Horsechestnut seed (*Aesculus hippocastanum* L.)

SYNONYMS

Hippocastani semen (Lat), Roßkastaniensamen (Ger), graine de marronier d'Inde, aescule (Fr), eschilo (Ital), hestekastanje (Dan).

WHAT IS IT?

The horsechestnut tree (*Aesculus hippocastanum* L.) is mainly grown as an ornamental in parks and gardens in Europe, although it is in fact a native of Asia minor. Horsechestnut seeds and bark have been extensively used in European traditional medicine since the 16th century and a wine based on the flowers was imbibed for neuralgia and arthritis. The flowers and flower buds are now used to make two of the Bach Flower Remedies. However, this monograph will only describe the herbal use of the seed. Unlike true chestnuts, the seeds of the horsechestnut are not edible, although a specially prepared seed meal has been used as fodder.

EFFECTS

Increases venous tone, increases capillary resistance, decreases capillary permeability, improves circulation by toning veins; decreases oedema from lymphatic congestion or of inflammatory origin.

TRADITIONAL VIEW

Horsechestnut seed (hereafter referred to as horsechestnut) was traditionally used in the treatment of rheumatism and neuralgia and conditions of venous congestion, particularly with dull, aching pain and fullness. Other major uses include rectal complaints (particularly haemorrhoids, rectal neuralgia and proctitis) and reflex conditions attributed to rectal involvement (including headache, spasmodic asthma, dizziness, disturbed digestion). It was regarded as a remedy for congestion and engorgement. Uneasy and throbbing sensations, with dull aching pain in any part of the body, but especially in the hepatic region, was one specific indication.[1,2]

SUMMARY ACTIONS

Venotonic, antioedematous, antiinflammatory.

CAN BE USED FOR

INDICATIONS SUPPORTED BY CLINICAL TRIALS

Chronic venous insufficiency, varicose veins, oedema of the lower limbs. Prophylactic use to decrease the incidence of deep venous thrombosis following surgery. Topically for haematoma, contusions, non-penetrating wounds and sports injuries involving oedema.

TRADITIONAL THERAPEUTIC USES

Venous insufficiency (especially varicose veins, haemorrhoids); rheumatism; neuralgia; rectal complaints; disease states associated with inflammatory congestion.

MAY ALSO BE USED FOR

EXTRAPOLATIONS FROM PHARMACOLOGICAL STUDIES

To improve circulation by improving venous tone (peripheral vascular disorders, slow-healing leg ulcers); disorders where local tissue oedema may be involved (e.g. carpal tunnel syndrome, Bell's palsy, dysmenorrhoea, intervertebral disc lesions); conditions requiring treatment of the early phase of inflammation such as soft tissue injuries, swelling, minor surgery.

OTHER APPLICATIONS

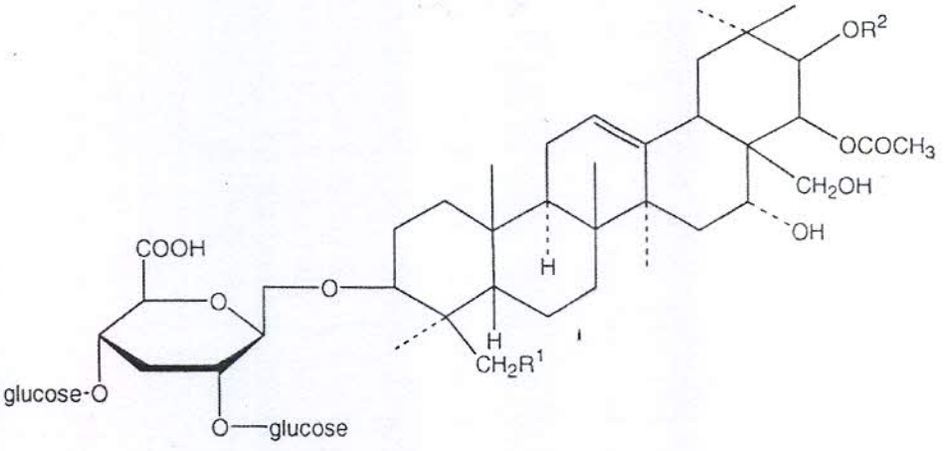
Skin care products: for normal skin, baby skin, sensitive skin; to tone the skin; as an antiinflammatory; to treat fragile capillaries, pimples, sunburn or cellulite.[3]

PREPARATIONS

Decoction of dried or fresh seeds, liquid extract and tablets for internal use. Decoction, extract, cream, gel or ointment for topical use.

DOSAGE

- 1–2 g of dried seed per day.
- Horsechestnut tablets (200 mg of 5:1 concentrated extract, standardized to contain 40 mg escin): 2–3 tablets per day.



R^1 = OH (aglycone: barringtogenol C)
R^1 = H (aglycone: protoaescigenin)
R^2 = tigloyl, angelicoyl, 2-methylbutyryl, or isobutyryl

Escin (aescin)

β-aescin: major glycosides consist of aglycones protoaescigenin or barringtogenol C esterified with tiglic acid, angelic acid, 2-methylbutyric acid or isobutyric acid

- 2–6 ml of 1:2 liquid extract, 5–15 ml of 1:5 tincture per day.
- Preparations containing 100 mg of escin per day.

DURATION OF USE

There is no suggestion that the long-term use of horsechestnut should be restricted.

