QUINONES

Medicinal Plants and Crude Drugs Containing Anthraquinones

Plan

- 1. The general characteristic of Anthraquinones
- 2. Physico-chemical properties of Anthraquinones
- 3. Qualitative and quantitative determination of Anthraquinones
- 4. Medicinal plants and crude drugs containing Anthraquinones

Quinones are divided into three groups: benzoquinone, naphthoquinone, anthraquinone

$$\begin{array}{c|c}
8 & 1 \\
7 & 3 \\
R & O
\end{array}$$

Benzoquinone (C₆)

Naphthoquinone (C₁₀)

$$\begin{array}{c|c}
R & O & R \\
\hline
8 & 9 & 1 \\
\hline
7 & & & & \\
R & 6 & & & & \\
\hline
0 & & & & & \\
\hline
0 & & & & & \\
\end{array}$$

Anthraquinone (C₁₄)

COENZYME Q_{10} , also known as UBIQUINONE, UBIDECARENONE, COENZYME Q, and abbreviated at times to CoQ_{10}

This oil-soluble, vitamin-like substance is present in most eukaryotic cells, primarily in the mitochondria. It is a component of the electron transport chain and participates in aerobic cellular respiration, generating energy in the form of ATP.

95% of the human body's energy is generated this way. Therefore, those organs with the highest energy requirements—such as the heart, liver and kidney —have the highest CoQ_{10} concentrations. There are three redox states of Coenzyme Q10: fully oxidized (ubiquinone), semiquinone (ubisemiquinone), and fully reduced (ubiquinol)

$$H_3C$$
 O
 CH_3
 H_3C
 O
 CH_3
 CH_3
 CH_3
 CH_3

Factors affecting CoQ₁₀ levels

Various factors **reduc**e the concentration of CoQ_{10} in different organs; the following are known:

- Use of statins reduce CoQ₁₀ levels .
- Aging, in individuals older than 20 years, reduces CoQ₁₀ levels in internal organs.
- UV exposure reduces CoQ₁₀ levels in the skin.

Coenzyme Q10 is the 3rd most sold dietary ingredient in the United States after omega-3 and multivitamins.

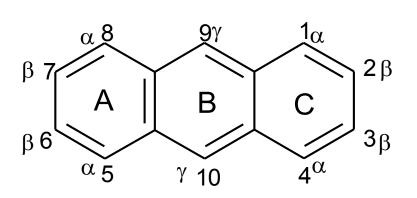
According to the Mayo Clinic, "CoQ10 has been used, recommended, or studied for numerous conditions, but remains controversial as a treatment in many areas." Further clinical results are needed to determine whether supplementation with coenzyme Q_{10} is beneficial for healthy people.

- Coenzyme Q10 helps to maintain a healthy cardiovascular system. There is evidence of CoQ10 deficiency in heart failure. Recently, CoQ10 plasma concentrations have been demonstrated as an independent predictor of mortality in chronic heart failure, CoQ10 deficiency being detrimental to the long-term prognosis of chronic heart failure. CoQ10 is available as medicine in several European countries, but is in these countries also available as a food supplement.
- There are several reports concerning the effect of CoQ₁₀ on blood pressure in human studies. A recent (2007) meta-analysis of the clinical trials of CoQ₁₀ for hypertension reviewed all published trials of coenzyme Q₁₀ for hypertension, and assessed overall efficacy, consistency of therapeutic action, and side-effect incidence. Meta-analysis was performed in 12 clinical trials (362 patients) comprising three randomized controlled trials, one crossover study, and eight open-label studies. The meta-analysis concluded that coenzyme Q₁₀ has the potential in hypertensive patients to lower systolic and diastolic blood pressure without significant side-effects.
- \bullet CoQ₁₀ is also being investigated as a treatment for cancer, and as relief from cancer treatment side-effects.

