

REFERENCES

Aesculus hippocastanum HORSE CHESTNUT

1. According to Fluck (Hans Fluck: Medicinal Plants, 1988 W.Foulsham & Co. Ltd. ISBN 0-572-00996-8.) the parts of horse chestnut used are the fresh seeds, freed from the seedcoat, more rarely the bark from the branches or the fruit walls.

Constituents are described as the saponin aescine, flavones, coumarin and tannins. Their action is to strengthen the blood vessels, to prevent thrombosis, to strengthen the veins and to relieve haemorrhoids. The seeds are poisonous and have resulted in accidents to children. Previously the seeds and dried bark were used in domestic medicine for bleeding piles and bleeding of the womb. Today, under medical control, extracts of horse chestnut either as drops or injections are used for venous stasis, varicose veins and thrombosis.

2. Lust (J.Lust: The Herb Book, 1986, 16th. impression, Bantam Publishing. ISBN 0-553-17273-5.) gives alternative names as Buckeye or Spanish chestnut. Uses are listed as astringent, expectorant, treatment of leg ulcers, varicose veins, haemorrhoids, recurrent neuralgia and sunburn. The bark is useful for diarrhoea and the fruit for bronchitis and respiratory catarrh. In European folk medicine, carrying the fruit in one's pocket is believed to be good for preventing and curing arthritis. Lust also warns that the leaves, seeds and green capsule shells sometimes cause poisoning if taken in sufficient amounts. Roasting the seeds seems to destroy the poison in them.

3. Mrs Grieve (M.Grieve: A Modern Herbal, 1984 Savvas Publishing. ISBN unknown.) tells how the bark has tonic, narcotic and febrifuge properties and is used in intermittent fevers, given in an infusion of 1oz to the pint in tablespoonful doses, three or four times daily. As an external application to ulcers this infusion has also been used with some success. The fruits have been employed in the treatment of rheumatism and neuralgia and also in rectal complaints and for haemorrhoids.



4. Hoffmann (D.Hoffmann: The Herb Users Guide. 1987 Thorsons Publishing. ISBN 0-7225-1288-0.) lists the constituents as :- Saponins, tannins, flavones, starch, fatty oil, the glycosides aesculin and fraxin. He recommends horse chestnut as an astringent and circulatory tonic and describes its action as unique on the vessels of the circulatory system. It seems to increase the strength and tone of the veins in particular, it may be used internally to aid the body in the treatment of problems such as phlebitis, inflammation of the veins, varicosity and haemorrhoids. Externally it may be used as a lotion for leg ulcers.

5. In Potter's (R.C.Wren: Potter's New Cyclopaedia of Botanical Drugs and Preparations, 1985 8th impression, published C.W.Daniels. ISBN 0-85032-009-7.) we read that horse chestnut is a tonic, narcotic, febrifuge and astringent. The fruits have been employed with success in treatment of rheumatic and neuralgic disorders, also for rectal complaints, backache, piles etc.

The term horse chestnut arises from the fact that horses are said to eat the fruit and by it cure coughs.

6. Dr Winter Griffiths (H. Winter-Griffith: The Vital Vitamin Fact File. 1988. Thorsons Publishing ISBN 0-7225-1693-2.) lists the known effects: - Increases bleeding time (a laboratory test for blood clotting), irritates mucous membrane. Eating even a few nuts can cause toxic symptoms. Unproved speculative benefits are as a sunscreen in 4% solution.

7. Weiss (R.F. Weiss. Herbal Medicine. (translated from the 6th. German edition of Lehrbuch der Phytotherapie by A.R. Meuss). The Bath Press. 1986. ISBN 0-906584-19-1.) refers to *Aesculus hippocastanum* as Horse Chestnut. This provides a valuable remedy specifically for diseases of the venous system, in the shiny brown fruits. Distinction must be made between the Sweet Chestnut *Castanea vesca*, which produces edible chestnuts - these are not used medicinally. The leaves of the sweet chestnut are used as an expectorant in bronchitis and whooping cough.

Extracts from the seed of the horse chestnut act on the connective tissue barrier between blood vessels and tissue, where nutrients and gases diffuse, inhibiting exudation and the development of oedema and reducing vascular fragility. The wall of the vein becomes less permeable, and this inhibits oedema.

Active principle

Two principles found in the chestnut have been identified as the most important: aesculin, which is a coumarin derivative, and aescin, a saponin. In addition there are a number of flavones.

Aescin is the major principle. Like all saponins it has haemolytic properties, though this is minimal with therapeutic doses, when it does not interfere. The special characteristic of aescin is its effect on capillary permeability. The number and diameter of the small pores in the capillary membranes is reduced, making them less permeable to fluids. In animal experiments, the anti-oedematous activity of aescin was found to be six hundred times that of the classical drug rutin. An important second effect is an improvement of the tone in the walls of the vein.

Saponins are found in many medicinal plants, some being neutral, others acid. Many saponins, primula saponin for instance, are well known cough remedies. The term saponin derives from the ability of these compounds to reduce the surface tension of water, producing a foam in the same way that soap (sapo) does. It suggests good surface absorption. In the case of aescin the effect is particularly on the vascular walls, increasing the wettability of the inner walls. This makes it easier for tissue fluids to drain into the capillaries. Increased oncotic (= colloid-osmotic) pressure causes perivascular oedema to be sucked into the capillaries at the same time.

The anti-oedematous effect is very useful in a whole range of conditions, not only acute thrombophlebitis, but also to reduce swelling within bruises, fractures, brain trauma and even strokes, and to remove fluid from the spinal ganglia and relieve the pressure on nerve strands in intervertebral disc abnormality.

Aescin is given by mouth for varicose veins, though it can be applied externally in the form of ointments or gels. The preparations must not be massaged on, but applied gently to avoid inflammation of the vein.

The German Drugs Commission issued a statement that it was important to follow the manufacturer's directions carefully when using β -aescin i.v. The daily dose for adults should not exceed 20mg, that for infants of up to 3 years is 0.1mg per Kg of body weight, whilst the daily dose for children aged 3 to 10 years is 0.2mg/Kg. Doctors were also asked to monitor kidney function carefully, particularly with postoperative use of aescin, and to report any relevant observations.

8. In *Extracts From Nature* (Christina Probert Jones: Marks and Spencer: *Extracts from Nature*. 1989 Tigerprint. no ISBN No.) it is reported to; tone veins, have a strong action on the circulation and so is used to treat varicose veins, haemorrhoids, phlebitis and leg ulcers.

9. Stuart et al (M.Stuart: *The Encyclopaedia of Herbs and Herbalism*. 1986. Orbis ISBN 0-85613-700-6.) also lists uses; tonic, narcotic, antipyretic. Bark employed traditionally in intermittent fevers. Combined action of constituents of seeds strengthens arteries and veins, preventing thrombosis. Seed extract relieves haemorrhoids. The reference also points out that the seeds are poisonous and should be used by medical personnel only.

10. In an *Illustrated book of Herbs* (S.Bunney: *The Illustrated Book of Herbs*. 1984. Octopus ISBN 0-7064-1489-6.) by Bunney we read that externally horse chestnut is used to treat cuts, frostbite, ringworm and haemorrhoids. A coumarin component aesculoside is included in some sunscreen preparations.

11. In a data sheet from *Plantextrakt* (through Aston Chemicals) we read that it contains triterpensaponins. It is characterised by the reduction of the permeability of the capillaries, anti-oedematous. It is used for the treatment of oedemas, haemorrhoids, preparation for varicose veins.

12. In a data sheet from *Exsymol* (through Paroxite) we learn that it contains triterpenic saponosides and flavonoids (quercetine and kaempferol glycosides). It also contains amidon, catechic tannins and leucoanthocyanes, amino acids, adenine and group B vitamins. It is astringent and has vitaminic activity. It is recommended for all anti-sebhorreic treatment, anti-spot preparations, etc.

13. In a data sheet from William Ransom we read that it is an astringent, stimulating and anti-inflammatory. Medicinally it is a tonic for varicose veins, diuretic, anti-inflammatory. It is a treatment for haemorrhoids, phlebitis and diarrhoea.

14. Schauenberg and Paris (P.Schauenberg, F.Paris: *Guide to Medicinal Plants*. 1990 First paperback edition (Paris 1974). Lutterworth Press ISBN No. 0-7188-2820-8) say that it contains various saponins, of which the most important is aescine; tannins; a glycoside, esculoside, whose aglycone is esculetol (coumarin); and flavones. It is an effective antiphlogistic and diuretic in cases of venous origin (varicose veins, haemorrhoids). It increases the rate of blood circulation and is used in cases of gastritis, enteritis and prostate malfunction. A fluid extract is made to protect the skin from the harmful effects of the sun. The horse chestnut, originally from Asia Minor, was introduced into central Europe in the 16th century. In 1720 it was recommended as a febrifuge in place of quinine.

15. Kay van Rietschoten: *Plants with anti-inflammatory action*. *The British Journal of Aromatherapy* Vol.1, numbers 3/4, Autumn/Winter 1990. The fruit and the bark of the horse chestnut have traditionally been used for ailments of the circulatory system, including varicose ulcers, haemorrhoids, chilblains and thrombophlebitis.

Research has shown (Berti et al. 1977) that the horse chestnut saponin aescin has an anti-exudative property that it increases the tone of isolated veins.

It is active in the first phase of inflammation, which is characterised by an increased vascular permeability of the venous side of the circulation.

Experiments on animals (Longiave et al, 1978) indicate that aescin stimulates the production and release of prostaglandins of the F-alpha type, which induce contraction of veins. This contraction is antagonised or reduced by the inhibition of cyclooxygenase, the enzyme responsible for prostaglandin formation from arachidonic acid.

Research into the anti-exudative property of aescin using further animal experiments (Rothkoph, n.d.) showed that aescin has some 'sealing' effect on the walls of the capillaries. It was able to antagonise the effect of bradykinin (a potent increaser of vascular permeability) by normalising the permeability of the plasma/lymph barrier dose-dependently (dependency?).

Weiss states that the aescin reduces the number and diameter of the small pores in the capillary membrane, making them less permeable to fluids. It also makes it easier for tissue fluids to drain into capillaries.

The ability of aescin to improve the venous return via local synthesis of prostaglandin F₂ alpha coupled with the anti-exudative property explains the use of *Aesculus* in the treatment of haemorrhoids and varicose veins.

16. In the Lawrence review of Natural Products July 1991 (updated Feb 1995) we read that the chestnuts are members of the genus *Aesculus*. *A. hippocastanum* (Horse Chestnut), *A. californica* (California Buckeye) and *A. glabra* (Ohio buckeye). There is also a related species of the genus *Castanea dentata* but this has largely been exterminated by blight.

Has been used in traditional medicine and for a variety of commercial preparations. Extracts of the bark have been used as a yellow dye and the wood has been used for furniture, packing cases etc. In the western United States, the crushed unripe seeds of the California buckeye were scattered into streams to stupefy the fish (caused by the saponins - ACD), and the leaves were used as a remedy for congestion. The seeds are toxic, and various methods have been tried to detoxify them, including burying them in swampy ground over winter, then boiling them before eating. The Indians roasted the poisonous nuts, peeled and mashed them, then leached the meal in lime water for several days, creating a meal from which bread could be made. The horse chestnut is used as a traditional remedy for arthritis and rheumatism. Extracts are made commercially available for oral, topical and parenteral administration for the management of varicose veins and haemorrhoids.

Some members of the *Castanea* are used in cooking. Most commonly, the sweet chestnut (*Castanea sativa*) is roasted and used in stuffings and holiday meals. The chestnut is derived from a genus separate from the horse chestnut and represents an edible chestnut of commercial importance.

Chemistry: The seed oil contains about 65-70% of oleic acid. Several species contain phenolic acids, coumarins such as aesculetin, cyclitols and saponins such as aescin. Members of the genus produce the toxic glycoside esculin (aesculin in some texts). This poorly characterised toxin is found in the twigs, sprouts, leaves and nuts.

Pharmacology: Medicinally, an extract of the plant containing 50mg of triterpene glycosides decreases venous capillary permeability and appears to have a "tonic" effect on the circulatory system.

The bark of the horse chestnut has been found to possess anti-inflammatory activity, primarily due to the presence of steroids stigmasterol, alpha-spinasterol and beta-sitosterol.

Toxicology: *Aesculus* is classified by the FDA as an unsafe herb; all members of this genus should be considered potentially toxic. A number of components have been attributed toxic properties including glycosides and saponins. Potential toxins identified in the genus include nicotine, quercetin, quercitrin, rutin, saponin and shikimic acid.

The most significant toxic principle is esculin. Poisoning is characterised by muscle twitching, weakness, lack of coordination, dilated pupils, vomiting, diarrhoea, depression, paralysis and stupor. The nut is the most toxic part of the plant. Children have been poisoned by drinking tea made from the leaves and twigs and by eating the seeds; deaths have been reported following ingestion. Amounts as little as 1% of a child's weight may be poisonous. Gastric lavage and symptomatic treatment have been suggested.

The LD50 of a single dose of water-soluble portion of alcoholic extracts of horse chestnut seeds was calculated to be 10.6 mg/g body weight of chicks and 10.7 mg/g in hamsters. Extracts of the seeds of the Ohio buckeye were nontoxic to chicks and hamsters fed 80 mg/g in this study.

Honey made mainly from the California buckeye has been reported to be toxic. A potential association between nasal cancer and long-term exposure to wood dusts, including dust from the chestnut trees has been reported. Aflatoxins have been identified in some commercial skin cleansing products containing horse chestnut; since aflatoxins are potent carcinogens that can be absorbed through the skin, it is imperative that strict quality control be applied to topical products containing potentially contaminated horse chestnut material.

Horse chestnut pollen is allergenic and often associated with the development of allergic sensitization, particularly in urban children.

Not recommended for internal use, to be considered toxic.

17. In a data sheet from Maruzen Pharmaceuticals (through K&K Greeff) we read that the nuts are used to prepare an extract that is astringent, antiphlogistic and haemostatic .

18. In a data sheet from Indena (through K&K Greeff) we read that the seeds are used, which contain escin and other triterpenic saponins, purinic derivatives, aminoacids, vitamins of the B group, flavonoids.

It is a mild astringent, skin lightener. Coadjutant in treatment of cellulitis. It is used in tonics, lotions for reddish or sensitive skins, sun products, clearing preparations for hands. Foam baths and personal hygiene preparations. Products for the treatment of cellulitis.

