Horse chestnut

BOTANY

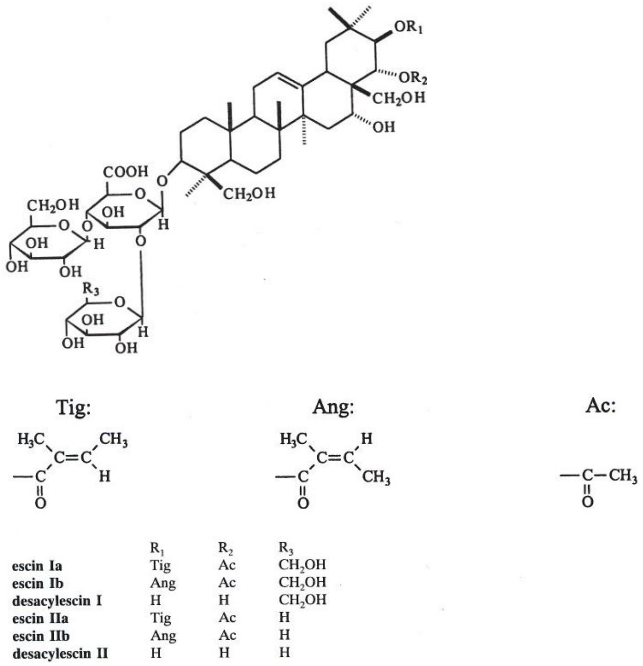
Aesculus hippocastanum L., common name Horse chestnut, belongs to the Hippocastaneae family. This tree may grow up to 20-30m tall. The bark is soft in young trees and scaly-like in aged trees. Leaves are deciduous, divided into 5-7 irregularly toothed leaflets, from 8 to 20 cm long. Flowers appear by the beginning of the summer; with irregular corollas made of five ovate petals; flowers in different colors: white, yellow, reddish-pink, arranged in spikes about 30 cm long; calyx bell-shaped with seven stamens, which support reddish-brown anthers. The fruit is a large spiky capsule with three valves, containing globose seeds; the seeds are covered with a glossy brown tegument with whitish spots and have two large cotyledons. Horse chestnut is native to the Caucasus and the Balkan Peninsula, particularly to the north of Greece, where it still grows in the wild. Horse chestnut is currently cultivated worldwide; it is completely adapted to temperate climates.

Horse chestnut extract is produced from the seeds of *Aesculus hippocastanum* L.

CHEMISTRY

Triterpene saponins

Saponins are the most relevant active principles in horse chestnut seeds. Saponins account for 10% of the seed cotyledons composition. The main constituent is β-escin (escin); aphrodaescin, argyraescin and cryptoaescin are also present. Escin is a mixture of more than 30 different saponins, basically derived from 2 aglycones: protoaescigenin and barringtogenol C, which only differ in a C-24 hydroxyl group on the second aglycone. Saponins give the seeds their pungent bitter flavor.

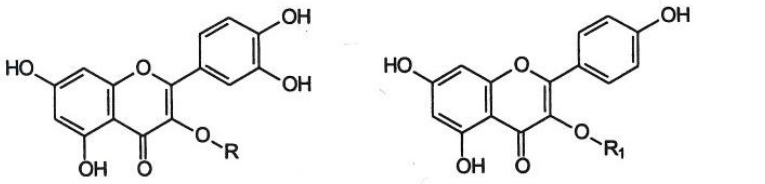


	R_1	R_2	R_3
escin Ia	Tig	Ac	CH_2OH
escin Ib	Ang	Ac	CH_2OH
desacylescin I	H	H	CH_2OH
escin IIa	Tig	Ac	H
escin IIb	Ang	Ac	H
desacylescin II	H	H	H

Fig.1. Structure of the main saponins in escin (Wilkinson, J.A. & Brown, A.M.G., 1999).

Flavonoids

Several flavonoids have been identified in *A. hippocastanum* seeds, mainly heterosides of quercetin and kaempferol; they include astragalin, isoquercitrin, leucocyanidin and rutin.



R = Rutinoside: **Rutin**
R = Rhamnoside: **Quercitrin**
R = Glucose: **Isoquercitrin**
R = Arabinoside: **Quercetin 3-arabinoside**

R_1 = Rutinoside: **Kaempferol 3-O-rutinoside**
R_1 = Rhamnoside: **Kaempferol 3-O-rhamnoside**
R_1 = Glucose: **Astragalin**
R_1 = Arabinoside: **Kaempferol 3-arabinoside**

Fig.2. Strucure of the flavonoids in *A.hippocastanum* (Wilkinson, J.A. & Brown, A.M.G., 1999).

Proanthocyanidins

Horse chestnut seeds also contain proanthocyanidins.