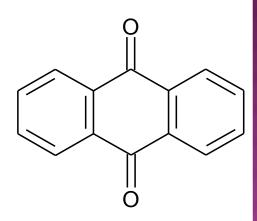
Besides endogenous synthesis, CoQ_{10} is also supplied to the organism by various foods. However, despite the scientific community's great interest in this compound, a very limited number of studies have been performed to determine the contents of CoQ_{10} in dietary components. $(CoQ_{10} \text{ concentration } [mg/kg])$

Food	C [mg/kg])	Food	C [mg/kg])	
Beef heart	113	Soybean oil	54-280	
Beef liver	39-50	Olive oil	4-160	
Beef muscle	26-40	Grapeseed oil	64-73	
Chicken heart	116.2-132.2	Sunflower oil	4-15	
sardine	5-64	peanuts	27	
salmon	4-8	walnuts	19	
tuna	5	sesame seeds	18-23	
parsley	8-26	pistachio nuts	20	
broccoli	6-9	avocado	10	

Anthraquinone (9,10-anthrachinon) is an aromatic organic compound. It is oxidized derivative of anthracene



Anthracene



Anthraquinone

The relationships between oxidized and reduced forms of anthraquinone nucleus are shown:

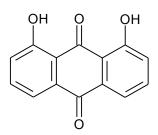
anthraquinone

CLASSIFICATION

Anthraquinones divided into two groups: <u>monomers</u> and <u>dimers</u> (*dianthrones*) of the anthrone skeleton.

Monomers

According to disposition hydroxyl groups anthraquinones could be divided on two subgroups: **chrysazin derivatives and alizarin derivatives**.



OH

Chrysazin (emodin)

(1,8-dihydroxyanthraquinone)

Alizarin

(1,2- dihydroxyanthraquinone)

R₁=CH₃, R₂=H – chrysophanol R₁=CH₃, R₂=OH – emodin R₁=CH₂OH, R₂=H – aloe-emodin R₁=COOH, R₂=H – rhein

Dimers

Depending on type of connection dimers could be divided on <u>dimers with</u> <u>single bond</u> and <u>condensed</u>.

Dimers with single bond – occur as reduced (connected to γ -C) – *chrysophanoldianthrone*, as oxidized (to α - or β -C) – *cassianine*

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Hypericine

PHYSICAL CHEMICAL PROPERTIES

- Yellow, orange or red crystals;
- ➤ When heating sublimable
- They are soluble in:
 - <u>free aglycons</u> in ether, chlorophorm, benzen; <u>not</u> soluble in water:
 - <u>anthraquinone glycosides</u> in water, aqueous-alcoholic solutions, <u>not</u> soluble in ether, chlorophorm, benzen;
 - •aglycons and glycosides in aqueous solution of alkali.
- Fluoresce yellow, red, orange and violet in UV-light.

QULITATIVE IDENTIFICATION

Bornträger's test

Chrysophanol (yellow)

react

don't react

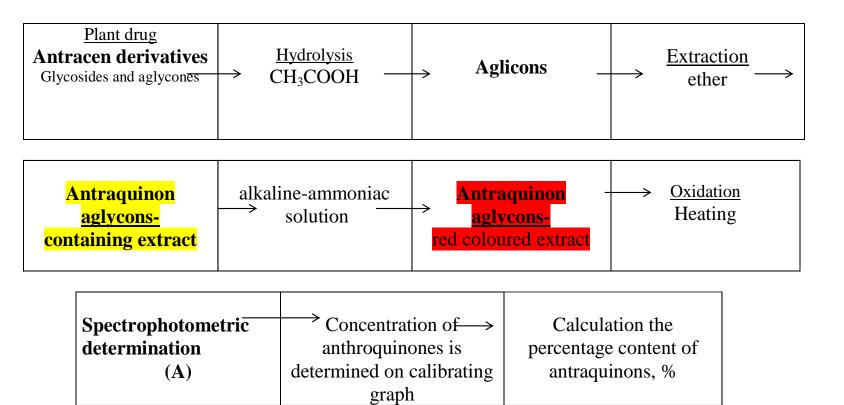
Emodin (yellow)

react

react

QUANTITATIVE DETERMINATION

Spectrophotometry



PHARMACOLOGIC ALACTIVITY

- >laxative
- >to treat nephrolithiasis
- **>**antispasmodic
- **>**diuretic
- **>**anti inflammatory
- **>**antiviral
- **>**anticancer
- **Antidepressant**



Side Effect

All anthracene glycozide drugs <u>should not be taken</u> <u>continuously (in cases of chronic constipation)</u> over a prolonged period because disturbances of water and electrolyte balance occur (potassium loss). They should not be used <u>during pregnancy</u> (reflex stimulation of the uterus) <u>and lactation</u> (the aglycones partially pass into the breast milk), or <u>in cases</u> <u>intestinal obstruction</u> (risk of intestinal rupture).

Anthraquinones are partly conjugated with glucuronic and sulfuric acids and are excreted in the urine, which then takes on a deep yellowish brown color and turns red to reddish brown upon becoming alkaline.