19. Chiej (Chiej, R.: The Macdonald Encyclopaedia of Medicinal Plants. 1984, reprinted 1988. Macdonald Orbis. ISBN No. 0-356-10541-5 (hb), -10542-3 (pb).) refers to *Aesculus hippocastanum* or *Hippocastanum vulgare* as Horse Chestnut. This tree originates in the Balkan Peninsular and was taken to Italy by the Sieneese doctor P.A.Mattioli, whence it spread throughout western Europe, including Britain. The bark, the pericarp and the seeds are used.

The bark contains esculin, tannin, ash. The pericarp contains ethereal oil, saponin, pectin, potash, calcium, phosphorus. The seeds contain phytosterol, starch, sugar, linoleic acid, palmitic acid, stearic acid.

The bark is astringent, vasoconstrictive, antithermic. The pericarp is peripherally vasoconstrictive. The seeds are tonic and decongestant.

The form of use is as decoction, powder, tincture, medicinal wine, ointment, fluid, dry and semi-fluid extracts, suppositories, poultice in powder form.

Horse chestnuts can be made into a type of edible flour. If the seeds are roasted they can be used as a substitute for coffee.

20. In a data sheet from Haarman and Reimer we read that it is antiphlogistic, spasmolytic, astringent, and promotes circulation. It contains several methyl esters of kaempferol and quercetin with detectable amounts of aescin.. Fructose, galactose, maltose, raffinose etc. have been the sugars found.

21. Harry (R.G.Harry: The Principles and practice of modern cosmetics - vol 2. Cosmetic Materials. 2nd. edition 1963 published Leonard Hill.) refers to aesculin, or polychrome, esculinic acid. 6,7-dihydrocoumarin-6-glucoside. Aesculin is obtained from the inner bark of the horse chestnut tree (*Aesculus hippocastanum*), it occurs in the form of white crystals, which decompose at 205°C.

Like other fluorescent materials, aesculin absorbs ultraviolet rays and is employed in some toiletry preparations as a sun-screening agent. It is sometimes employed to enhance the effect of heliotherapy. It has been considered to have the action of the citrous flavonoid compounds found in citrous fruits, rose hips and blackcurrants which are claimed to have an effect in maintaining normal conditions in the walls of minor blood vessels when administered orally.

So far as is known, in concentrations of 4% and less in toilet preparations, aesculin appears to be innocuous.

22. In a botanical information sheet from A.Webster of English Grains we read that the seeds are used which contain escin (triterpene glycosides).

The effect is antiexudative, improving the circulation. The escin of horse chestnut acts on the symptoms of all forms of chronic venous insufficiency such as cramps in the calves, itching, pain and sensations of heaviness in the legs, varicose veins and postthrombotic syndrome. Additional fields of application: ulcers of the leg as well as posttraumatic and postoperative swelling of soft tissue.

Since the middle of the last century horse chestnuts have been used in the treatment of various intestinal diseases such as chronic diarrhoea, myxorrhoea and dysentery. They have established themselves as substitutes for red cinchona bark. A great number of approved OTC preparations for haemorrhoids and for the improvement of venous circulation contain horse chestnut extracts.

Internally, there may be the side effect of irritations of the gastro-intestinal mucosa.

23. Hutchens (Hutchens, A.R.: Indian Herbalogy of North America. 1973 First paperback edition. Shambhala. ISBN No. 0-87773-639-1.) refers to *Castanea dentata* as

Chestnut, Spanish Chestnut, Horse Chestnut, Sweet Chestnut. The leaves or inner bark are used for their tonic, mild sedative and astringent properties.

The green or dried leaves can be used, and it is considered a particular herb for whooping cough or nagging distressing coughs, controlling the paroxysmal; and in frequent hiccoughs and other irritable and excitable conditions of the respiratory organs. Fevers, ague respond to the soothing of the mucous surfaces and the nervous system, acting as an antispasmodic. *Lobellia inflata*, Blue Cohosh and *Caulophyllum thalictroides* are most successfully combined for the above mentioned.

Called Konsky cashtan in Russia, known as Horse Chestnut, does not grow wild, but has long been cultivated in European Russia, Middle Asia and Kaukaz (Eaucasus).

Folk Medicine: Its value is recognised and is used for arthritis, rheumatism, female bleeding, haemorrhoids and chronic inflammation of the intestines.

Clinically; Extracts used for bleeding haemorrhoids, varicose veins, arteriosclerosis. (I think Hutchens is confused with Horse Chestnut and Sweet Chestnut - ACD).

24. Council of Europe. Plant Preparations used as ingredients of cosmetic products. 1st. edition. Strasbourg 1989. HMSO. ISBN No. 92-871-1689-X

Index of abbreviations

c: chronic toxicity
e: eye irritation
f: skin irritation
h: subchronic toxicity
i: metabolism study
j: photosensitisation
k: phototoxicity
l: sensitisation animals
m: sensitisation man
n: mutagenicity
o: acute oral toxicity
p: acute dermal toxicity
q: special toxicity studies
r: reproduction studies
s: teratogenicity

If in parenthesis, letters indicate toxicity data concerning relevant active principles.

Aesculus hippocastanum is also known as Marronnier d'Inde (French), Rosskastanie (German), Ippocastano (Italian), Castano de Indias (Spanish), Paarde-Kastanje (Dutch).

The seeds are used.

Chemical composition

- Triterpenic saponins: 8-12% mainly escin (afrodescin, argirescin, escin [up to 14%], kryptoescin).
- Flavonoids (quercetin, quercitrin, kaempferol)
- amino acids
- purins

- Anthocyanins
- Catechic tannins up to 2%
- Phytosterols (friedelin, butyrospermol, taraxerol, triacontane, α -spinasterol)
- Coumarins (esculoside)
- Vitamins (B group, K₁, C, provitamin D)
- Fatty acids 2-5% (oleic, linoleic, linolenic, stearic, palmitic acids)
- Starch 30-40%
- Sugars 9%
- Proteins 8-10%

Intended cosmetic effects and recommended maximum concentration in cosmetic products

Tonic, astringent, "anticouperose"

up to 2% dry extract

up to 5% glycolic extract

in preparations for skin and scalp, lotions, creams and gels for cellulitis, astringent shampoos.

up to 4% dry extract

up to 10% glycolic extract in tonic baths for body and feet.

Other possible effects

Anti-oedema, vasoprotective, periferic vasoconstrictor.

Toxicological data

f anim., f man, e, l, m, o, p.

Evaluation and remarks

Group 3 (recommended for use)

Selected toxicological references

Hazelton (1980). Acute dermal LD50 study in rabbit, L 0344 B.A. 5553. Inverni della Beffa. Unpublished report.

Inverni della Beffa (1985). Horse Chestnut glycolic extract: Primary irritation on rabbit skin and assessment of eye irritation, 60/85/LFT. Unpublished report.

25. A new molluscicidal triterpenic glycoside from *Aesculus indica*. Sati O.P., Rana U.: Int. J. Crude Drug Res. 25(3) 158-60, Sep 1987.

26. In a Health and data sheet from Optima (for Coletica). Esculoside: also known as esculin, bicolorin, enallochrome, polychrome, escosyl, 6-(β -D-Glucopyranosyloxy)-7-hydroxy-2H-1-benzopyran-2-one, 6,7-dihydroxycoumarin-6-glucoside.

Esculoside is a glucoside compound extracted from the leaves and bark of the Horse Chestnut tree (*Aesculus hippocastanum*).

Toxicological data

EOCD guideline 405, concerning the study of "acute irritant/corrosive effect on the eyes", Esculoside may be considered as non irritating to the eye, according to the 91/326 EEC directive.

EOCD guideline 404, concerning the study of "acute irritant/corrosive effect on the skin", Esculoside may be considered as non irritating to the skin, according to the 91/326 EEC directive.

EOCD guideline 401, concerning the study of "oral toxicity", Esculoside did not induce abnormal toxicity in a single oral administration, at the dose 5 g/kg in distilled water. according to the 91/326 EEC directive.

Evaluated on guinea pig skin, a preparation containing 5% of Esculoside did not induce phototoxicity under UVA or UVB irradiation.

Product activity

Esculoside does the following:-

increases vasoconstriction
increases capillary resistance and veinotonicity
decreases capillary permeability.

Esculoside is used for these activities in "dermaceutical formulations" on basis of topical applications, where **capillary resistance is poor** (ecchymosis, couperosed skins, erythrosais, petechia...).

As Esculoside increases blood circulation, it is used in pharmaceutical formulations in order to treat symptoms due to **veino-lymphatic insufficiencies**; heavy legs, cramps, pains, dysaesthesia...

Esculoside is a stable hydrosoluble vitamin factor which has vitamin P actions:

the protection of several biochemical compounds (adrenaline, vitamin C...) against oxidation, increases their half life time and, as a consequence their biological activities.

the protection of adrenaline with this antioxidant action, increases adrenaline action, with a stimulation (via cyclic Adenosyl Mono Phosphate, used as a second messenger) of glycogenolysis and lipolysis.

the protection of vitamin C with this antioxidant action, increases its action, with a synthesis stimulation of connective tissue components like collagens, a higher protection against free radicals.

It also has a UVA protection effect.

27. R. Maffei Facino, M. Carini, G. Aldini, R. Stefani, E. Bombardelli, P. Morazzoni: Free radical Scavenging Action and Anti-enzyme Activity of Proanthocyanidine A2, a new polyphenol from *Aesculus hippocastanum* L.

Key words: Proanthocyanidine A2, *Aesculus hippocastanum* L., Phosphatidylcholine liposomes, radical scavenging activity, anti-enzyme activity.

Summary: The antioxidant activity of proanthocyanidine A2 from *Aesculus hippocastanum* L. was tested in unilamellar phosphatidylcholine liposomes (PCL), a structural model for biological membranes, alternative to conventional cell membranes from animal source.

PCL were exposed to a flux of HO° radicals generated by water sonolysis for 15 min (induction phase) and the spontaneous lipid peroxidation under air atmosphere, involving lipid radicals (propagation and breakdown phases), followed by 48 h, by measuring formation of intermediate (conjugated dienes) and end products (total carbonyl functions) of lipid peroxidation.

Proanthocyanidine A2 was able to inhibit all the stages of the peroxidative phenomenon in a dose-related fashion and with a different potency.

In addition, Proanthocyanidine A2 exhibits a remarkable inhibitory effect, of non-competitive type, on the activity of some key proteolytic enzymes: collagenase, elastase and glycosidases: hyaluronidase and β -glucuronidase which regulate the turnover of the main components of the extracellular matrix of the subcutaneous tissue.

Proanthocyanidine A2 can prevent photooxidative skin aging, through a dual mechanism of action: directly, by scavenging carbon and oxygen-centered free radicals, by which skin surface lipids and collagen, elastin and hyaluronic acid are markedly affected, and indirectly, restraining the radical mediated increased degradation of these extracellular matrix constituents, through an inhibition of the enzyme systems involved in their turnover.

28. M. Carini, R. Maffei Facino, A. Brambilla, R. Stefani, C. Scesa: Anti-hyaluronidase and anti-elastase activity of saponins from *Hedera helix*, *Aesculus hippocastanum* and *Ruscus aculeatus*: an explanation of their efficacy in the cosmetic treatment of liposclerosis.

Summary

Triterpene and steroid saponins and sapogenins of plant origin (*Hedera helix*, *Aesculus hippocastanum*, *Ruscus aculeatus*) are claimed to be effective for the treatment/prevention of panniculopathy edemato-fibrosclerotica (so-called "cellulitis"). but until now it has never been elucidated the mechanism(s) by which these compounds can be active. In this work we evaluated the inhibitory effects of these plant constituents on the activity of elastase and hyaluronidase, the enzyme systems involved in the turnover of the main components of the perivascular amorphous substance.

The results showed that for *Hedera helix*, the sapogenins only non-competitively inhibit hyaluronidase activity in a dose dependent fashion; both the saponins Hederacoside C and α -Hederin are very weak inhibitors. The same behaviour is observed for serin protease porcine pancreatic elastase: the glycosides are devoid of inhibitory action, while genins are potent competitive inhibitors.

Constituents from *Aesculus hippocastanum* show inhibitory effects only on hyaluronidase, and this activity is mainly linked to the saponin Escin, less to its genin Escinol.

By contrast, Ruscogenins from *Ruscus aculeatus*, ineffective on hyaluronidase activity, exhibit remarkable, anti-elastase activity. The mechanism of elastase inhibition by triterpene and steroid aglycons, with a nitroanilide as substrate, is discussed.

All these findings provide a biochemical support for the efficacy of these extracts in the treatment of liposclerosis, since the recovery of the integrity of hyaluronic acid and elastin (and of their functional interactions with proteoglycans) might lead to a reconstruction of the extracellular matrix in which the pericyte microvascular system is embedded.

29. In a data sheet from Laboratoire Phybiotex.

Esculoside is obtained from the bark of Horse Chestnut branches (*Aesculus hippocastanum* L.) by extraction with hot water, followed by precipitation of the tannins and fractionated recrystallisation with active carbon filtration steps. It can also be obtained by partial synthesis from esculetin. 6,7-dihydroxycoumarin-6-glucoside (DAB Xth edition).

Esculoside has also been found in an Australian Pittosporaceae, *Bursaria spinosa* and in *Fraxinus japonica*.

Biological activity

Esculoside is listed in the 9th edition of the French Pharmacopoeia. No toxicity related phenomena have been reported. On the contrary, esculoside containing pharmaceutical specialities and folk lore remedies abound.

Alcoholic or aqueous extracts of bark are described as veinotonic, antipyretic, and congestion relief preparations by internal or external use¹⁻⁴.

Treatment of red skin blotches, of heavy legs and oedemas^{5,6} as well as increasing the capillary resistance (vitamin P), decreasing capillary permeability and participating in anti-inflammatory activities⁷ are some of the uses to which esculoside is commonly put.

Marinova et al. described the antioxidant activity of esculetin (the aglycone of esculoside, i.e. esculoside without the sugar moiety) as manifested by protection of triglycerides against auto-oxidation at high temperatures. This antioxidant property might explain some of the anti-inflammatory activities of esculoside.

Yamagami et al.⁹ showed reduction of carragenin induced oedema and UV related erythema as well as diuretic effects.

The cosmetic applications of horse chestnut extracts include therefore local hyperemia treatment (sun exposure), the reduction of irritation and skin rashes, and the increase of local microcirculation in association with lipolytic slimming and anti-cellulite treatment.

Other activities

Huei-Chen Huang et al. studied antiproliferative effects of esculoside and esculetin and showed inhibitory activity on protein tyrosine kinase¹⁰.

Kostova et al.¹¹ described antimicrobial activity of esculoside and esculetin as well as skin regeneration after wounding, at the same time confirming the absence of irritation or toxicity of esculoside¹².