Proanthocyanidins are included in the condensed tannins or proanthocyanidols group. These compounds are flavan polymers. Flavan polymers are made up of flavan-3-ols units attached one to each other by carbon-carbon bonds, generally 4→8 or 4→6, which result from the attachment between the electrophilic C-4 of a flavanyl (coming from a flavan-4-ol or a flavan-3,4-diol) and a nucleophilic position (usually C-8 and less frequently C-6) of another unit, generally flavan-3-ol (Bruneton J., 2001).

Coumarins
Esculin and fraxin.

The name coumarin comes from “coumarou”, the vernacular name for the Tonka bean (*Dipteryx odorata* Willd.), from which coumarins were first isolated, in 1820. Coumarins are 2*H*-1-benzopyran-2-ones, which can be initially considered as the lactones of the 2-hydroxy-Z-cinnamic acids. More than a thousand coumarins have been described, the simplest ones being distributed throughout the vegetable kingdom (Bruneton, J. ,2001).

Other active principles
Vitamins of the B, K_1 and C groups, provitamin D, phytosterols, catechin tannins (≤2%), adenine, adenosine, guanine, L(+)lysine, L(-)tryptophan, fatty acids (2-5%) mainly oleic, linoleic, linolenic, stearic and palmitic acids, starch (30-40%), sugar (9%) and proteins (8-10%).

TRADITIONAL USES

The origin of the botanical name of this plant is uncertain. *Aesculus* is the ancient name for some oak trees, which resemble horse chestnut. *Hippocastanum* refers to the fact that the fruits were usually fed to horses. Horse chestnut is recommended to prevent and treat chronic venous insufficiency, varicose veins, tired legs, edemas of different origins, sequela of phlebitis and hemorrhoids, and as a coadjuvant in treatments for cellulite and arthritis with edema. It has been found useful to treat ecchymosis, hemorrhagic diathesis, metrorrhagia and capillary fragility. For these purposes, infusion or extract of the seeds are used.

COSMETIC PROPERTIES

Anti-inflammatory, anti-edema and venotonic activities
Chronic venous insufficiency is a condition that may include leg swelling, varicose veins, leg pain, itching, and skin ulcers. There is evidence from laboratory, animal, and human research that horse chestnut seed extract may be beneficial to patients with this condition. Studies report significant decreases in leg size, leg pain, itchiness, fatigue and "tenseness." There is preliminary evidence that horse chestnut seed extract may be as effective as compression stockings.
(http://www.nlm.nih.gov/medlineplus/spanish/druginfo/natural/patient-horsechestnut.html).

Due to their escin content, horse chestnut seeds have anti-inflammatory and venotonic properties, which decrease blood-vessels permeability and produce an important anti-edema effect. Horse chestnut seeds extract reduces lysosomic enzymatic activity (β-glucuronidase and arylsulfatase) – which is augmented in chronic venous pathologies – thus reducing the hydrolysis of proteoglycans in the capillary walls. Furthermore, reduced vascular permeability reduces the leakage of low molecular-weight proteins, electrolytes and water to the interstitial space. These escin properties are based on a molecular mechanism that improves calcium ions intake, which results in *in vivo* as well as *in vitro* increase in venous tension. Further mechanisms, such as prostaglandin F2 (PGF2) release, antagonism to histamine and reduction of tissue mucopolysaccharides catabolism, contribute to the former pharmacological actions (www.fitoterapia.net).

Topical applications of escin and its aglycone, escinol, have been demonstrated to possess non-competitive anti-hyaluronidase activity. *A. hippocastanum* has protective effects on the connective tissues, which surround the capillary vessels. In chronic venous insufficiency, the capillaries become highly permeable; the outcome is that water and proteins leave the vascular system, which in turn cause swelling. This may be as a result of the degradation of the extracellular matrix surrounding the capillaries. The main component of this extracellular matrix is hyaluronic acid; levels of this compound are usually regulated by the enzyme hyaluronidase, which promotes the degradation of hyaluronic acid. This inhibition of hyaluronidase should lead to the recovery of the integrity of hyaluronic acid, and consequently of the extracellular matrix surrounding the capillaries (Wilkinson, J.A. & Brown, A.M.G., 1999).

The venotonic effects of escin were evaluated on isolated human saphenous veins. Stimulation with escin always increased venous tone; this effect was not blocked by phentolamine and was not mediated by adrenergic receptors. PGE seemed to be the venous tone relaxing agent, while PGFα seemed to produce contraction. These findings suggested that escin extracts exert *in vitro* improving effects on venous tone associated to PGFα increase (Alonso, J., 2004).

In a study, 15 patients with different kinds of varicose veins were daily administered 900mg horse chestnut extract for twelve days. The outcome was a reduction of the deleterious actions of certain enzymatic systems (glycosaminoglycanase) on the proteoglycans present in the vein-walls. Proteoglycans and collagen prevent leakage of macromolecules through the walls, thus determining the rigidity and size of the capillaries. Horse chestnut stabilizes lysosomal membranes, thus preventing leakage of deleterious enzymes (Alonso, J., 2004).

