phenolic compounds

Raw material of cowberries and bearberry is harvested in two terms - early spring before flowering and in autumn from the beginning of fruit ripening until the snow cover appears. Drying is air-shaded or artificial drying at a temperature not exceeding 50-60 ° C in a thin layer. It may be harvested again in 5-6 years, from the same bushes.

Raw Rhodiola rosea (golden root) is harvested in the phases of the end of flowering and fruiting. Dried at a temperature of 50-60 ° C. Repeat harvesting on the same bushes is possible after 10-15 years.

Raw male shield-fern (Rhizomata Filicis maris) is collected in autumn, do not wash, dried in the shade or in dryers at a temperature not exceeding 40 ° C. The same planting can be harvested again in 20 years.Cotton raw material, root bark (Cortex radicum Gossypii), is harvested after the cotton harvest.The raw material is stored according to the general list in a dry and well-ventilated room. Shelf life - 3 years. Male fern rhizomes are stored for 1 year.

# Medicinal plant material containing simple phenolic compounds

***COMMON BEARBERRY FOLIA - ARCTOSTAPHYLOS UVAE URSI FOLIA***

***common bearberry - Arctostaphylos uva-ursi (L.) Spreng.***

***Family Ericaceae***

**Bearberries** (indigenous **kinnickinnick**) are three species of dwarf shrubs in the genus *Arctostaphylos*.
*Arctostaphylos uva-ursi* is a small procumbent woody groundcover shrub growing to 5–30 centimetres high. Wild stands of the species can be dense, with heights rarely taller than 15 cm. Erect branching twigs emerge from long flexible prostrate stems, which are produced by single roots. The trailing stems will layer, sending out small roots periodically. The finely textured velvety branches are initially white to pale green, becoming smooth and red-brown with maturity. The small solitary three-scaled buds are dark brown.

The leaves are shiny, small, and feel thick and stiff, measuring about 4 cm long and 1 cm wide. Their tops are darker green than their undersides. They have rounded tips tapering back to the base, held vertically by a twisted leaf stalk in an alternate arrangement on the stem. The leaves remain green for 1–3 years before falling in autumn, when their colour changes to a reddish-green or purple, pale on the underside.

Terminal clusters of small urn-shaped flowers bloom from May to June. The flowers are white to pink, and bear round, fleshy or mealy, bright red to pink fruits called drupes. The smooth, glossy skinned fruits range from 6 to 13 mm in diameter. The red fruits persist on the plant into early winter. The fruits are bittersweet when raw, but sweeter when boiled and dried. Each drupe contains 1 to 5 hard seeds.

Distribution: circumpolar, at high latitudes, from Scotland east
across Scandinavia, Russia, Alaska, Canada and Greenland; southern limits in Europe in the  Alps, in Asia to the Altay Mountains, and in North America to British Columbia in the west.

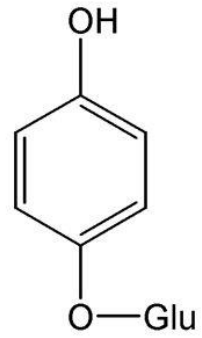
**Harvesting.**

Leaves should be harvested at two times: in spring, before or at the very beginning of flowering (from late April to mid-June) and in autumn, from the time the fruit ripens until it falls off (from late August to mid-October). After flowering, young shoots begin to grow; leaves harvested at that time become fulvous when dried and also contain small amounts of arbutin. When harvesting raw material, the leafy shoots (twigs) are cut off with a special knife or by hoeing. The cut branches are collected, shaken of sand and moss, and transported to the drying place.

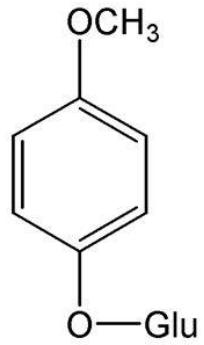
**External features.** Integument. Leaves small, leathery, dense, brittle, smooth-edged, obovate or oblong-obovate, rounded at the top, sometimes with a small depression, cuneately narrowed toward the base, with a very short petiole. Leaves are 1-2.2 cm long and 0.5-1.2 cm wide. Veining is reticulate. Leaves dark green, glossy, with clearly visible depressed veins on upper side, slightly lighter, matt, glabrous on lower side. It has no smell. The taste is strongly astringent and bitter.

**Chemical composition.**

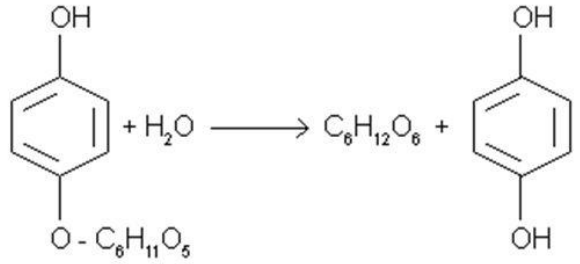
The active ingredient is phenologlicoside arbutin, which is a beta-D-glucopyranoside hydroquinone (8-16%). Leaves are rich in tannins of hydrolysable group (7.2 to 41.6 %). Methylarbutin, hydroquinone, galloylarbutin, as well as triterpenoids - ursolic acid (0.4-0.7%), flavonoids, catechins, phenolcarboxylic acids - gallic acid, ellagic acid are found in smaller amounts. The leaves of bearberry have a lot of iodine (2.1-2.7 mkg / kg). The glycoside arbutin is hydrolyzed to hydroquinone and glucose under the influence of arbutase enzyme.