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7. Tetenyi P., Les principes actifs du marron d'inde, 1977 Plant Med. Phytotherap. 11, 158-164.
8. Marinova E.M. et al., 1994, Food Chemistry 51, 125-132.
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10. Huei-Chen H. et al. 1993, Eur. J. Pharmacol. 268, 73-78.
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12. Klouček E. et al. 1994, Dokl. Akad. Nauk. 47, 125-128.

Cosmetic activities

The paper discusses the tests which were carried out on:

- action against blotches

The venotonic and anti-inflammatory properties of esculoside led us to test its cosmetic action in treating blotches. Blotches consist initially of a symmetrical inflammation of the face (transient erythema) following stress, changes in temperature, or alcohol consumption. This inflammation may become persistent (erythrosis) and give rise to the telangiectases known as facial blotchiness. The precise cause of these symptoms is not known, but their onset and progress are probably determined by microcirculatory vascular disturbances in the facial angular veins, which are directly involved in cooling the brain.

- free radical scavenger activity

30. Potter (R.C.Wren, rewritten by E.M. Williamson and F.J. Evans: Potter's New Cyclopaedia of Botanical Drugs and Preparations, 1994, published C.W.Daniels. ISBN 0-85207-197-3.) refers to Horse Chestnut as *Aesculus hippocastanum* (Fam: Hippocasanaceae) [Syn. *Hippocastanum vulgare* Gaertn.]. It is native to Northern Asia, but widely cultivated, common in Britain. The bark and seeds are used.

Constituents: Saponins, a complex mixture known as "aescin", composed of acylated glycosides of protoaescigenin and barringtogenol-C and including hippocaesculin and many others. The acyl groups are usually tiglic, angelic or acetic acids.

Medicinal uses: Anti-inflammatory, febrifuge, astringent. Extracts of Horse Chestnut. or more usually, preparations of aescin, are used for rheumatism, venous congestion,

haemorrhoids, and in cosmetics. Aescin has been shown to eliminate oedema and reduce exudation, it antagonises the effects of bradykinin, although it is not a direct bradykinin antagonist. It has anti-inflammatory activity and causes an increase in plasma levels of ACTH, corticosterone and glucose in rats. Aescin is also active against the influenza virus *in vitro*. Hippocaesculin and barringtogenol-C-21-angelate have anti-tumour activity *in vitro*.

Preparations: Liquid Extract (fruit), dose: 0.5-1.2 ml; Liquid Extract (bark), dose: 2-4 ml.

Regulatory status: GSL.

31. S. Srijayanta, A. Raman, B. Goodwin: A comparative study of *Aesculus hippocastanum* and *Aesculus indica*.

Journal of Pharmacy and Pharmacology **49**, Suppl. 4, September 1997. ISSN 0022-3573. British Pharmaceutical Conference 1997. Science Proceedings, 134th Meeting, Scarborough. September 15-18, 1997. Paper 207, p.111.

Aesculus hippocastanum L. (Hippocastaceae) is a common plant in Europe. Aescin, a complex mixture of triterpene glycosides, extracted from seeds of this plant exhibits anti-inflammatory and anti-oedema effects in various experimental models (Bruneton, 1995). It has been widely used in the therapy of peripheral vascular disorders and the cosmetics field. *Aesculus indica* Colebr. is an indigenous plant in India and Pakistan used for the treatment of rheumatism (Chopra et al, 1956). Most studies on their phytochemistry have been carried out on *A. hippocastanum*, with only occasional studies on *A. indica* (Ikram et al, 1978).

The aim of this work is to establish a direct comparison of the two species grown under comparable conditions. The plant materials (seeds, husks and leaves) were collected from close geographical locations in order to minimise variations occurring due to geographical and climatic factors.

TLC zone profiles showed that the constituents of the leaves, seeds and husks differed within a single species. Comparing *A. castanum* and *A. indica* revealed similar respective profiles for the seeds and leaves of the two species, whereas the husks differed.

An investigation for the presence of coumarin, aesculetin, and its glycoside aesculin, was carried out using TLC, followed by detection under UV light. The results indicated an absence of aesculin and aesculetin from seeds, husks and leaves of both species. The absence of the compounds was not due to the unsuitability of the method, since it was effective in extracting aesculin and aesculetin from the bark of *A. hippocastanum* which had been reported to contain the two compounds (Matysik et al, 1994). *A. indica* bark was not available for comparison.

Aescin was found only in the seeds of both species, but not in the leaves and husks. The content of aescin in the seeds of the two species was determined using TLC-densitometry. Aescin which gave a dark brown zone occurred in dried *A. hippocastanum* seeds at 9.46 +/- 0.095% w/w and in *A. indica* at 13.4 +/- 0.46% w/w (n=3, separate determinations). These results suggest that *A. indica* seeds may be a viable alternative commercial source of aescin.

32. M. Howard: Traditional Folk Remedies, A comprehensive Herbal. Century paperbacks. 1987. ISBN No. 0-7126-1731-0.

Folklore: In classical times the word *Aesculus* was used to denote oak trees, but the specific part of the horse chestnut's botanical name may derive from the fact that the fruit was used as a cattle and horse feed. The tree was first imported into Europe from Asia as late as the sixteenth century. Its medical properties for easing the discomfort of piles soon became apparent to herbalists and folk healers. The nut-like fruits were carried as a charm against rheumatism by country people, but were said to be effective only if they had been stolen or obtained by begging.

General Medical Properties: Astringent, tonic, antirheumatic and antiphlogistic.

Specific properties: Horse Chestnut fruits, or conkers, as school children call them, are used in folk medicine as a tonic, to treat rheumatic pain, to thin the blood and cure piles. The active ingredient is escin, medically recognised as an anti-inflammatory agent.

Application and use: Use with caution, as large doses can be toxic, and only under the direction of a medicinal herbalist.

33. Genders (B196). One of the most handsome of assiduous trees, is one of a genus of 13 species indigenous to South East Asia and North America. The horse chestnut is native to East Europe and West Asia. It is a light loving tree, rarely found in woodlands, almost always in hedgerows or growing soundly in fields and usually in a sandy soil. It will retain a height of 100 feet with a girth of up to 16 to 17 feet with smooth light brown bark. The dark green palmate leaves are composed of 5-7 lance shaped leaflets joined at the same point and held on long footstalks. They turn gold, then brown before they fall in autumn. The flower buds are born in the axis of the leaves of the previous season, the buds being covered with overlapping scales protected by a sticky resinous substance.

The white flowers are born in a large upright in fluorescent in May and are visited by bees. They are followed in autumn by large, shiny dark red single fruits enclosed in a prickly green leathery capsule which school boys remove, fastening the fruits to string to play the game known as conkers. From the fruits, after removing the hard polished outer skin, the juice is extracted and used in bath oils for a foam bath which will tone the flesh and make it soft and supple.

34. Bunney (B27). Children have been poisoned, though not fatally, after eating the green outer casing of the fruit and they should be warned about this

Horse chestnut is native to South Eastern Europe and seems to have been introduced into England around 1550. The tree's generic name, *Aesculus*, comes from the Latin word *esca* (=food). The name was given originally to a type of oak, the acorns of which were ground to make a flour. How it came to be transferred to horse chestnut is not known. There is also confusion about the origin of the tree's specific and common names. *Hippocastanum* is a Latin translation of horse chestnut, and this name could be derived from a Turkish custom of feeding chestnuts to horses ailing from respiratory diseases. At one time the plant was used to treat malaria.

The fully ripe chestnut, sometimes the bark, are used medicinally. The constituents include up to 28% of saponins of which escin is the most important, the coumarin glycosides aesculin, aesculoside and fraxin and tanins.

Horse chestnut has astringent, antipyretic and antithrombotic properties. In some countries it is included in proprietary medicines used to treat cardiovascular diseases. It is also used for varicose veins, respiratory infections and severe diarrhoea. A tincture of

fresh chestnuts is used in homeopathy. All internal use of horse chestnut should be medically supervised.

Externally horse chestnut is used to treat cuts and bruises, frostbite, ringworm and haemorrhoids. A coumarin component aesculoside is included in some sunscreen preparations.

35. Ody (B138) *Aesculus Hippocastanum* or horse chestnut used for varicose veins swollen or stretched veins in the legs, associated with poor venous return or raised abdominal pressure as in obesity, pregnancy or persistent constipation. Key symptoms: obvious enlarged and stretched veins. Pain in the legs.

The action is astringent and internally strengthening to the blood vessels, possibly due to the presence of aescin. Take up to 2.50ml tincture three times a day; use a dilute tincture for compresses. Combinations: use with liver herbs such as goldenseal or dilute with witchazel for compresses.

36. Lesley Bremness (B82) cites the use of *Aesculus hippocastanum* for haemorrhoids and for varicose veins.

37. Jean Palaiseul (B118) Some 50 patent medicines turn to good account its incomparable action on the venous circulation, and it has long been known under its scientific name as a homeopathic remedy, advocated in the treatment of haemorrhoids and varicose veins (for which it is also the allopathic remedy) as well as of a very painful kind of lumbago, pains that are alleviated by cold and aggravated by heat, and of acute attacks of rhinopharyngitis

Ever since a physician named Bachelier introduced it here at the beginning of the seventeenth century, it is actually a native of India, we have assiduously discovered other uses for it than those for which it seemed to have been created: to lend its magnificent and ornamental presence to our surroundings (gardens, avenues) and provide food that, reduced to flower mixed with oats and administered in the amount of 100 grams a day, eased broken winded horses, a purpose for which it is still used by the Turks, and to which it owns both its scientific and common name.

It has also been used to increase the natural subscriptions of the nose and produce sneezing; the bark of its branches was prescribed as a febrifuge in place of quinine which was unattainable under the Continental system; the chestnuts, containing saponins, were macerated and used for laundering, and also made into soap; its flour gave an excellent wood size which, being bitter, also kept away woodworm and which, mixed with tallow, was used to make candles that were longer lasting but unhappily gave less light than ordinary candles.

Popular medicine made use of its virtues long before it was scientifically established that a principle of horse chestnut acts as a venous tonic and thins the blood.

Taken internally, a decoction of the outer covering of the fruit, dried and crushed (30 grams to a litre of water; boil for 5 minutes; leave to infuse for the same length of time; one or two cupfuls per day, between meals) is recommended for disturbances of circulation, congested conditions of the venous system (varicose vein, haemorrhoids), enlarged prostate.

The prescription for external use is simply that you should always carry one or two horse chestnuts in your pocket, replacing them once they have become as hard as rock.

This is the classic country remedy for dramatic pains and painful haemorrhoids. Does it work through auto - suggestion or through the evaporation and absorption by osmosis of an essential oil modestly employed in the treatment of doubt? What matters is that it does work, and you risk nothing by trite. It appears that sweet chestnuts share the same virtues, if one is to judge by a letter written by Madame de Sevigne in October 1671: "the other day I had three or four basketfuls to hand: some I boiled some I roasted some I put in my pocket...."

38. Talalaj & Czechowicz (B262). Active constituents: triterpenoid saponins mainly aescin (5%). Also coumarins and flavonoids.

Pharmacological action: anti-oedemic, vasotonic, haemostatic.

Medicinal uses: internally, horse chestnut preparations have primarily been used in the treatment of deficient peripheral circulation and oedematous conditions. It strengthens the tone of the veins, increases capillary resistance, and shows capillary sealing effects. It is useful in the treatment of varicose veins, leg ulcers, and haemorrhoids. Externally, it has been employed in the treatment of leg ulcers, skin inflammation, burns, and frost bite. It is extensively used in homeopathic medicine to treat varicose veins and haemorrhoids.

Toxicity: horse chestnut preparations, particularly of the seeds, are toxic in overdose. Cases of severe poisoning occur mostly in children who have eaten the seeds. Symptoms include vomiting, diarrhoea, uncoordinated twisting of muscles, dilated pupils, depression and even paralysis.

Contraindications: it should be avoided during pregnancy and in cases of acute kidney dysfunction.

Remarks: the doctor should be informed when this plant is being used.

39. Powell (B66). Horse chestnut .

Probably the best of all remedies for piles. May be used in fluid extract form, or homoeopathically. The dose for the fluid extract is 5 to 10 drops in hot water before or after meals, three times daily. We favour the homeopathic dilution. Ask or Aesculus hip 30. Does: five pills on rising and again on retiring. If necessary may be taken for several weeks.

40. Grieve – A modern herbal.

Chestnut, Horse

Botanical: *Aesculus hippocastanum*

Family: N.O. Sapindaceae

---**Synonym**---*Hippocastanum vulgare* (Gaertn.).

---**Parts Used**---Bark and fruit.

The Horse Chestnut, *Aesculus hippocastanum*, which has also been known as *Hippocastanum vulgare* (Gaertn.), is an entirely different tree from the Sweet Chestnut, to which it is not even distantly related, and is of much more recent importation to English soil. It is a native of northern and central parts of Asia, from which it was introduced into England about the middle of the sixteenth century.

The name *Æsculus* (from *esca*, food) was applied originally to a species of oak, which according to Pliny, was highly prized for its acorns, but how it came to be transferred to the Horse Chestnut is very uncertain; perhaps, as Loudon suggests, it was given ironically, because its nuts bear a great resemblance, externally, to those of the Sweet Chestnut, but are unfit for food. *Hippocastanum* (the specific name of the common sort) is a translation of the common name, which was given - Evelyn tells us - 'from its curing horses brokenwinded and other cattle of coughs.' Some writers think that the prefix 'horse' is a corruption of the Welsh *gwres*, meaning hot, fierce, or pungent, e.g. 'Horse-chestnut' = the bitter chestnut, in opposition to the mild, sweet one.

The tree is chiefly grown for ornamental purposes, in towns and private gardens and in parks, and forms fine avenues, which in the spring, when the trees are in full bloom, present a beautiful sight.

---Description---The trunk of the tree is very erect and columnar, and grows very rapidly to a great height, with widely spreading branches. The bark is smooth and greyishgreen in colour: it has been used with some success in dyeing yellow. The wood, being soft and spongy, is of very little use for timber.

It is often used for packing-cases.

The sturdy, many-ribbed boughs and thick buds of the Horse Chestnut make it a conspicuous tree even in winter. The buds are protected with a sticky substance: defended by fourteen scales and gummed together, thus no frost or damp can harm the leaf and flower tucked safely away within each terminal bud, which develops with startling rapidity with the approach of the first warm days after the winter. The bud will sometimes develop the season's shoot in the course of three or four weeks. The unfolding of the bud is very rapid when the sun melts the resin that binds it so firmly together.

The large leaves are divided into five or seven leaflets, spreading like fingers from the palm of the hand and have their margins finely toothed. All over the small branches may be found the curious marks in the shape of minute horse-shoes, from which, perhaps, the tree gets its name. They are really the leaf scars. Wherever a bygone leaf has been, can be traced on the bark a perfect facsimile of a horse-shoe, even to the seven nail markings, which are perfectly distinct. And among the twigs may be found some with an odd resemblance to a horse's foot and fetlock.