Escin is proposed as anti-edema agent, especially for topical preparations, to treat venous-lymphatic insufficiency related symptoms. The 1998 *Note Explicative* states that horse chestnut-based medicines can be claimed useful for: symptomatic treatment of functional disorders related to capillary fragility, such as ecchymosis or petechiae, for subjective symptoms of venous insufficiency, such as tired legs, and for hemorrhoid symptoms (Bruneton, J., 2001).

Escin anti-edema effects on formalin-, dextran-, or ovalbumin-induced mice plantar edema are rather long lasting. The effects of intravenous 0.5mg/kg escin persist for several days with a broader therapeutic spectrum than rutin (Alonso, J., 2004).

Flavonoids are active principles with a wide range of actions; remarkably, reduction of capillary fragility and permeability, anti-inflammatory action and free radical scavenging action (Wilkinson, J.A. & Brown, A.M.G., 1999).

It is also important to take into account the known actions of proanthocyanidols on blood capillaries (venotonic and blood vessel-protection activities), as well as their anti-oxidant action and inhibitory activity on the elastase, collagenase and hyaluronidase enzymes (Bruneton, J., 2001).

Proanthocyanidin A_2 in horse chestnut seeds showed a similar range of biological activities than escin (venotonic and vessel-protection actions). However, this compound also showed wound healing, anti-oxidant, anti-inflammatory and anti-enzymatic activities (Wilkinson, J.A. & Brown, A.M.G., 1999).

Therefore, horse chestnut seeds extract is recommended to formulate cosmetic products to improve general blood circulation.

Free radical scavenging activity
The relationship between skin aging and reactive oxygen species is well-known, especially in combination with UV radiation. Horse chestnut extract demonstrated good *in vitro* efficacy to reduce the production of oxygen reactive species and their associated damages, in biochemical and biological assays (Wilkinson, J.A. & Brown, A.M.G., 1999).

A. hippocastanum has been demonstrated *in vitro* to act as a potent scavenger of active oxygen, being almost 20 times more effective at absorbing superoxide anions than ascorbic acid, a recognized anti-oxidant. Similarly, *A.hippocastanum* extract reduced the release of hydroxyl radicals and singlet oxygen, thus demonstrating a broad spectrum of active oxygen scavenging properties. In a further *in vitro* experiment, horse chestnut effectively inhibited lipid peroxidation. Horse chestnut activity was similar to that of α-tocopherol (Wilkinson, J.A. & Brown, A.M.G., 1999).

Different horse chestnut extracts demonstrated *in vitro* and *in vivo* scavenging actions by inhibiting lipid peroxidation, due to their proanthocyanidin A_2 concentration (Alonso, J., 2004).

Thus, horse chestnut extract is recommended to formulate anti-aging cosmetics.

Activity on UV radiation
Ramos, M.F.S. et al (1996) investigated the potential use of plant extracts, including *A. hippocastanum* seeds extract, as novel sun-protection agents, based on their ability to absorb light. Such absorption is of particular interest in the ultra-violet region of the spectrum, as UV radiation has been linked with a number of cutaneous conditions including sunburn, photosensitivity, actinic elastosis, cutaneous degeneration, etc. Horse chestnut alone did not absorb UV radiation significantly. However, adding *A.hippocastanum* extract to a 2% solution of the synthetic photo-protector octylmethoxycinnamate, significantly increased the sun-protection factor (SPF) of the later, from 4 to 6. Thus, even when horse chestnut extract is not an effective sun-protector, it increases SPF values. The authors also remark the emollient and moisturizing properties of this product, which are also useful to protect the skin against sunlight damages.

Several horse chestnut extracts have demonstrated protective effects against UV radiation-induced erythema. Such an action has been attributed to proanthocyanidin A_2.

Therefore, *A.hippocastanum* extract is recommended to formulate cosmetic products with photo-protective activity.

Finally, we would like to mention that the publication *Plants preparations used as ingredients of cosmetic products* (Council of Europe Publishing, 1994) includes a monograph on the dry and glycolic extracts of *A.hippocastanum* seeds. This publication attributes them the following properties:

- tonic, astringent, anti-couperosis
  Maximum recommended concentrations are:
  -up to 2% of the dry extract
  -up to 5% of the glycolic extract
  for skin and scalp care preparations, lotions, anti-cellulite cream and gel and astringent shampoo
  -up to 4% of the dry extract
  -up to 10% of the glycolic extract, when added to tonic bath and shower gel for body and feet

Other possible cosmetic properties:

- anti-edema, blood vessels-protection, peripheral vasoconstriction

COSMETIC APPLICATIONS

Action	Active	Cosmetic Application
Anti-inflammatory anti-edema & venotonic	Triterpene saponins Flavonoids Proanthocyanidins	-Blood circulation activation -Anti-cellulite
Free radical scavenger	Proanthocyanidin A_2 Flavonoids	-Anti-aging
UV radiation	Proanthocyanidin A_2 Flavonoids	-Photo-protection

RECOMMENDED DOSE

The recommended dose is between 0.5% and 5.0%.

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