Arbutin




Methylarbutin




Arbutin Hydroquinon

**Pharmacotherapeutic group.** Diuretic, antiseptic.

**Uses.** Decoction of bearberry leaves are used in diseases of the urinary tract (urolithiasis, cystitis, urethritis) as a disinfectant and diuretic. At high doses may vomiting, nausea, diarrhea and other side effects. The leaves of bearberry slightly irritate the epithelium of the urinary system, so they are combined with plants that have anti-inflammatory, styptic and diuretic effects.

***COWBERRY LEAVES - VACCINII VITIS-IDAEA FOLIA***
***cowberry - Vaccinium vitis-idaea L.***
***Family Ericaceae (Vaccinioideae)***

***Vaccinium vitis-idaea***, the **lingonberry**, **partridgeberry**, **mountain cranberry** or **cowberry**, is a small evergreen shrub in the heath family Ericaceae, that bears edible fruit. It is native to boreal forest and Arctic tundra throughout the Northern Hemisphere, from Europe and Asia to North America. Lingonberries are picked in the wild and used to accompany a variety of dishes in Northern Baltoscandia, Russia, Canada and Alaska.

*Vaccinium vitis-idaea* spreads by underground stems to form dense clonal colonies. Slender and brittle roots grow from the underground stems. The stems are rounded in cross-section and grow from 10 to 40 cm in height. Leaves grow alternately and are oval, 5–30 mm (1⁄4–1+1⁄8 in) long, with a slightly wavy margin, and sometimes with a notched tip.

The flowers are bell-shaped, white to pale pink, 3–8 mm (1⁄8–3⁄8 in) long, and produced in the early summer.

The fruit is a red berry 6–10 mm ($\frac{1}{4}$–$\frac{3}{8}$ in) across, with an acidic taste, ripening in late summer to autumn. While bitter early in the season, they sweeten if left on the branch through winter.

**Harvesting.**

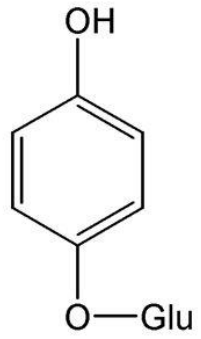
Lingonberry leaves are harvested in two periods in spring and autumn: in spring before flowering, when there are no buds or before they turn white; in late autumn when the fruit is fully ripe. Leaves harvested in summer dry out, which decreases the quality of the raw material. Raw material can be collected by plucking leaves from a shrub, cut with scissors or gently breaking off above ground shoots, from which leaves can easily be detached after drying. The best quality raw material is the leaves harvested immediately after or during snowmelt.

**External features.**

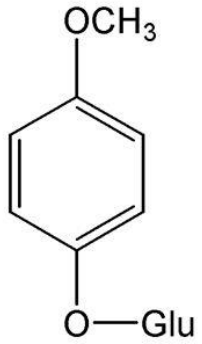
Leaves are short-cellular, leathery, elliptical or obovate, blunt or slightly emarginate at the top, with solid or slightly dentate edges turned to the bottom side, 7-30 mm long and 5-15 mm wide. Leaves are dark green above, light green below with clearly visible dark brown dots (glandules). The veining is pinnate. The leaves lack smell. The taste is bitter, astringent.

**Chemical composition.**

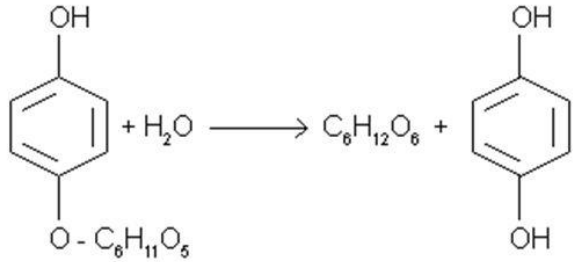
Lingonberry leaves contain arbutin (4-9%), free hydroquinone, as well as flavonoids, tannins, mainly of the condensed group (up to 15%), ursolic, ellagic and quinic acids.




Arbutin




Methylarbutin




Arbutin Hydroquinon

**Pharmacotherapeutic group.** Diuretic, antiseptic.

**Pharmacological properties.** Cowberry leaves have antimicrobial, astringent and anti-inflammatory effect due to the presence in the plant phenolic glycoside glycoside arbutin, as well as ursolic acid and phytoncides. The preparations have astringent and capillary-strengthening properties due to the flavonoids, vitamins, ursolic acid and tannins; they also have demineralizing effect, increase antibiotics efficiency, stimulate phagocytosis and other defensive forces of the body, regulate nitrogenous exchange.

**Uses.**

Lingonberry leaves are used in urolithiasis, pyelonephritis, cystitis, prostatitis and gonorrhea as a diuretic, disinfectant, demineralizing and nitrogen-regulating agent. The leaves of cowberry compared with bearberry leaves contain fewer tannins and almost no methylarbutin, not always useful in kidney diseases and affect the mucosa of the gastrointestinal tract, which should be considered when prescribing the leaves of cowberry in patients with renal pathology. Decoction of lingonberry leaves is used in nephropathy and edema in pregnant women, in diabetes mellitus in pregnant women, as an adjunct in pyelonephritis in pregnant women and in the postpartum period.


THANK YOU
FOR YOUR
ATTENTION