The flowers are mostly white, with a reddish tinge, or marking, and grow in dense, erect spikes. There is also a dull red variety, and a less common yellow variety, which is a native of the southern United States, but is seldom seen here.

The fruit is a brown nut, with a very shining, polished skin, showing a dull, rough, pale-brown scar where it has been attached to the inside of the seed-vessel, a large green husk, protected with short spines, which splits into three valves when it falls to the ground and frees the nut.

---Cultivation---The Horse Chestnut is generally raised from the nuts, which are collected in the autumn and sown in the early spring. The nuts should be preserved in sand during the winter, as they may become mouldy and rot. If steeped in water, they will germinate more quickly. They will grow 3 foot the first summer and require little care, being never injured by the cold of this climate. They thrive in most soils and situations, but do best in a good, sandy loam.

---Part Used Medicinally---The bark and the fruit, from both of which a fluid extract is made. The bark is stripped in the spring and dried in the sun, or by slight artificial heat, and when dry, occurs in commerce in flattened pieces, 4 to 5 inches long and about 1 to 1 1/2 inch broad-about 1 to 1 1/4 inch thick, greyish-brown externally, showing corky elongated warts, and on the inner surface pinkish-brown, finely striated longitudinally. The bark is odourless, but has a bitter astringent taste.

---Medicinal Action and Uses---The bark has tonic, narcotic and febrifuge properties and is used in intermittent fevers, given in an infusion of 1 OZ. to the pint, in tablespoonful doses, three or four times daily. As an external application to ulcers, this infusion has also been used with success.

The fruits have been employed in the treatment of rheumatism and neuralgia, and also in rectal complaints and for haemorrhoids.

---Preparations---Fluid extract, fruit, 5 to 20 drops. Fluid extract, bark, 1/2 to 2 drachms.

Horse Chestnuts as Fodder

In Eastern countries considerable use is made of Horse Chestnuts for feeding horses and cattle, and cattle are said to eat them with relish, though pigs will not touch them. The method of utilizing them is to first soak them in lime-water, which deprives them of the well-known bitter flavour inherent in the nuts, and then to grind them to a meal and mix them with the ordinary provender.

---Constituents---Analysis has shown that the nuts contain 3.04 per cent. water; 2.66 per cent. ash; 10.99 crude protein; oil, 5.34 per cent.; and 73.97 per cent. carbohydrates. Experiments conducted at Wye College proved that the most satisfactory way to prepare the Horse Chestnuts as food for animals was to soak partly crushed nuts in cold water overnight, then boil them for half an hour or so and strain off the water. The nuts were then dried, partially husked and reduced to a meal, which, though slightly bitter, had a pleasant taste and appearance. The meal was fed to a calf, a sheep and two pigs. The calf received up to 5 lb. of the meal per day and made good increase in live weight, and the sheep suffered no ill effects, but the pig refused to eat the food containing the meal. It is concluded that Horse Chestnuts are not poisonous to any of the farm animals experimented with, within the limits of what they can be induced to eat, and that they form a highly nutritious food. Chestnut meal is a fairly concentrated food, and contains about 14 per cent of starch, it being calculated that 1 lb. of Horse Chestnut meal would be equivalent to 1 lb. 1 OZ. of feeding barley, 1 lb. 4 OZ. of oats, 1 lb. 8 oz. of bran, and 3 lb. 5 OZ. of good meadow hay.

Experiments made during the Great War proved that for every ton of Horse Chestnuts which are harvested, half a ton of grain can be saved for human consumption, and thus the Horse Chestnuts, though totally unfit for human food, can be utilized indirectly to increase the national food supply.

The genus *Pavia* is so closely allied as to be now generally grouped with the *Æsculus*. The Red Buckeye (*Æ. pavia*) is a handsome small tree with dense and large foliage, together with bright red flowers in large loose clusters in early summer. Sometimes it rises from 15 to 20 feet high, but some of its varieties are only low-spreading or trailing shrubs. The Yellow Buckeye (*Æ. flava*) is common and sometimes 40 feet high. It has somewhat the habit of the Red Horse Chestnut (*Æ. rubicunda*), but has smoother leaves. The DWARF HORSE CHESTNUT (*Æ. parviflora*) is a handsome shrub, 6 to 10 feet

high, flowering in later summer. Its foliage is much like that of other *Æsculi*, and its small, white, fragrant flowers are in long, erect plume-flowers.

41. Cornell University Web page.

General poisoning notes for *Aesculus hippocastanum*

Horse-chestnut (*Aesculus hippocastanum*) is an introduced tree that is found in the southern parts of Ontario and Quebec. It has poisoned cattle, horses, and pigs, causing sickness and death (Reynard and Norton 1942, Muenscher 1975). Human poisoning has also occurred.

References:

Cooper, M. R., Johnson, A. W. 1984. Poisonous plants in Britain and their effects on animals and man. Her Majesty's Stationery Office, London, England. 305 pp.

Hardin, J. W., Arena, J. M. 1969. Human poisoning from native and cultivated plants. Duke University Press, Durham, N.C., USA. 167 pp.

Lampe, K. F., McCann, M. A. 1985. AMA Handbook of poisonous and injurious plants. American Medical Assoc. Chicago, Ill., USA. 432 pp.

Reynard, G. B., Norton, J. B. 1942. Poisonous plants of Maryland in relation to livestock. Univ. MD. Agric. Exp. Stn. Bull., A10. 312 pp.

Image or illustration for *Aesculus hippocastanum*

[Aesculus hippocastanum](#)

These images or illustrations are provided courtesy of Drs. [Dan Brown](#), Robert Hillman and Mary Smith of Cornell University. Please see their [Cornell University Poisonous Plants page](#).

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Nomenclature

Botanical name: *Aesculus hippocastanum* L.

English Common name: horse-chestnut

French Common name: marronnier

Botanical family name: Hippocastanaceae

English family name: horse-chestnut

French family name: marronnier

References:

Agriculture Quebec. 1975. Noms des maladies des plantes du Canada/ Names of plant diseases in Canada. , Quebec City, Que., Canada. 288 pp.

Alex, J. F., Cayouette, R., Mulligan, G. A. 1980. [Common and botanical names of weeds in Canada/Noms populaire et scientifiques des plantes nuisibles du Canada](#). Revised. Agric. Can. Publ., Ottawa, Ont., Canada. 132 pp.

Bailey, L. H., Bailey, E. Z. 1976. Hortus third. Revised. MacMillan, New York, N.Y., USA. 1290 pp.

Scoggan, H. J. 1978, 1979. The flora of Canada. Nat. Mus. Nat. Sci. (Ottawa) Publ. Bot. 7(1)-7(4). 1711 pp.

Van Wijk, H. L. 1911. A dictionary of plant names. Martinus Nijhoff, The Hague, The Netherlands. 1444 pp.

Victorin, M. 1964. Flore Laurentienne. 2nd ed. Univ. Montreal, Montreal, Que., Canada. 952 pp.

Distribution

The plant, *Aesculus hippocastanum* is a plant or plant product used around the home.

References

Bailey, L. H., Bailey, E. Z. 1976. Hortus third. Revised. MacMillan, New York, N.Y., USA. 1290 pp.

Boivin, B. 1966, 1967. Énumération des plantes du Canada. Provencheria 6. Nat. Can. (Que.) 93: 253-274; 371-437; 583-646; 989-1063. 94: 131-157; 471-528; 625-655.

Notes on poisonous plant parts

Horse-chestnut fruits, leaves, and flowers contain the chemical aesculin. Young leaves and flowers are especially toxic to cattle (Reynard and Norton 1942). Children occasionally ingest the fruit but few authenticated cases of poisoning are found in the literature, although death has been reported (Lampe and McCann 1985).

Toxic parts

flowers
leaves
mature fruit

References:

Cooper, M. R., Johnson, A. W. 1984. Poisonous plants in Britain and their effects on animals and man. Her Majesty's Stationery Office, London, England. 305 pp.

Hardin, J. W., Arena, J. M. 1969. Human poisoning from native and cultivated plants. Duke University Press, Durham, N.C., USA. 167 pp.

Lampe, K. F., McCann, M. A. 1985. AMA Handbook of poisonous and injurious plants. American Medical Assoc. Chicago, Ill., USA.

432 pp.

Reynard, G. B., Norton, J. B. 1942. Poisonous plants of Maryland in relation to livestock. Univ. MD. Agric. Exp. Stn. Bull., A10. 312 pp.

Notes on toxic chemicals

Aesculin is a saponin (7-hydroxycoumarin 6-glucoside) that yields aesculetin (6,7-dihydroxycoumarin) upon hydrolysis. Aesculin is related to hydrocoumarin found in spoiled sweet-clover hay (Cooper and Johnson 1984). LD-50 measurements from nut extracts were as follows (Williams and Olsen 1984):

10.6 mg/g of body weight for chicks
10.7 mg/g of body weight for hamsters.

Toxic chemicals

- aesculin

References:

Cooper, M. R., Johnson, A. W. 1984. Poisonous plants in Britain and their effects on animals and man. Her Majesty's Stationery Office, London, England. 305 pp.

Reynard, G. B., Norton, J. B. 1942. Poisonous plants of Maryland in relation to livestock. Univ. MD. Agric. Exp. Stn. Bull., A10. 312 pp.

Williams, M. C., Olsen, J. D. 1984. Toxicity of seeds of three *Aesculus* spp to chicks and hamsters. Am. J. Vet. Res., 45: 539-542.

Animals/Human Poisoning

Note: When an animal is listed without additional information, the literature (as of 1993) contained no detailed explanation.

Cattle

Humans

General symptoms of poisoning for Humans

death
depression
diarrhea
gastroenteritis
muscle twitching
paralysis
pupil dilation
restlessness
unconsciousness

vomiting
weakness

Notes on Poisoning

Horse-chestnut poisoning is usually limited to severe gastroenteritis because the saponins (including aesculin) are poorly absorbed. Serious and fatal cases can result from frequent multiple ingestion of the plant (Lampe and McCann 1985).

References:

Cooper, M. R., Johnson, A. W. 1984. Poisonous plants in Britain and their effects on animals and man. Her Majesty's Stationery Office, London, England. 305 pp.

Hardin, J. W., Arena, J. M. 1969. Human poisoning from native and cultivated plants. Duke University Press, Durham, N.C., USA. 167 pp.

Lampe, K. F., McCann, M. A. 1985. AMA Handbook of poisonous and injurious plants. American Medical Assoc. Chicago, Ill., USA. 432 pp.

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42. From the Internet. **Horse Chestnut** exhibits astringent and anti-inflammatory properties. Do not confuse this herb with its North American relative *Aesculus glabra*, called Buckeye. The unique actions of Horse Chestnut are on the vessels of the circulatory system. It seems to increase the strength & tone of the veins in particular. Horse Chestnut may also be used internally to aid the body in the treatment of problems such as phlebitis, inflammation in the veins, varicosity, and hemorrhoids.

Externally, Horse Chestnut may be used in a lotion for these same conditions (*phlebitis, inflammation in the veins, varicosity, and hemorrhoids*), as well as for leg ulcers.

Use Horse Chestnut in combination with other cardiovascular tonics such as Hawthorne, Linden, Ginkgo and Yarrow.

43. Launert (B94). Active ingredients: saponins and fatty oil (mainly in the seed), glycoside (aesculin, fraxin), tannin, flavones.

Effect: astringent (bark); arrests bleeding, prevents spasms.

Parts used: mainly the seed but also the flower and bark of young trees.

Application: for domestic purposes a wine based on the dried or fresh flowers (1 liqueur glass three times a day) is taken against neuralgia, rheumatic pain, arthritis; a decoction or infusion of bark is used internally against uterine and haemorrhoidal bleeding, chronic bronchitis, intestinal or stomach inflammations, arthritis, neuralgia, rheumatism; can be used externally as a compress (or added to bath water) against eczema, cuts and bruises, boils, eruptions of the skin and chilblains, etc. The powdered seed is occasionally added to snuff.

44. cosmetochem ag data file
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Fax. CH - (0)41 / 748 33 44

I INCI name:

Aqua, Propylene Glycol, Horse Chestnut (*Aesculus Hippocastanum*) Extract.

II General information from literature:

Botanical Family: Hippocastanaceae

Common Name:

Latin: *Aesculus Hippocastanum* L.

English: Horse Chestnut

French: Marron d'Inde

German: Rosskastanie

Among the finest of ornamental shade trees are the buckeye and the horse chestnut. With their showy flowers, luxuriant leaves, and graceful, pyramid-shaped crowns, they are a popular planting for streets and parks. The wood of both types of tree, which comprise the genus *Aesculus*, is used in the making of artificial limbs, furniture, bowls, boxes, and crates.

The horse chestnut, *Aesculus hippocastanum*, is a deciduous hardwood tree of the buckeye family, Hippocastanaceae. Native to the Balkan peninsula, it has been planted worldwide as a landscape tree. It was introduced into the United States as an ornamental tree in about the middle of the 18th century and has become naturalized on the east coast. It can reach 130 feet (40 meters).

The trees are dicots characterized by large winter buds covered with sticky scales. The common horse chestnut tree, *A. hippocastanum*, bears five to nine leaves on one stem, and large clusters of attractive yellow, red or whitish irregular flowers with four or five petals. The fruit is a brown nut, with a very shining, polished skin, showing a dull, rough, pale-brown scar where it has been attached to the inside of the seed-vessel, a large green husk, protected with short spines, which splits into three valves when it falls to the ground and frees the nut. The nuts are inedible for humans, but they are eaten by deer and squirrels. The fruits have been employed in the treatment of rheumatism and neuralgia.

Scientific classification: Horse chestnuts make up the family Hippocastanaceae. The common horse chestnut is classified as *Aesculus hippocastanum*, the Ohio buckeye as *Aesculus glabra*, the yellow buckeye as *Aesculus octandra*, and the California buckeye as *Aesculus californica*.

(Microsoft (R) Encarta Multimedia Encyclopedia)

(Comptons Interactive Encyclopedia)

(Comptons Interactive Encyclopedia)

(Mrs. M. Grieve: A Modern Herbal)

III Main components:

The following substances are listed in the literature as actives of the plant:

Bark: 3 % Aesculin (Camarinynglycosid), Aeculetin (Aglykon), Fraxin, Scopolin, Fraxetin, Scopoletin, Guercitrin (Flavonolglykosid), Quercetin, Aescin (Saponinglykosid), Allantoin, Phytosterine, Leukoanthocyanes, tannin, resin, starch, fatty oil.