Cascara Bark – Cortex Rhamni purshiani Cascara sagrada – Rhamnus purshiana DC (Frangula

purshiana DC)

Fam. - Rhamnaceae

It is native to western North America.

The bark is brownish to silver-grey with light splotching.

The bark is harvested mostly from wild trees. Once stripped from the tree, the bark is aged for about 1 year to make its effect milder.

(Ph. Eur. USP)

The drug consist of the quilled channeled pieces, 1-5 mm thick and varying in length and width, fairy smooth, mostly slightly shiny, with occasionl horizontally elongated lenticels, and frequently covered with lichen and moss. Upon careful scrapping, red colored tissue becomes visible. The inner surface is yellowish-brown and finely striated longitudinally. The fracture is short and granular, and in the inner part, somewhat fibrous.

If the <u>inner surface</u> is spotted with ammonia solution, it takes on red color (*Bornträger's test*)



Cascara Sagrada

• Act . Const.

- 6-9 % anthracene derivatives.
- Cascarosides A,B,C and D;
- Two aloins, barbaloin derived from alor emodin antrones;
- A number O-glycosides derived from emodin, aloe-emodin, crysophanol and free aglicones.
- Other important constituents include resins, tannins, and lipids which make up the majority of the other bark ingredients.

HO OH OH OH

cascarosides

The are 2 proposed mechanisms of anthracen derivatives laxative effect:

- 1. Influence on colonic motility (stimulation of propulsive contractions and inhibiting stationary contractions), which results in accelerated intestinal passage as well as a reduction in fluid absorption.
- 2. Influence on secretion process (stimulation of mucous and active chloride secretion), which results in increased fluid secretion.

Defecation occurs after 8-12 hours.

Uses

- Cascarosides exhibit a cathartic effect that induces the large intestine to increase its muscular contraction (peristalsis), causing a bowel movement.
- In1890 in America it replaced the berries of the European buckthorn (R. cathartica) as an official laxative.

Cautions

- Only the aged bark (at least 1 year prior to use) should be used.
- Fresh cut, dried bark causes vomiting and violent diarrhea.

Frangula or Buckthorn Bark – Cortex Frangulae Buckthorn – Frangula alnus (Rhamnus frangula)

Fam. - Rhamnaceae

It is found in Europe. Commercial supplies are available from Russia and Ukraine.

The plant differs from the common buckthorn, in that it does not possess thorn; it has leaves with 7-8 pair veins.

The bark occurs in quills 0,5-2mm thick. It has a purplish cork and transversely elongated, whitish lenticels. On removing the outer cork cells, a dark crimson inner cork is exposed. (*Bornträger's test*)

Act. Const.

6,0% hydroxyanthracene derivatives calculated as glucofrangulin A;

The fresh bark contains anthranols and anthrones which are unstable and readily oxidize to the correspondent anthraquinones.

Glucofrangulin A

 $\textbf{Glucofrangulin} \ B$



° Frangulin B

Frangulin A

Uses. Only the aged bark should be used. Fresh cut, dried bark causes vomiting and violent diarrhea. **Syrup, dry extract, "Rhamnil" – laxative**,

Common buckthorn fruit – Fructus Rhamni catharticae

Common (european) buckthorn - Rhamnus cathartica

Fam. - Rhamnaceae

Common buckthorn is a shrub or small tree that can grow to 7.6 m in height. The bark is dark gray and the inner bark is orange (easily seen when the tree is cut). Twigs are usually tipped with a sharp spine. The leaf arrangement is usually subopposite, but examples of opposite and/or alternate arrangements are commonly found. Leaves are dark green, oval 3.8-7.6 cm long, slightly serrate with 3 to 4 pairs of curving veins and a somewhat folded tip. Flowering occurs in the spring, when yellow-green, 4petaled flowers develop in clusters of 2 to 6 near the base of the petioles. Plants are dioecious (male and female flowers occur on separate plants).



Fruits are small, black berries that are 0.6 cm in diameter, which have a wrinkled and shrunken surface. At the top, there are the remains of the 4-part pistil. The stalk, or part of it, which is often still present, is thin and somewhat curved. Inside, the 4 locules each contain the hard, ovoid and keeled seed.

Act const.

- Oxidised anthracen derivatives 4%: frangulaemodine, crysophanol, glucofrangulin, frangulin,
- Reduced anthraquinones;
- Flavonoids;
- Pectin,
- Gum,
- Organic acids.