Flower: Kämpferol-3-glykosid, Kämpferol-3-arabinosid, Kämpferol-3-rhamnoglykosid, Rutin, Isoquercitrin, Aescin (Saponinglykosid), tannins, cholin, Purin-derivatives, Adenosin, Adenin, Guanin, Urea.

Seed: Starch, 8-28 % Aesculussaponin, ca. 9 % sugars, 8-10 % proteins, fatty oil with mainly Olein, Catechin- tannins, Flavoglycosides, Phytosterines, Purinderivatives: Adenin, Adenosin, Guanin, Urea, Vitamines (B1, C, K) Cholin, Proteases, colours, gum.

Leaves: Aesculin, Fraxin, Scopolin, Flavonolglykosides, Aescin, tannin, Vitamin K1, Phytosterines, Purinderivates, resin, Leukoanthocyanes, Phosphor- compounds, Castaprenoles.

(Hoppe: Drogenkunde)

(Das Beste: Geheimnisse und Heilkräfte der Pflanzen)

IV Cosmetic applications:

The following cosmetic related activities of the plant are extracted from the literature:

Anti-inflammatory, astringent, tonic, against skin diseases, skin and hair cleaning products (saponins), stimulating, tonic, general skin and hair care.

(Hoppe: Drogenkunde)

(Das Beste: Geheimnisse und Heilkräfte der Pflanzen)

Recommended level of use: 2 - 10 %.

Use in hair- and skin care products.

V Storage and safety:

Storage:

We recommend storing this Herbasol Extract at room temperature (20 - 30 °C), protected from direct sun light.

Maximum recommended storage time:

One year in original sealed cans or drums.

Once the container is opened, the product must be handled with care to avoid microbiological contamination.

Safety for Use:

We assure to the best of our knowledge and belief the good compatibility and the non-toxicity of this HERBASOL EXTRACT. It is safe for use in usual dosages in skin and hair cosmetics. Nevertheless, this statement does not discharge the producer of the finished cosmetic product from compatibility tests required by the authorities.

Options:

On request, most of our Plant Extracts are available in the following variations:

- oil soluble
- IPA (Isopropylalcohol)
- Special
- Super Herbasol
- Forte
- Herbasol Distillate
- Herbasol Complex

45. Foster & Duke (B164). Horse chestnut.

Aesculus Hippocastanum.

Uses as in *Aesculus glabra* (see above) also, peeled roasted nuts of this tree were brewed for diarrhoea, prostate ailments. Thought to increase blood circulation. In Europe, preparations of the seeds are believed to prevent thrombosis, and are used to treat varicose veins and haemorrhoids; thought to help strengthen weak veins and arteries. Also used in gastritis and gastroenteritis. Leaf tea tonic; used for fevers. Flower tincture used on rheumatic joints. Bark tea astringent; used in malaria, dysentery; externally, for lupus and skin ulcers.

Warning: outer husks poisonous; all parts can be toxic. Fatalities reported. Seeds (nut) contain 30 to 60% starch, but can be used as a foodstuffs only after the toxins have been removed.

46. Mindell (B201). Horse chestnut, *Aesculus hippocastanum*

Facts

Although traditionally used as a remedy to bring down a fever and relieve cold symptoms, horse chestnut is being rediscovered in Europe for its ability to reduce swelling of varicose veins and soothe haemorrhoids. Horse chestnut extract has also been used as a sunscreen. According to folklore, carrying around the fruit of this tree in your pocket can prevent and cure arthritis. Many herbalists predict that as the baby boomers approach middle age, horse chestnut will soon enjoy new popularity in the United States.

47. Winter Griffith (B24).

Horse chestnut, *Aesculus hippocastanum*.

Part used for medicinal purposes: bark, leaves, seeds or nuts.

Chemicals this herb contains: aesculin, argyroschin, capsuloescinic acid, escin.

Known effects: increases bleeding time (a laboratory test for blood clotting). Irritates mucus membrane.

Miscellaneous information: these are more reliable, safer anti-coagulants. Eating even a few nuts can cause toxic symptoms.

Unproved speculated benefits: is used as anti-coagulant. 4% solution is used as sunscreen.

Toxicity. Rated slightly dangerous, particularly in children, persons over 55 and those who take larger than appropriate quantities for extended periods often.

48. Dragoco data sheet

Common names for the horse chestnut include the conker tree, wild chestnut and buck-eye.

The horse chestnut is indigenous to northern Greece. From there, in 1576, it was brought by the Turks to Vienna via Constantine. A short time later it came to France, Germany and England. Since then it has become widely distributed as a decorative tree and accepted as a well loved foodstuff by the larger of our wild animals this carbohydrate-rich fruit has found no acceptability for human consumption due to its bitter taste.

In medicine, the horse chestnut was first mentioned in the sixteenth century by the Italian doctor and botanist Mattioli. He recommended it as an agent against malaria and other intermittent fevers. The seeds, flowers and bark of the horse chestnut are all used as extractives. The seeds contain the following components: fatty oil, phytosterins, purine derivatives, vitamins B1, C, K, saponins, sugar, protein, catechin tannins, flavonoid glycosides, choline, starch.

The horse chestnut flowers contain purine derivatives, campherol compounds, rutin, isoquercetrin, aescin, tannin and choline.

Horse chestnut leaves contain: vitamin K1, phytosterins, purine derivatives, leucoanthocyanogens, aesculin, fraxin, scopoline, flavone glycoside, aescin, tannins, phosphorous compounds, castaprenols and gum.

The bark contains: phytosterins, leucoanthocyanogens, fatty oils, aesculin, aesculetin, fraxin, scopoline, fraxetine, scopoletine, quercetrin, aescin, allantoin, chestnut tannic acid, gum and starch.

The following medicinal effects have been attributed to the horse chestnut:

Blood-purifying, astringent, oedema-dispersing, reduces inflammation, encourages the circulation and capillary-dilating.

The internal application of horse chestnut is recommended against intestinal catarrh, diarrhoea, colics and haemorrhoids. The positive effects of horse chestnut on the whole blood vessel system have led to its use today as a vasodilator in numerous mechanical preparations in the forms of salves, drops, tablets, capsules, Suppositories and injections.

In homeopathy extracts of horse chestnut are used for catarrh in the nose and throat, haemorrhoids and ulcers of the lower leg.

In country medicine a tincture from the flowers and leaves is used against complaints associated with the veins and rheumatic disorders as well as stomach and intestinal cramps.

The external application of horse chestnut is useful for the treatment of rheumatism, chilblains, herpes, scrofula, varicose veins and sun burn.

In cosmetics horse chestnut extracts are primarily used for their saponin content. As a result of their vitalising, capillary dilating and permeability increasing properties horse chestnut extracts find use in skin care products, face lotions, bubble baths, shower gels and hair care products.

The constituencies of horse chestnut have vitalising, capillary dilating and permeability increasing effects and therefore offer excellent possibilities for use in cosmetic products. They are particularly suitable for preparations for the care of normal and skins; in the hair care sector, they are recommended for use in products for normal and greasy hair

49. In a data sheet from Rahn

Horse chestnut

Action and application: at externally as a vasoconstrictor, astringent, and to inhibit oedema. It is use on varicose veins, phlebitis, haemorrhoids, oedema, lower leg ulcers, disturbed circulation, abdomen injury, effusions of blood.

Used in cosmetics: lotions, skin creams, cosmetics in ampules, soaps, hair lotions, shampoos, masks, body milks.

Recommended concentration for use: 3-10%

32. Carol A. Newall, Linda A. Anderson and J. David Phillipson: Herbal Medicines - a guide for health-care professionals. London. The Pharmaceutical Press. 1996. ISBN no. 0-85369-289-0.

HORSE-CHESTNUT

Species (Family)

Aesculus hippocastanum L. (Hippocastanaceae)

Synonyms(s)

Aesculus

Part(s) Used

Seed

Pharmacopoeial Monographs

Martindale 30th edition

Pharmacopoeias: Ger., Port., and Span.

Legal Category (Licensed Products)

GSL (for external use only)

Constituents

Coumarins Aesculetin, fraxin (fraxetin glucoside), scopolin (scopolin glucoside)

Flavonoids Flavonol (kaempferol, quercetin) glycosides including astragalín, isoquercetrin, rutin; leucocyanidin (quercetin derivative)

Saponins A mixture of saponins collectively referred to as "aescin" (about 13%); α - and β -escin as major glycosides.

Tannins Type unspecified but likely to be condensed in view of the epicatechin content (formed during hydrolysis of condensed tannins)

Other constituents Allantoin, amino acids (adenine, adenosine, guanine), choline, citric acid, phytosterol.

Food Use

Horse-chestnut is not used in foods.

Herbal Use

Traditionally, horse-chestnut has been used for the treatment of varicose veins, haemorrhoids, phlebitis, diarrhoea, fever, and enlargement of the prostate gland.

Dose

Fruit: 0.2 - 1.0 g three times daily

Pharmacological Actions

Documented studies have concentrated on the actions of the saponins, in particular aescin.

Animal studies Anti-inflammatory activity in rats has been documented for both a fruit extract and the saponin fraction. Anti-inflammatory activity in the rat has been reported to be greater for a total horse-chestnut extract compared to aescin. In addition, an extract including aescin also exhibited activity suggesting horse-chestnut contains anti-inflammatory agents

other than aescin. No difference in activity was noted when the horse-chestnut extracts were administered prior to and after dextran (inflammatory agent). It has been proposed that aescin affects the initial phase of inflammation by exerting a “sealing” effect on capillaries and by reducing the number and/or diameter of capillary pores.

In addition, the saponin fraction has been reported to exhibit analgesic and antigranulation activities in rats, to reduce capillary permeability, and to produce an initial hypotension followed by a longer lasting hypertension in anaesthetised animals. Prostaglandin production by venous tissue is thought to be involved in the regulation of vascular reactivity.

Prostaglandins of the E series are known to cause relaxation of venous tissues whereas those of the F_α series produce contraction. Increased venous tone induced by aescin *in vitro* was found to be associated with an increased PGF_{2α} synthesis in the venous tissue.

The saponin fraction has been reported to contract the isolated rabbit ileum.

Considerable antiviral activity *in vitro* towards influenza virus (A₂/Japan 305) has been described for aescin.

Metabolism studies of aescin in the rat have concluded that aescin toxicity is reduced by hepatic metabolism.

Flavonoids and tannins are generally recognised as having anti-inflammatory and astringent properties, respectively.

Human studies Results of a controlled double-blind trial over 4 weeks involving 40 patients with chronic venous insufficiency have confirmed the antioedematous effect and beneficial influence on subjective parameters (pain, tiredness, feeling of tension and pruritis in the legs) of a horse-chestnut extract. A randomised placebo-controlled cross-over double blind trial of 22 patients with chronic venous insufficiency concluded that 1200 mg of horse-chestnut extract (standardised to 100 mg aescin) had an antioedematous effect via a decrease in transcapillary filtration.

Glycosaminoglycan hydrolases are enzymes involved in the breakdown of substances (proteoglycans) that determine capillary rigidity and pore size (thus influencing the passage of macromolecules into the surrounding tissue). Proteoglycans also interact with collagen, stabilising the fibres and regulating their correct biosynthesis. The activity of these enzymes was found to be raised in varicose patients compared to healthy patients. Treatment of 15 varicose patients with horse-chestnut extract (900 mg daily) for 12 days was found to cause a significant reduction in the activity of these enzymes. The proposed mode of action suggested that horse-chestnut acts at the site of enzyme release, exerting a stabilising effect on the lysosomal membrane.

The cosmetic applications of horse-chestnut have been reviewed and are attributed to properties associated with the saponin constituents.

Side-effects, Toxicity

Two incidences of toxic nephropathy have been reported and were stated as probably secondary to the ingestion of high doses of aescin. In Japan, where horse-chestnut has been used as an anti-inflammatory drug after surgery or trauma, hepatic injury has been described in a male patient who received an intramuscular injection of a proprietary product containing horse-chestnut. Liver function tests showed a mild abnormality and a diagnosis of giant cell tumour of bone (grade 2) by bone biopsy was made. Other side-effects stated to have been reported for the product include shock, spasm, mild nausea, vomiting, and urticaria.

The effect of aescin, both free and albumin-bound, on renal tubular transport processes has been studied in the isolated, artificially perfused frog kidney. Aescin was found to primarily affect tubular, rather than glomerular, epithelium and that binding to plasma protein (approximately 50%) protects against this nephotoxicity. Aescin was thought to be neither secreted nor reabsorbed in the tubules and the concentration of unbound aescin filtered through the kidney (13%) was considered to be too low to have toxic effects. The authors commented that the symptoms of acute renal failure in man are caused primarily by interference with glomeruli and in view of this, the nephrotoxic potential of aescin is probably only relevant when the kidneys are already damaged and also if the aescin is displaced from its binding to plasma protein.

A proprietary product containing horse-chestnut (together with phenopyrazone and cardiac glycoside-containing plant extracts) has been associated with the development of a drug-induced auto-immune disease called 'pseudolupus syndrome' in Germany and Switzerland. The individual component in the product responsible for the syndrome was not established. It has been noted that death occurs rapidly in animals given large doses of aescin, due to massive haemolysis. Death is more prolonged in animals given smaller doses of aescin. LD₅₀ values for aescin have been estimated in mice, rats, and guinea pigs and range from 134 to 720 mg/kg (by mouth) and from 1.4 to 15.2 mg/kg (intravenous injection). The total saponin fraction has been reported to be less toxic in mice (intraperitoneal injection) compared to the isolated aescin mixture (LD₅₀ 46.5 mg/kg and 9.5 mg/kg, respectively). The haemolytic index of horse-chestnut is documented as 6 000 compared to 9 500 to 12 500 for aescin.

Contra-indications, Warnings

Horse-chestnut may be irritant to the gastro-intestinal tract due to the saponin constituents. Saponins are generally recognised to possess haemolytic properties but are not usually absorbed from the gastro-intestinal tract following oral administration. Horse-chestnut may interfere with anticoagulant/coagulant therapy (coumarin constituents). Aescin, the main saponin component in horse-chestnut, binds to plasma protein and may affect the binding of other drugs. Horse-chestnut should be avoided by patients with existing renal or hepatic impairment.

Pregnancy and lactation The safety of horse-chestnut during pregnancy and lactation has not been established. In view of the pharmacologically active constituents present in horse-chestnut, use during pregnancy and lactation is best avoided.