Uses: Tea – laxative.

Rhubarb root – Radices Rhei Rhubarb – Rheum palmatum L. Fam. - Polygonaceae

Native to the northwestern China and eastern Tibet, also cultivated to some extent in Europe.

The drug consist of the whole or cut, peeled underground parts (turned shaped roots with very small rhizomes). The ochre-yellow to brownish pieces are often covered on the outside with powder, exhibiting orange striations or orange-red mottling. The fracture is granular, crumbly (not fibrous) and reddish brown. Odor is characteristic and faintly smoky; taste is somewhat bitter and harsh.









ACT. CONST

1. Anthraquinone O-

glycosides of aloe—emodin, emodin, chrysophanol and physcion; dianthrone glycosides of rhein (sennosides A and B) and their oxalates; free anthraquinones mainly aloe emodin, chrysophanol, emodin, physcion and rhein.

2. Tannins

Hydrolysable and condensed including glucogallin, free gallic acid, (–)-epicatechin gallate and catechin.

Anthraquinone aglycones

Homodianthrones

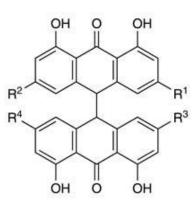
rheidin A

rheidin B

rheidin C

sennidin C,D

Dianthrone aglycones



aloe-emodin dianthrone chrysophanol dianthrone emodin dianthrone physcion dianthrone	CH ₂ OH CH ₃ CH ₃ CH ₃		H OH OCH ₃		CH ₂ OH CH ₃ CH ₃ CH ₃		H OH OCH
sennidin A,B	COC	ЭН	Н		COO	Н	Н
Heterodianthrones							
palmidin A (CH_3	OH	4	CH	2OH	H	
palmidin B (CH ₃	H		CH	2OH	Н	
palmidin C	CH ₃	H		CH	3	OH	ĺ.

OH

OCH₃

CH₃

CH₃

CH₃

CH₂OH

R1

 R^2

 R^3

COOH

COOH

COOH

COOH

Н

H

Н

Other constituents

Calcium oxalate, fatty acids, rutin, resins, starch (about 16%), stilbene glycosides, carbohydrates, volatile oil (trace) with more than 100 components.

Uses

The laxative action of anthraquinone derivatives is well recognised. Rhubarb also contains tannins, which exert an astringent action. At low doses, rhubarb is stated to act as an antidiarrhoeal because of the tannin components, whereas at higher doses it exerts a cathartic action.

Side—effects, Toxicity

Rhubarb leaves are toxic because of the oxalic acid content and should not be ingested. A case of anaphylaxis following rhubarb ingestion has been documented.

Contra-indications

For contra—indications and warnings associated with anthraquinone—containing drugs. The astringent effect of rhubarb may exacerbate, rather than relieve, symptoms of constipation. It has been stated that rhubarb should be avoided by individuals suffering from arthritis, kidney disease or urinary problems.

Aloe – Folia Aloes Aloe arborescens A. Barbadensis (A. vera) Fam. - Liliaceae

(Ph. Eur. USP)

Aloe arborescens occurs naturally in areas of South Africa, Mozambique, Zimbabwe and Malawi

The aloes are typical xerophytic plants that have fleshy leaves, usually have spines at the margins. The leaves are cut in March and April and placed cut-end down on a V-shaped trough. The latter is inclined so that the latex that is contained in specialized cells just beneath the epidermis of the leaf can be led into a vessel. The latex is evaporated in a copper kettle and, when of the proper consistency, is poured into metal containers and allowed to harden.





Aloes consist of the dried and concentrated cell sap from various species of the genus Aloe.

Act. Const

- Mostly 1,8-dihydroxyanthracene derivatives with 25-49% aloin.
- The drug also contains low amounts of aloe-emodin and chrysophanol and their glycosides.
- Other characteristic constituents are 8-glucosylchromone derivatives known as "aloe-resin"
- Bitter glycosides (phenyl-2-pyrone derivatives) (*A.vera* doesn't contain).
- Polysaccharides.
- Glycoproteins.

Uses

Aloeresin A

CH₂OH

aloin

O-Ara

Due to its anthraquinone derivative content, Aloes is used as a potent laxative. Some C-glucosyl chromones have exhibited strong antiphlogistic effects

Martindale 35th edition(G85) WHO volume 1 1999

Aloe vera

The mucilaginous fresh juice from the leaves is used in cosmetics and it has trade name *Aloe vera*.