Pharmaceutical Comment

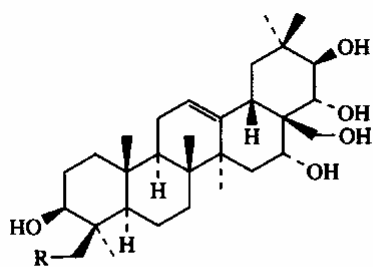
Horse-chestnut is traditionally characterised by its saponin components, in particular aescin which represents a mixture of compounds. However, horse-chestnut also contains other pharmacologically active constituents including coumarins and flavonoids. The traditional use of horse-chestnut in peripheral vascular disorders has largely been substantiated by studies in animals and humans, in which anti-inflammatory and capillary stabilising effects have been observed. Many of the documented activities can probably be attributed to the saponin and flavonoid constituents in horse-chestnut.

33. Krochmal, Arnold & Connie: A guide to the Medicinal plants of the United States. Quadrangle, the New York Times Book Co. 1973. ISBN No. 0-8129-0261-0.

Common names: Buckeye tree, horsechestnut.

Uses: In Appalachia, people have carried horsechestnuts in their pockets to prevent rheumatism. A tincture of the seeds has been used to treat haemorrhoids. An infusion of the bark or nuts has been used to cure skin sores and ulcers. The flowers have been used to treat rheumatism, the bark and fruit as a tonic and to treat fever. The fruit has been used to treat rectal complaints, haemorrhoids, rheumatism and neuralgia.

34. Paul M. Dewick: Medicinal Natural Products - a biosynthetic approach. John Wiley & Son. ISBN No.0-471-97478-1 (ppb), 0-471-97477-3 (hardback).



R = OH, protoaescigenin
R = H, barringtonol

Seeds of horsechestnut (*Aesculus hippocastanum*) sometimes used in herbal preparations as anti-inflammatory and anti-bruising remedy, contain a complex mixture of saponins termed **aescin**, based on the polyhydroxylated aglycones **protoaescigenin** and **barringtonol**. Several of these hydroxyls are esterified with aliphatic acids, e.g. acetic, tiglic and angelic acids.

35. Charles F. Millspaugh: American Medicinal Plants - an illustrated and descriptive guide to plants indigenous to and naturalised in the United States,

which are used in medicine. Dover Publications, New York. 1974. ISBN No. 0-486-23034-1. Originally published by John C. Yorston & Co., Philadelphia in 1892 under the title *Medicinal Plants*.

AESCVLUS HIPPOCASTANUM.

Horse chestnut. A tincture of the fresh, ripe, hulled nut of *Aesculus hippocastanum*, Linn.

Description.--This stately, umbrageous tree usually attains a growth of about 60 feet in height, and 50 feet in diameter of foliage. Trunk erect; ovate, and smooth-barked when young; oval, tending to quadrilateral, when old; bark of the full grown tree greyish, rough, and fissured; inner bark smooth, greenish-white, tough, fibrous, astringent, and bitter; wood light, not durable. Leaves opposite, digitately 7-lobed; leaflets 7, obovate, with a cuneate base, acute tip, and doubly-serrate margin; straight-feather veined, early deciduous. Inflorescence dense, pyramidal, upright, hyacinthine thyrsi, terminal upon the shoots of the season; flowers many, often polygamous, the greater proportion of them sterile; pedicels articulated. Calyx tubular or bell-shaped, oblique or inflated at the base; lobes 5-lobed. Corolla spreading, white, spotted with purple and yellow: petals 4-5~ usually 5, more or less unequal, nearly hypogynous, clawed and undulate margined. Stamens 6-8, usually 7, declined; filaments unequal, awl-shaped, long and slender; anthers oval, 2-celled. Ovary ovate, stipitate, 3-celled; style 1, filiform; stigma acute; ovules 1 in each cell. Fruit a roundish, echinate, 1-celled, 1-valved capsule, splitting into 4 dissepiments, disclosing 1-2 full formed, somewhat hemispherical nuts, and sometimes an aborted third; seed a large amylaceous nut, having a dense shining testa marked with a large roundish hilum; cotyledons 2, thick, sarcochering; radicle conical, curved.

Sapindaceae.--This large and variable order is chiefly tropical, especially the typical suborder, of which the genus under consideration is the only North American can

representative. The family is composed of trees, shrubs, or tendril-bearing climbers, showing widely different characters of leaf, flower, and fruit; and includes the soapberries, bladder-nuts, and maples. The leaves are usually alternate (Exe. *Aesculus*), simple or compound. E2bwcrs mostly irregular and unsymmetrical; sepals 4-5, imbricate in aestivation: petals 4-5 alternate with the sepals, and sometimes wanting. Disk sarcous, regular, expanded, or glandular, protruding between the petals and stamens. Stamens 5-10, perigynous or hypogynous; filaments free or cohering at their bases: anthers introrse. Ovary 1-3 celled and lobed; ovules 1-2 in each cell; style simple, or 2-3 cleft. Fruit a capsule, samara, or fleshy indehiscent drupe; embryo curved or convolute (Exe. *Staphylea*): albumen wanting.

The plants that are of particular interest to us in this family, beside the two under consideration here, are: Guarana or Brazilian Cocoa (*Paulinia sorbilis*, Mart.), and the Brazilian timbo-sipo (*Paulinia pinnata*, D. C.). Economically the berries of *Sapindus saponaria* and the bark and roots of other species are used in lieu of soap in cleansing woollens. The genus *Paullinia* contains many species in which a deleterious narcotic constituent is developed in the juice or seeds; the native Brazilians prepare a slow but potent and certain poison from *Paullinia pinnata*; *P. australis* is supposed to be the origin of a venomous honey round in the Brazilian woods; and *P. curruru* yields an arrow poison to the natives of Guiana, who also prepare a narcotic intoxicating drink from *P. cupana*. The products of most species of this order are to be regarded with suspicion, yet the Chinese *Lee Chee* (*Nephelium Litchi*) and Longan (*Nephelium Litchi*) are delicious fruits; the Brazilian Fruta de Pavao (*Schmidelia edulis*) is sweet and palatable; and the Jamaica wing-leaved honey-berry (*Melicocca bijugis*) edible, sub-acid, and pleasant. The berries of many species of the genus *Sapindus* are edible, though the seeds, used by the natives of the country of their growth to poison fish, are active narcotic toxicants.

History and Habitat.--The horse chestnut is a native of Asia; it was introduced into Europe about the middle of the sixteenth century by seed, and first cultivated in England by Tradescant in 1633;+ alter this its growth became quite general, as the tree accommodates itself quickly to all temperate regions. It is one of our first trees to bud in the spring, and Bowers in April and May, its fruit being fully ripe at the first autumn frost. Being one of our most dense shade trees, dark, cool, and clean, it is extensively planted in the yards and along the streets of almost every American city and village. The nuts are eaten greedily by horses, sheep, goats, cows, and pigs, and form an excellent fattening food for those animals when prepared in such a manner as to drive off the acrimony. This is best accomplished by boiling them in potash and washing them with water. Germination, however, renders them pleasant food through change of the bitter principles to saccharine, a result similar to that produced in malting barley. The nuts are said to yield a starch of finer quality than that of any cereal (Parmentier); paste made of the powdered nuts is claimed to be very tenacious and not attacked by moths and vermin; the saponaceous property of the seeds, when used in lieu of soap, is highly esteemed in cleaning and fulling woollens, especially in France and Switzerland (Marcandier). The nuts of *Aesculus Californica* are largely used by the natives of that State for making into bread, after removing the bitterness by freely washing the powdered cotyledons. The fruit of *Ae. pavia* is used by the Aborigines for stupefying fish; this species is so common in Ohio that it has become an emblem, and given rise to the sobriquet "Buckeye State."

The use of Cortex hippocastani dates from the writings of Matthiolus.* In Europe it was put forward, especially by Zannichelli, as an efficient remedy for intermittent fevers of various types; this use has been upheld by many able medical writers, from whose works it would

appear equal if not superior at that time to Peruvian bark. The usual dose given was from one to four scruples of the powder, repeated from two to six times in twenty-four hours; this use seems never to have extended to England or America. The bark and nuts were introduced into the Edinburgh College with a view to their errhine power; it being known that insufflation of the powder caused violent sneezing, it was recommended for the purpose of producing or promoting nasal discharge.

In this country, especially among the laity, the nuts have been greatly esteemed as a remedy for haemorrhoids and rheumatism, used either as a decoction or as a salve prepared with lard. So great is the faith of many people afflicted with either of these diseased conditions, that they carry a few nuts in their pockets from season to season, fully confident that the disorder is warded off by this means. In Europe, the oil procured by means of ether is used largely in neuralgia and rheumatism. An infusion of the bark or nuts is said to act favourably in the healing of indolent and gangrenous ulcers. The testa of the nuts is narcotic; according to Dr. McDowell 10 grains are equal to 3 grains of opium.

Aesculus is not officinal in the U. S. Ph., nor has it an officinal preparation in the Eclectic Materia Medica, though used--especially as an extract--under the name Aesculin.

PART USED AND PREPARATION.--The fresh, ripe, hulled nut is pounded to a pulp and weighed. Then two parts by weight of alcohol are taken, the pulp mixed thoroughly with one-sixth part of it, and the rest of the alcohol added. After stirring the whole well, and pouring it into a well-stoppered bottle, it is allowed to stand at least eight days in a dark, cool place.

The tincture, separated from the mass by filtration, has a clear brownish-orange colour by transmitted light; no characteristic odour; an extremely bitter, acrid, and astringent taste, and an acid reaction. An amylaceous deposit takes place on standing, which, being of no value to the preparation, may be filtered off.

CHEMICAL CONSTITUENTS.--Aesculin. This aromatic glucoside exists in the bark of many trees of the genera *Pavia* and *Aesculus*. It crystallizes in fine, snowy needles and globules, which lose their water of crystallization and fuse at 160°C (320° F), decomposing at higher temperatures. They are soluble in both hot and cold water and in alcohol, their solutions exhibiting a fine light-blue fluorescence. Boiling with dilute mineral acids decomposes this body into glucose and

Aesculetin, another glucoside, which also exists in a free state in the bark. This body is only sparingly soluble in water, and crystallizes in bitter needles, which break down under the action of boiling potash into formic, oxalic, and protocatechinic acids.

Paviin. This glucoside is considered identical with fraxin, and will be found described under *Fraxinus Americana*.

Oil of Aesculus. This oil is readily obtained from the nuts of this species by etherial extraction. It results as a beautiful yellow liquid, congealing at 1" (f 3·8" F.), and becoming solid at -50 ('3" F.).

Quercetrin. This coloring matter of quercitron, occurs in the testa of the nut and in the flowers.

Aesculetinic acid is one of the resultants of a still farther decomposition taking place in glucose and aesculetin when they are decomposition products of the action of baryta water upon aesculin.

Aescinic acid. This amorphous body is a decomposition product of aphrodaescin when boiled with liquor potassa.

Argyraecin. This acrid, amorphous glucoside was discovered by Rochelder in 1862 as a constituent of the seed. It is soluble in alcohol and water; a watery solution forming a soapy foam on agitation. This body together with

Aphrodaescin, another acrid, amorphous principle, having the same properties of solubility and saponification, and breaking down under the action of a concentrated mineral acid into sugar and aescigenin, so markedly resemble saponin that a question arises as to whether they are specific principles, or are to be considered together as

Saponin. This peculiar glucoside, existing in the roots of *Saponaria officinalis*, many species of *Lychnis*, *Polyga senega*, *Gypsophila struthium*, *Lucuma glycyphloea*, *Monnina polystachya*, *Quillaja saponaria* and many other plants, including ferns; has, before the observation of Rochelder, been accounted a principle of the nuts of this plant. It is a white, amorphous, sternutatory powder, having at first a sweetish, then a pungent and lastingly acrid taste. It is readily soluble in water, the solution frothing like that of soap on agitation, and is resolved under the action of concentrated hydrochloric acid into an amorphous sugar and sapogenin.

Although our tincture is made of the nuclei of the nuts only, still it would seem as if the bitterness, astringency, and agrimony present were due to all or nearly all of the above constituents found in the bark.

PHYSIOLOGICAL ACTION.--We have no accessible accounts of poisonings by this drug, still the provings, being made with goodly sized doses of the tincture, are sufficient to give us an insight into the physiological action. *Aesculus hippocastanum* causes inflammation of the mucous membranes of the respiratory and digestive tracts, and especially of the rectum; this is shown in the following list of symptoms: Dryness, heat, burning and swelling of the mucous membranes of the nose, larynx, and trachea, with a subsequent copious catarrhal discharge: the same symptoms prevail in the mouth and oesophagus, followed by profuse ptyalism and mucous discharge; the tongue becomes coated with a thick white or yellow fur. and reels as if scalded; the throat becomes congested, raw, and burning followed by a sense of constriction, and renders deglutition painful and difficult. Constant burning in the stomach and epigastrium, followed by nausea, retching, and violent vomiting with great tenderness and colic throughout the abdomen. are markedly present. Severe dryness, burning, and soreness of the rectum, with prolapse, and sufficient inflammation of the haemorrhoidal veins to result in purple tumors, indicate the severity of the action of the drug in this locality. Ineffectual efforts at stool, with great urging, and constant severe pain in the lumbar region, extending to the hips and sacrum, are constant symptoms of the drug. Its action upon the liver and portal system is marked by severe congestion, and attendant burning, constrictive pains and deep soreness. The provings, however, fail to substantiate its previous use in intermittent fever and neuralgia; its febrile symptoms being only slight and its pains, other than those referable to the alimentary tract, slight and not characteristic of nerve irritation.

36. Prof. S. Talalaj & Dr. A.S. Czechowicz: Herbal Remedies - harmful and beneficial effects. Published by Hill Content Publishing. 1989 (first edition). ISBN No: 0-85572-1898.

Parts used: Seeds, flowers, bark.

Active constituents: Triterpenoid saponins, mainly aescin (5%). Also coumarins and flavonoids

Pharmacological action: Anti-oedematic, vasotonic, haemostatic.

Medicinal uses: Internally, horse-chestnut preparations have primarily been used in the treatment of deficient peripheral circulation and oedematous conditions. It strengthens the tone of the veins, increases capillary resistance, and shows capillary sealing effects. It is useful in the treatment of varicose veins, leg ulcers, and haemorrhoids. Externally, it has been employed in the treatment of leg ulcers, skin inflammations, bums, and frostbite. It is extensively used in homeopathic medicine to treat varicose veins and haemorrhoids.

Toxicity: Horse-chestnut preparations, particularly of the seeds, are toxic in overdose. Cases of severe poisoning occur mostly in children who have eaten the seeds. Symptoms include vomiting, diarrhoea, uncoordinated twisting of muscles, dilated pupils, depression and even paralysis.

Contra-indications: it should be avoided during pregnancy and in cases of acute kidney dysfunction.

Remarks: doctor should be informed, when this plant is being used.