Aloe vera is obtained from the mucilaginous tissue in the centre of the Aloe vera leaf and consists mainly of polysaccharides and lipids. It should not be confused with aloes, which is obtained by evaporation of water from the bitter yellow juice that is drained from the leaf. Unlike aloes, aloe vera does not contain any anthraquinone compounds and does not, therefore, exert any laxative action.





Aloe vera – dried drug substance (leaf gel).

Act. Const

Aloe vera is reported to contain mono- and poly saccharides, tannins, sterols, organic acids, enzymes (including cyclooxygenase), saponins, vitamins and minerals.

It possess re-epitelising, anti-erythematous, moisture-binding and absorptive properties.

Hypoglycaemic activity has been documented for an aloe vera fresh and preserved.

Uses:

Traditionally, aloe vera has been used in ointments and creams to assist the healing of wounds, burns, eczema and psoriasis.

Horse sorrel roots – Radices Rumicis

Horse sorrel (Asiatic dock) – Rumex confertus

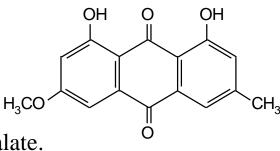
Fam. - Polygonaceae

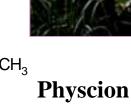
Native to the eastern Europe, Siberia, Kazakhstan. The drug consist of the whole or cut, underground parts (chunky straight roots with small rhizomes).

The outer surface is brown, with slight wrinkles. The rough transverse surface is yellowish-brown. Odor slight, specific. Taste slightly bitter, astringent.

Act const.

- emodin, chrysophanol, aloe-emodin,
- physcion,
- tannins,
- flavonoids,
- free gallic acid,
- resin, vitamin K,
- volatile oil (trace), Calcium oxalate.





Uses

At low doses, rhubarb is stated to act as an antidiarrhoeal because of the tannin components, whereas at higher doses it exerts a cathartic action.

Senna leaf – Folia Sennae; Alexandrian senna – Cassia acutifolia; Tinnevelly senna - Cassia angustifolia. Fam. - Fabaceae

BHC 1992, BHP 1996, BP 2007, Complete German Commission E, ESCOP 2003, Martindale 35th edition, Ph Eur 2007, USP, WHO volume 1 1999

Cassia angustifolia is native to Arabia, and it is cultivated in India. Cassia acutifolia is native and cultivated in Africa.

The drug consist of entire, lanceolate to narrowly lanceolate, pinnate leaflets having a short petiole and measuring 2-6cm long and 7-12 mm wide. The leaflets have asymmetrical base and a tin, stiff and brittle, light green lamina which appears as if glabrous. The leaflets are often marked with transverse or oblique lines. Odor is faint, characteristic, Taste is sweetish at first, then bitter.



ACTIVE. CONST.

Dianthrone glycosides (sennosides A, A₁, B-F) more than 3%;

Anthraquinone glycosides (small amounts):

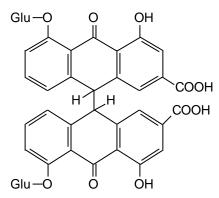
Rhein-8-glucoside and rein-8-sophoroside;

Hydroxyanthracene glycosides -2.5%;

Mucilage -2-3%;

Flavonoids;

Essential oil -0.05%.



Sennosides A - C

Uses

It is one of the most frequently botanical employed laxative remedies. The drug is used for acute constipation and in all cases in which defecation with a soft stool is advisable (hemorrhoids, surgical interventions in the rectum, etc.) no longer than 1-2 weeks.

Making the tea

Pour warm or hot water over 0,5-2g of cut dried leaf. Steep for 10-20 min and then strain. ("resins" which are responsible for causing abdominal pains, are dissolved in cold solution). The laxative effect take place 10-12 hours after drinking a tea.

Alexandrian senna pods – Sennae fructus acutifoliae; Tinnevelly senna pods - Sennae fructus angustifolia

Alexandrian senna – Cassia acutifolia; Tinnevelly senna – Cassia angustifolia. Fam. – Fabaceae

The drug consist of flattened, brownish green, membranaceous-leatheraly pods, which are up to 5 cm long and about 15-18 (*C. angustifolia*) or 20-25(*C. acutifolia*) mm wide and slightly reniform. The fruits normally contain 5-7 or 7-10 seeds, which are more or less cordate, whitish to grayish green and very hard with a dimpled, reticulately ridged surface. Odor is faint, characteristic. Taste is mucilaginous and sweetish at first, then bitter and harsh.