37. The British Herbal Pharmacopoeia 1996. The British Herbal Medicine Association (BHMA). 4th edition 1996. ISBN No. 0-903032-10-4.

Hippocastani semen

Horse-chestnut Seed consists of the dried seeds of *Aesculus hippocastanum* L.

CHARACTERISTICS

Macroscopical Description:

Dense, hard seeds, up to 2.53 cm, irregularly ovoid or subspherical, a few somewhat hemispherical, with an almost plane facet; surface smooth, dark, marbled reddish-brown, a little uneven and with dull lustre; large, nearly circular, rough, greyish-brown scar of hilum; larger seeds show a narrowish V-shaped ridge, marking the position of the radicle of the embryo, extending approximately one fifth of the circumference, the point terminating near a minute perforation in the testa close to the hilum. In section, tests 1-1.6 mm, dark brown, hard and brittle, closely surrounding the embryo of two large, horny, off-white cotyledons and radicle; endosperm absent.

Microscopical Description

HORSE CHESTNUT

Source: *Aesculus hippocastanum* L. (Family Hippocastanaceae).

GENERAL DESCRIPTION

Deciduous tree to 25 m; leaves opposite, digitate with five to seven obovate, irregularly crenate-serrate leaflets; glabrous above, tomentose beneath. Flowers white, with yellow to pink spot at base, in large cylindrical panicle. Spiny globose fruits 2 to 6 cm in diameter with large brown smooth seed, 2-4 cm in diameter; found in mountain woods, indigenous to central Balkan peninsula, widely planted and established throughout the northern hemisphere as a shade and ornamental tree (TUTIN 2). The parts used are the seed, branch bark, and leaves.

CHEMICAL COMPOSITION

The seeds and bark contain a mixture of triterpene saponins known as aescin (escin), composed of acylated glycosides of protoaescigenin and barringtogenol-C, hippoesculin and others; quinones, including plastoquinone 8; flavones, including 3,5-dihydroxy-3',4',7-trimethoxyflavone, myricetin 3',4',7-trimethyl ether; sterols, including stigmasterol, campesterol, and sitosterol; linolenic, palmitic, and stearic acids; and others. The glycoside aesculin (esculin) (7-hydroxycoumarin 6-O-glucoside) is considered the most toxic component of the seed (GLASBY 2; WREN).

PHARMACOLOGY OR BIOLOGICAL ACTIVITIES

Horsechestnut extracts, notably aescin, has antiinflammatory, antiedema, antiexudative, and venotonic activity.

Aescin was found to be responsible for antiexudative and edema-protective activity [3]. Aescin acts on the capillary membrane, normalizing vascular permeability, enhancing capillary resistance, and reducing the outflow of fluid into the extracapillary space [4]. Aescin has a "sealing" effect on the capillaries and reduces the number and diameter of the small pores of the capillary wall by which exchange of water occurs. Anti-inflammatory activity at the initial exudation phase of inflammation has been confirmed in various in vitro and in vivo models. [5,6]

In vitro aescin has been found to stimulate an increase in venous tone, with a decrease in the volume of venous district of the saphenous vein and its collaterals facilitating return blood flow to the heart. [2,7]

Efficacy of a 2%-aescin-containing gel in reducing tenderness of experimentally induced hematoma has recently been confirmed. [8]

In vitro antitumor activity has been observed from hippoesculin and barringtogenol-C-21-angelate. [2, 9]

Horsechestnut seeds are considered inedible and poisonous. The bitter flavor prevents consumption of large amounts. The leaves, flowers, young sprouts and seeds are toxic. Symptoms of poisoning include nervous muscle twitching, weakness, dilated pupils,

vomiting, diarrhoea, depression, paralysis and stupor (HARDIN AND ARENA). Incidents of anaphylactic shock after i.v. injections of horsechestnut have been reported, along with renal toxicity or failure (PROHNE AND PFANDER). [2]

USES

Medicinal, Pharmaceutical, and Cosmetic.

Horsechestnut extract or aescin (0.25-0.5%) has reportedly been used in shampoos, shower foams, foam baths, skin care products, body and hand creams, lotions, and toothpastes. Cosmetic use in Europe has been based on its clearing and redness reducing properties, and its effectiveness in preventing cellulitis. [10]

Numerous clinical studies and published case reports confirm the efficacy of aescin containing topical products, especially in the treatment of sports injuries, including blunt trauma of the lower limbs, [11] joint sprains, tendonitis, hematomas, muscle strain, traumatic edema, [12] Achilles' tendonitis; surgical outpatient trauma, including fractures, sprains, crush injuries, and contusion; [13] postoperative or postpartum oedema in gynaecology and obstetrics; [4] and others.

Intravenous (never extraveneous) administration of aescin in ampoules is used clinically by physicians in Germany and other European countries for treatment of posttraumatic, intraoperative or postoperative conditions of cerebral oedema, and other surgical specialities.[14]

Traditional Medicine. Fruits, bark, or seed has reportedly been used externally for ulcers; a folk cancer remedy. Seeds used for gastritis, enteritis, and hemorrhoids (DUKE 2). Bark tea astringent, used in malaria, dysentery; externally for lupus and skin ulcers (FOSTER AND DUKE).

Leaf preparations used in European traditions for eczema, varicose veins, supportive treatment of varicose ulcers, phlebitis, thrombophlebitis, hemorrhoids, menstrual spastic pain, soft tissue swelling from bone fracture and sprains, and other uses. Effectiveness of leaf preparation claims is unsubstantiated. [15].

COMMERCIAL PREPARATIONS

In Germany and other countries topical gels contain 1% aescin; ampoules containing 5.1 mg sodium aescinate (equivalent to 5 mg aescin); sugar-coated tablets; and liquid oral preparations are available. Topical products are available in Canada.[2]. No horsechestnut or aescin-containing drug formulations are available in the United States, though aescin is available in bulk.

Regulatory Status. Undetermined in the United States. In Germany, horse chestnut seeds are the subject of a positive therapeutic monograph, indicated for chronic venous insufficiency, including oedema, cramps in the calves, itching, pain and sensations of heaviness in the legs, varicose veins, post-thrombotic syndrome, plus posttraumatic and postoperative swelling of soft tissue, in average daily doses equivalent to U)-150 mg of aescin in liquid or solid preparations for oral administration." Horse chestnut leaf preparations claims are not substantiated, therefore, therapeutic use is not recommended. [15]

REFERENCES

See the General References for BLUMENTHAL; DUKE 2; FOSTER AND DUKE; FROHNE AND PFANDER; OLASBY 2; HARDIN AND ARENA; LIST AND HORHAMMER; MABBERLY; MARTINDALE; STEINMETZ; TUTIN 2; WEISS; WREN.

1. T. Konoshima and K. H. Lee, *J. Nat. Prod.*, 49, 4, 650.
2. R. F. Chandler, *Can. Pharm. J.*, 297 (July/Aug. 1993).
3. D. M. Lorenz and M. L. Marek, *Arzneim. Forsch.*, 10, 263 (1960).
4. D. Tenhaeff, *Arztliche Praxis*, 24(12), 559 (1972).
5. G. Vogel et al. *Arzneim. Forsch.*, U(5), 699 (1970).
6. M. I. Rothkopf and G. Vogel, *Arzneim. Forsch.*, 26(2), 225 (1976).
7. F. Annoni et al., *Arzneim. Forsch.*, 29(4), 672 (1979).
8. C. C. Calabrese and P. Preston, *Planta Med.*, 59(5), 394 (1993).
9. J. De Meirsmen and N. Rosselle, *Ars. Mad.*, 9(3), 247 (1980).
10. G. Properpio et al., *Fitoterapia*, 2, 113 (1980).
11. J. Rothhaar and W. Theil, *Med. Wochenschr.*, 33(27), 1006 (1982).
12. C. Zuinen, *Rev. Med. Liege*, 31(5), 169 (1976).
13. F. Jakob and B. Fassbender, *Fortschr. Med.*, 87(20/21), 893 (1969).
14. F. Heppner et al., *Wein. Med. Wochenschr.*, 117, 706 (1967).
15. Monograph *Hippocostani folium*, *Bundesanzeiger* (July 14, 1993).
16. Monograph *Hippocostoni semen*, *Bundesanzeiger*, no. 228 (Dec. 5, 1984).

LATEST REFERENCES FOR

Aesculus hippocastanum

1. Oschmann, R; Biber, A; Lang, F; Stumpf, H; Kunz, K. Pharmacokinetics of beta-aescin after administration of different *Aesculus*-extract containing formulations. [Pharmakokinetik von beta-Aescin nach Gabe verschiedener *Aesculus*-Extrakt enthaltender Formulierungen.] *Pharmazie* (1996) 51(8): 577-581. [German, en, 19 ref.] [Dr. Willmar Schwabe Arzneimittel, Willmar-Schwabe-Str. 4, D-76227 Karlsruhe, Germany.]

Using a specific radioimmunoassay, the pharmacokinetics and relative bioavailability of aescin were measured after administration of different formulations containing *Aesculus*-extract. Of special interest was the relative bioavailability of aescin after administration of a newly developed film-coated tablet with sustained release in comparison to a reference formulation. In a cross-over, steady-state study in 24 volunteers, bioequivalence of the test and reference preparations could be demonstrated.

2. Dittgen, M; Zimmermann, H; Wober, W; Hoflich, C; Breitbarth, H; Timpe, C. Study on the bioavailability of beta-aescin after oral administration of different formulations. [Untersuchung der Bioverfugbarkeit von beta-Aescin nach oraler Verabreichung verschiedener Darreichungsformen.] *Pharmazie* (1996) 51(8): 608-610. [German, 8 ref.] [Jenapharm GmbH, Otto-Schott-Strasse 15, D-07745 Jena, Germany.]

3. Diehm, C; Trampisch, HJ; Lange, S; Schmidt, C. Comparison of leg compression stocking and oral horse-chestnut seed extract therapy in patients with chronic venous insufficiency. *Lancet* (British edition) (1996) 347(8997): 292-294. [English, 10 ref.] [Department of

Internal Medicine/Vascular Medicine, Affiliated Teaching Hospital, University of Heidelberg, Guttmanstrasse 1, 76307 Karlsbad-Langensteinbach, Germany.]

A randomized, partially blind, placebo-controlled clinical trial was carried out in Germany on 240 patients with chronic venous insufficiency. Patients were treated for 12 weeks with compression stockings, 50 mg aescin (horse-chestnut [*Aesculus hippocastanum*] seed extract; Venostasin retard) twice daily, or placebo twice daily. The lower leg volume of the more severely affected limb decreased on average by 43.8 ml in the aescin group, decreased by 46.7 ml in the compression stocking group and increased by 9.8 ml in the placebo group. Significant oedema reduction was achieved by the seed extract and the stockings, and the two therapies were shown to be equivalent.

4. Hartisch, C; Kolodziej, H; Bruchhausen, F von. Dual inhibitory activities of tannins from *Hamamelis virginiana* and related polyphenols of 5-lipoxygenase and lyso-PAF:acetyl-CoA acetyltransferase. *Planta Medica* (1997) 63(2): 106-110. [English, 20 ref.] [Institut für Pharmazie II, Pharmazeutische Biologie, Freie Universität Berlin, Berlin, Germany.]

The effects were studied of tannins from *H. virginiana*, *Crataegus oxyacantha* [*C. laevigata*], *Prunus spinosa* and *Aesculus hippocastanum* on the activity of 5-lipoxygenase (5-LOX) and lyso-PAF:acetyl-CoA acetyltransferase (AT). With IC₅₀ values in the range 1-18.7 µM, hamamelitannin and the galloylated proanthocyanidins isolated from *H. virginiana* were the most potent inhibitors of 5-LOX. Unlike the 5-LOX study, hamamelitannin proved to be ineffective in the AT assay. Potent candidates are represented by the group of B-type proanthocyanidins. Structure-activity relationships regarding the *in vitro* inhibitory potency of the polyphenols in the biological assays are discussed.

5. Bombardelli, E; Morazzoni, P; Griffini, A. *Aesculus hippocastanum* L. *Fitoterapia* (1996) 67(6): 483-511. [English, 143 ref., 10 col. pl.] [INDENA Spa, Scientific Department, Viale Ortles 12, 20139 Milan, Italy.]

Seeds and bark *A. hippocastanum* have been widely used in European traditional medicine. Today extracts and chemical constituents ([a]aescin, a pure saponin, and [a]aesculin, a coumarin) are used in clinical practice mainly for the treatment of peripheral chronic venous insufficiency. The botany, chemistry, pharmacology and therapeutic uses of *A. hippocastanum* extracts and constituent chemicals are presented. Esculin is reported to possess microvasculokinetic activity and is indicated for the treatment of cellulitis and hair loss. Proanthocyanidin A2, a catechin dimer isolated from bark, exhibits protection against UV damage, mainly due to its very strong antioxidant properties.

6. Izzo, AA; Capasso, R; Senatore, F; Seccia, S; Morrica, P. Spasmolytic activity of medicinal plants used for the treatment of disorders involving smooth muscles. *Proceedings of the VIII Congresso nazionale della Societa Italiana di Farmacognosia and 1st joint meeting of Belgian, Dutch, Spanish and Italian research groups on pharmacognosy, Naples, Italy, 9-14 June 1996* [edited by Capasso, F.; Evans, F. J.; Mascolo, N.]. *Phytotherapy Research* (1996) 10(Supplement 1): S107-S108. [English, 3 ref.] [Department of Experimental Pharmacology, University of Naples 'Federico II', via D. Montesano 49, 80131 Naples, Italy.]

Sixteen hydroalcoholic extracts of plants traditionally used in Italian folk medicine to treat gastrointestinal and respiratory diseases were screened for antispasmodic activity using guineapig ileum. The extracts (100-800 µg/ml) of 4 plants (*Angelica archangelica* roots, *Eucalyptus globulus* leaves, *Aesculus hippocastanum* skinned seeds, *Lavandula angustifolia*

flowering tops) significantly reduced spontaneous contractions of smooth muscle in circular pieces (IC₅₀ values of 265-738 ug/ml). These extracts (50-800 ug/ml) inhibited acetylcholine- and barium chloride-induced contractions of smooth muscle in longitudinal sections (IC₅₀ values of 137-598 ug/ml). *Angelica archangelica* was the most potent.

7. Rehn, D; Unkauf, M; Klein, P; Jost, V; Lucker, PW. Comparative clinical efficacy and tolerability of oxerutins and horse chestnut extract in patients with chronic venous insufficiency. *Arzneimittel Forschung* (1996) 46(5): 483-487. [English, de, 23 ref.] [Zyma GmbH, Medizin und Entwicklung, Munich, Germany.]