Act. Const.

The anthranoid composition is very similar to Sennae folium, but with a different content of sennosides and other ahthraquinone derivatives depending of the *Cassia* species.

Uses

Same as for Senna leaf. In spite of their somewhat higher anthracen content (in comparison to leaf, senna pods have a somewhat milder action and therefore are preferred for children. The milder action is dependent not on the absence of "resins" in the pods, but rather because pods contain only a small amount of the (strongly active) aloe-emodine glucoside.



St.Jon's wort herb — Herba Hyperici St.Jon's wort - Hypericum perforatum, Fam. - Clusiaceae

American Herbal Pharmacopoeia, BHP 1996, BP 2007, Complete German Commission E, ESCOP 2003, Martindale 35th edition, Ph Eur, USP, WHO volume 2

The material of commerce is obtained from wild collection in Europe, western Asia, and the US.

The drug consist of the whole or cut, dried flowering tops. Particularly distinct are the yellow to yellowish brown flowers, the petals have numerous dark spots and steaks; the lanceolate sepals are acute and at the time of flowering, twice as long as the ovary. Each flower contains about 60 stamens, usually fused into 3 groups. The glabrous light green and ovate-elliptical leaves are up to 3,5 cm long, often folded and shriveled with the entire margin and clearly visible, translucent dots. The yellowish green and round stem fragments show two longitudinal ridges opposite to each other. Odor is

mildly aromatic and somewhat balsamic; taste is bitter

and acrid.



ACT. CONST.

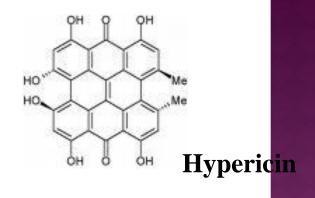
- \bullet Anthraquinone derivatives 0.1-0,3%,
- Flavonoids The concentrations of rutin, hyperoside and isoquercitrin have been reported as 1.6,
- 0.9 and 0.3%, respectively%.
- Tannins 8–9%; Oligomeric procianidins;
- > Essential oil (traces). Uses

Used as an antidepressive treatment for mild to moderate forms of endogenous, neurotic and larvate depression. It is also used for psychovegetative disturbances such as states of anxiety and nervous restlessness. Phytomedicines: **Tincture**; **DEPRIM**®

External: Oily Hypericum preparations for treatment acute and contused injuries, myalgia and first degree burns.

Side effect

Photosensitization is possible, especially in fair –skinned individuals.





Madder rhizome and root — Rhizomata et radices Rubiae Madder (dyer's-madder) — Rubia tinctorum Fam. Rubiaceae

The stalks of the Madder are so weak that they often lie along the ground, preventing the plant from rising to its maximum height of 8 feet. The stalks are prickly. The herb is used as fodder for animals.

The flower-shoots spring from the joints in pairs, the loose spikes of yellow, starry flowers.

The thick, fleshy fibers that compose the perennial are about 1/4 inch thick, and from their joining, or head, side roots run under the surface of the ground for some distance, sending up shoots. The main and side-roots are dried separately, their products being regarded as different, that of a young, parent root being the best.

The best European Madder is Dutch, but that from Smyrna is said to be even finer. The Turkey-red and other shades are adjective dyes, different mordants bringing many shades of red, pink, lilac, purple, brown, orange and black.

As a dye it colours milk, urine and bones, so that experiments in the growth of bones can be conducted with its help.



Act. const.

The root contains rubian, rubiadin, ruberythric acid, purpurin, tannin, sugar and especially alizarin.

- Pseudopurpurin yields the orange dye and xanthopurpurin the yellow.
- The astringent taste, slight odour and red colour, are imparted to water or alcohol.

Uses

Dry extract, «Cystenal», «Marelin» - litholitic, spasmolytic, diuretic.

- Although not as a general rule employed medicinally, Madder has been reputed as effectual in amenorrhoea, dropsy and jaundice.
- When taken into the stomach it imparts a red colour to the milk and urine, and to the bones of animals without sensibly affecting any other tissue. The effect is observed most quickly in the bones of young animals and in those nearest to the heart. Under the impression that it might effect some change in the nervous system, it has been prescribed in rachitis (rickets), but without noticeable favourable results.

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