Oxerutins (O-[beta-hydroxyethyl]rutosides, HR, Venoruton<reg trade mark>) and horse chestnut [*Aesculus hippocastanum*] extract (HCE) are used in the treatment of chronic venous insufficiency (CVI). Besides a direct comparison of the 2 compounds, the aim of this double-blind, randomized, placebo-controlled study was to investigate the initial dose/maintenance dose concept for HR. One hundred and thirty-seven female, postmenopausal patients with CVI grade II completed the study according to protocol. Following a 1-week placebo run-in, the patients were treated either with HR at 1000 mg/d or HCE at 600 mg/d for 12 weeks, or with HR at 1000 mg/d for 4 weeks and then at 500 mg/d for 8 weeks, and observed for a further 6 weeks. Efficacy was determined by reduction of leg volume. Subjective criteria were descriptively evaluated. HR (1000 mg/d) was proven to be equivalent or better than HCE, reducing the leg volume (AUB0-18) by -5273ñ11-418 ml/d compared with -3187ñ10-842 ml/d under HR (1000 mg/d and 500 mg/d), and -3004ñ7429 ml/d under HCE-treatment. Both compounds exhibited a substantial carry-over effect. The maintenance posology of HR is able to stabilize the therapeutic effect obtained under the initial dose conditions.

8. Yoshikawa, M; Murakami, T; Matsuda, H; Yamahara, J; Murakami, N; Kitagawa, I. Bioactive saponins and glycosides. III. Horse chestnut. (1): the structures, inhibitory effects on ethanol absorption, and hypoglycemic activity of escins Ia, Ib, IIa, IIb, and IIIa from the seeds of *Aesculus hippocastanum* L. *Chemical and Pharmaceutical Bulletin* (1996) 44(8): 1454-1464. [English, 36 ref.] [Kyoto Pharmaceutical University, 5 Nakauchi-cho, Misasagi, Yamashina-ku, Kyoto 607, Japan.]

A. hippocastanum seeds are used to treat peripheral vascular disorders and in cosmetics to prevent and treat cellulitis. Five bioactive triterpene oligoglycosides named escins Ia, Ib, IIa, IIb and IIIa were isolated from seeds of *A. hippocastanum*. The chemical structures of escins Ia, Ib, IIa, IIb, and IIIa were determined on the basis of chemical and physicochemical evidence, which included selective cleavage of the glucuronide linkage. Escins Ia, Ib, IIa, and IIb showed an ethanol absorption-inhibitory effect and hypoglycaemic activity in the oral glucose tolerance test in rats. Some structure-activity relationships are reported.

9. Profumo, P; Caviglia, AM; Gastaldo, P. Aescin formation in calli and embryoids from cotyledon and stem explants of *Aesculus hippocastanum* L. *Journal of Pharmacy and Pharmacology* (1994) 46(11): 924-925. [En, 11 ref.] [Institute of Botany, University of Genoa, 16136 Genoa, Italy.]

The aescin content of calli and embryoids, obtained from cotyledon and stem explants of *A. hippocastanum* (collected from the University Botanic Garden, Italy), and grown on MS medium containing kinetin, 2,4-D and NAA (all at 2 mg/litre), was analysed by HPLC. Aescin was produced in all the samples analysed. The callus cultures contained more aescin (31-47% DW) than the cotyledons from ripe seeds (11% DW).

10. Kockar, OM; Kara, M; Kara, S; Bozan, B; Baser, KHC. Quantitative determination of escin. A comparative study of HPLC and TLC-densitometry. *Fitoterapia* (1994) 65(5): 439-443. [En, 8 ref.] [Faculty of Engineering and Architecture, Anadolu University, Eskisehir, Turkey.]

Seeds of *Aesculus hippocastanum*, collected from Eskisehir, their 50% ethanol extract and a commercial *A. hippocastanum* extract were analysed for their escin contents, using either HPLC or TLC-densitometry. Both methods gave similar results and had a high degree of accuracy, with their linear calibration curves showing the same regression coefficient ($r=0.9998$).

1. Buchbauer, G; Jirovetz, L; Wasicky, M; Nikiforov, A. Volatiles of common horsechestnut (*Aesculus hippocastanum* L.) (*Hippocastanaceae*) peels and seeds. *Journal of Essential Oil Research* (1994) 6(5): 507-511. [En, 7 ref.] [Institute of Pharmaceutical Chemistry, University of Vienna, 1090 Vienna, Austria.]

The headspace, essential oil and dichloromethane extract of *A. hippocastanum* peel, and the essential oil of seeds (collected from Vienna) were analysed by GC, GC/FTIR/MS and GC-sniffing techniques. The headspace (fresh, green, weak dull odour, similar to peel odour) was rich in 3-hexenol (8.2%), 2-heptanol (5.2%), 2-heptenone (4.7%), benzyl alcohol (4.1%), 2-methylbutanyl (3.7%), 2-phenyl ethanol (3.5%), isovaleraldehyde (3.3%) and 2-octanol (3.3%). The peel essential oil and the peel extract showed a similar composition, but differed in olfactic impression; the essential oil had a weak green, dry, unpleasant burning and fatty side-note odour, whilst the odour of the extract was green, weak fruity, fatty-waxy in the background. The concentrations of the main compounds in both samples were less than in the headspace. The main volatile constituents of the seed essential oil were nonanal (5.3%), 3-hexenol (5.2%), nonanoic acid (4.6%), benzyl alcohol (3.9%) and 2-heptanol (3.2%). The seed essential oil had a bakery like, sweet, spicy with fatty by-notes odour; the odour of cut seeds was fatty, weak sweet and aromatic.

12. Yoshikawa, M; Harada, E; Murakami, T; Matsuda, H; Wariishi, N; Yamahara, J; Murakami, N; Kitagawa, I. Escins-Ia, Ib, IIa, IIb, and IIIa, bioactive triterpene oligoglycosides from the seeds of *Aesculus hippocastanum* L.: their inhibitory effects on ethanol absorption and hypoglycemic activity on glucose tolerance test. *Chemical and Pharmaceutical Bulletin* (1994) 42(6): 1357-1359. [En, 15 ref.] [Kyoto Pharmaceutical University, Misasagi, Yamashina-ku, Kyoto 607, Japan.]

The seeds of *A. hippocastanum* are known to contain the saponin, escin, which is used medicinally to treat peripheral vascular disorders and cellulitis. Five triterpene oligoglycosides, named escins Ia, Ib, IIa, IIb and IIIa, were isolated from *A. hippocastanum* seeds, and their structures were elucidated from chemical and physicochemical analyses. Escins-Ia, Ib, IIa and IIb inhibited ethanol absorption, and exhibited hypoglycaemic activity in oral glucose tolerance tests with rats. In both bioassays, escins IIa and IIb, which possess a 2'-O-xylopyranosyl group, showed higher activities than escins Ia and Ib, which possess a 2'-O-glucopyranosyl group in the oligosaccharide moiety.

13. Delitheos, A; Tiligada, E; Yannitsaros, A; Bazos, I. Antiphage activity in extracts of plants growing in Greece. *Phytomedicine* (1997) 4(2): 117-124. [English, 52 ref.] [Institute of Pharmaceutical Research and Technology, Pallini Attikis, Greece.]

Crude aqueous extracts of 255 plant taxa growing in various areas of Greece were screened for antiphage activity against 6 bacteriophages (T1, T2, T4, T7, MS2 and ϕ X 174). This laboratory model was used for the initial detection of antiviral and/or antineoplastic activity. Thirty-eight extracts showed antiphage activity against one or more of the bacterial viruses used. When the active extracts were tested in the presence of Tryptone Soya Broth, part of the antiphage activity remained in 7 extracts (*Aesculus hippocastanum*, *Cotinus coggygria*, *Epilobium angustifolium*, *Hypericum perforatum*, *Limonium graecum*, *Quercus coccifera* and *Rumex pulcher*), whereas when tested in the presence of fresh human plasma, the antiphage activity was abolished, possibly due to the precipitation of the active compounds by tannins or related substances.

14. Matsuda, H., Li, Y., Murakami, T., Ninomiya, K., Yamahara, J., Yoshikawa, M. Effects of escins Ia, Ib, IIa, and IIb from horse chestnut, the seeds of *Aesculus hippocastanum* L., on acute inflammation in animals. *Biological & Pharmaceutical Bulletin* 1997 20 10 1092-1095 En 4 ref. Kyoto Pharmaceutical University, 5 Nakauchi-cho, Misasagi, Yamashina-ku, Kyoto 607, Japan.

Seeds of *A. hippocastanum* are used in the therapy of peripheral vascular disorders and in cosmetics for the prevention and treatment of cellulitis. The effects of escins Ia, Ib, IIa, and IIb isolated from the seeds of *A. hippocastanum*, and desacylescins I and II obtained by alkaline hydrolysis of escins were studied on acute inflammation in rats and mice (p.o.). Escins Ia, Ib, IIa, and IIb (50-200 mg/kg) inhibited the increase of vascular permeability induced by both acetic acid in mice and histamine in rats. Escins Ib, IIa, and IIb (50-200 mg/kg) also inhibited that induced by serotonin in rats, but escin Ia did not. Escins Ia, Ib, IIa, and IIb (200 mg/kg) inhibited the hind paw oedema induced by carrageenin at the first phase in rats. Escin Ia (200 mg/kg) and escins Ib, IIa, and IIb (50-200 mg/kg) inhibited the scratching behaviour induced by compound 48/80 in mice, but escin Ia was weakest. Desacylescins I and II (200 mg/kg) showed no effect. With regard to the relationship between their chemical structures and activities, the acyl groups in escins were essential. Escins Ib, IIa, and IIb with either the 21-angeloyl group or the 2'-O-xylopyranosyl moiety showed more potent activities than escin Ia which had both the 21-tigloyl group and the 2'-O-glucopyranosyl moiety. *Aesculus hippocastanum*, seeds, inflammation, rats, mice, medicinal plants, medicinal properties, antiinflammatory properties, oedema, saponins, chemical structure, structure activity relationships, plant composition, pharmacology.

15. Griffini, A., Lolla, E., Peterlongo, F. Liquid chromatography-thermospray mass spectrometry analysis of β -escin. *Fitoterapia* 1997 68 6 520-526 5C00403 En 17 ref. Indena S.p.A., Research & Development Laboratories, Via Don Minzoni 6, 20090 Settala, Milan, Italy.

An HPLC-UV method was developed for the analysis of β -escin, the active principle obtained from the seeds of *Aesculus hippocastanum*. On-line combination with thermospray mass spectrometry, LC-MS (TSP), allowed identification of both main and minor saponin constituents. Positive thermospray mass spectra proved useful in providing information on the molecular weights and on the nature of sugars. *Aesculus hippocastanum*, saponins, mass spectrometry, analysis, plant composition, seeds, HPLC, analytical methods, medicinal plants.

16. Komissarenko, NF; Derkach, AI; Komissarenko, AN; Chermeneva, GV; Spiridonov, VN. Coumarins of *Aesculus hippocastanum* L. *Rastitel'nye Resursy* (1994) 30(3): 53-59. [Ru, 18

ref.] [Gosudarstvennyi Nauchnyi Tsentr Lekarstvennykh Sredstv Ukraina, Khar'kov, Ukraine.]

The coumarin content was determined in the flowers, leaves, seeds and seed coats, trunk and shoot bark, and wood. The data are tabulated. Eleven substances were extracted and identified, viz. umbelliferone, esculetin, scopoletin, isoscapoletin, fraxetin, skimmion, esculin, cichoriin, scopolin, isoscapolin and fraxin.

17. Kolodziej, H; Haberland, C; Woerdenbag, HJ; Konings, AWT. Moderate cytotoxicity of proanthocyanidins to human tumour cell lines. *Phytotherapy Research* (1995) 9(6): 410-415. [English, 31 ref.] [Institut für Pharmazeutische Biologie, Freie Universität Berlin, Königin-Luise Str. 2 + 4, D-14195 Berlin, Germany.]

The cytotoxicity of 16 proanthocyanidins, 12 of which were isolated from *Hamamelis virginiana*, *Prunus spinosa*, *Aesculus hippocastanum* and *Crataegus oxyacantha* [*C. laevigata*], was evaluated against GLC4 and COLO 320, using the microculture tetrazolium (MTT) assay. The proanthocyanidins exhibited low to moderate cytotoxicity (IC₅₀ values of 18 to >200 µM). Galloylated proanthocyanidins exhibited the highest cytotoxicity. An increase in the number of galloyl substituents increased cytotoxicity. Simple proanthocyanidins possessed low cytotoxicity, that was independent of the stereochemistry. Compounds with doubly linked units had negligible cytotoxic effects.

18. Masaki, H; Sakaki, S; Atsumi, T; Sakurao, H. Active-oxygen scavenging activity of plant extracts. *Biological & Pharmaceutical Bulletin* (1995) 18(1): 162-166. [English, 22 ref.] [Shiga Central Laboratory, Noevir Co., Ltd., 112-1, Okada-cho, Youkaichi 527, Japan.]

Of 65 plant extracts tested using the neotetrazolium method for evidence of superoxide anion-scavenging effects, 7 were selected for further investigation. The active oxygen scavenging activity (against superoxide anion radicals, hydroxyl radicals and singlet oxygens) and anti-lipid peroxidation activity of the 7 plant extracts (*Aesculus* [*Aesculus*] *hippocastanum*, *Hamamelis virginiana*, *Polygonum cuspidatum* [*Reynoutria japonica*], *Quercus robur*, *Rosemarinus* [*Rosmarinus*] *officinalis*, *Salvia officinalis* and *Sanguisorba officinalis*) were examined in detail by ESR spin-trapping and malondialdehyde generation, respectively. Furthermore, the active-oxygen scavenging activity of these plant extracts was evaluated using a murine dermal fibroblast culture system. Both *A. hippocastanum* and *H. virginiana* had strong active-oxygen scavenging activity and protective activity against cell damage induced by active oxygen. Both *A. hippocastanum* and *H. virginiana* are proposed as potent plant extracts with potential uses as anti-aging or anti-wrinkle materials for the skin.

19. Khan, L; Ahmad, N; Ahmad, KD; Kifayatullah, Q; Arfan, M. Commercial extraction of aescin. *International Journal of Pharmacognosy* (1995) 33(4): 344-345. [English, 8 ref.] [Natural Drugs Division, P.C.S.I.R. Laboratories, Peshawar Pakistan.]

A simple and economical method for the isolation of aescin from the dried seeds of *Aesculus indica* (collected from Pakistan) is presented. Aescin was selectively extracted in EtOH-H₂O. The extract was acidified with 4 N H₂SO₄ to pH 1, then placed in a water bath until the aescin precipitated out. The identity of the isolated compound was confirmed from spectral and physicochemical data, and from haemolytic and potentiometric characteristics.