SUMMARY ASSESSMENT OF SAFETY

Despite its inclusion in texts on poisonous plants, there is a very low risk associated with the oral or topical administration of horsechestnut seed.[4]

TECHNICAL DATA

BOTANY

The horsechestnut, a member of the Hippocastanaceae (buckeye family), is a deciduous tree with grey bark which grows to 25 m. The leaves are opposite and palmate with 5–7 strongly ribbed leaflets. The flowers are white with yellow to pink spots, contain five petals and are arranged in noticeable panicles up to 30 cm long. The fruit has a leathery, prickly capsule and contains 1–2 brown seeds with large whitish scar.[5,6]

KEY CONSTITUENTS

- Saponins (3–6%), referred to as escin (which is a complex mixture of over 30 individual pentacyclic triterpene diester glycosides).[7]
- Flavonoids, lipids, sterols.[8,9]

PHARMACODYNAMICS

Escin (also spelt 'aescin') is a registered drug in Germany and is the active ingredient in a number of preparations used either topically or orally for the treatment of peripheral vascular disease, in particular that related to altered capillary permeability and resistance. But it is mainly used by injection for conditions associated with oedema.

Venotonic, vascular protective and antioedema activity

Escin reduces the localized oedema associated with inflammation[10] and acts by reducing capillary permeability to water, thus decreasing exudation into intercellular spaces.[11] Escin induced contraction of isolated portal vein and stimulated the generation and release of prostaglandin F_2-alpha in vitro. Thus the antiexudative activity of escin may be mediated by prostaglandin F_2-alpha.[12] Escin administered by injection has inhibited oedema induced by several agents in rat paw, but was not effective in models representing the late reparative phase of inflammation.[13,14] This suggests that it acts on the initial stages of inflammation. Parenteral administration of escin to rats indicated the antiexudative activity to be the result of an influence on the small pores of the capillary wall through which fluid is exchanged.[15] Tests conducted on adrenalectomized and hypophysectomized animals indicate that normal production of corticosteroids is necessary for its antioedema activity. Escin thus mimics and relies upon the activity of corticosteroids.[16–18] Oral administration of escin has demonstrated antiexudative and antiinflammatory activity in vivo. The activity occurred in both prophylaxis and treatment and was due to a beneficial effect on permeability and diuresis.[19] Topical application of escin significantly inhibited exudation in vivo.[20]

In a randomized, double-blind, placebo-controlled crossover study, the influence of oral doses of escin on capillary resistance was tested on 12 healthy subjects. After 7 days of treatment with escin, capillary resistance was significantly improved as measured by the petechiae test. There was no effect from the placebo.[21]

The whole extract of the horsechestnut also shares these properties of escin. In fact, some writers suggest that the combination of escin with flavonoids, as found in the natural plant extract, is a superior treatment to escin alone. Horsechestnut extract demonstrated venotonic activity in vitro by inducing contraction of isolated vein preparations. Perfusion with horsechestnut extract increased the venous pressure of normal veins and, with prior administration, pathological veins also. During perfusion in inverse direction to the bloodstream, a clear contracting effect on the valves was obtained. Horsechestnut extract (2.5, 5.0 mg/kg IV) increased femoral venous pressure and flow, as well as thoracic lymphatic flow, with no change in arterial parameters.[22]

Oral administration of a standardized horsechestnut extract (50–400 mg/kg, containing 70% escin) reduced the cutaneous capillary hyperpermeability induced in rat and rabbit. It also increased skin capillary resistance in guinea pigs fed a vitamin C-deficient diet, as measured by the petechiae method. The extract (200–400 mg/kg) decreased the formation of oedema of lymphatic or inflammatory origin induced in rat hind paw. The horsechestnut extract suppressed plasmatic extravasation and leucocyte emigration into the pleural cavity in experimental pleurisy (200–400 mg/kg oral and 1–10 mg/kg IV) and decreased connective tissue formation in subchronic inflammatory granuloma (400 mg/kg oral and 5–10 mg/kg SC).[22]

Pharmacological and clinical studies indicate that oral administration of horsechestnut extract improved the tone of connective tissue and improved circulation by toning the veins. In a double-blind, placebo-controlled study, a decrease in the vascular capacity (i.e. increased flow) and in filtration coefficients was observed in volunteers with healthy circulation treated with standardized horsechestnut extract (600 mg per day, containing 100 mg escin).[23,24] The antioedematous activity demonstrated by standardized horse-chestnut extract in chronic venous insufficiency was mainly dependent on the inhibition of proteoglycan degradation and lysosomal enzyme activity.[25]

The effect of oral administration of horsechestnut extract (total of 360 mg, containing 90 mg escin) to 14 healthy volunteers on the venous tone of a segment of the lower leg was compared to placebo controls. Horsechestnut resulted in significant reduction of the pressure-dependent vein capacity ($p<0.02$), which is an indication of reduced deformation of the veins and an increase in vein tonus. An intravenous infusion of escin did not result in a noticeable change.[26]

In a double-blind, placebo-controlled trial on 20 healthy volunteers, 100 mg of horsechestnut extract (containing 16% or 70% escin) demonstrated similar venotonic activity on peripheral venous pressure-volume curves as placebo.[27] The lack of a positive effect may reflect on inadequate dosage.

In an uncontrolled trial, the velocity of blood in varicose veins of the lower extremities of patients was assessed after patients received horsechestnut extract for 12 days. Blood viscosity was significantly lowered and correlated to subjective improvement in 73% of cases.[28] A single dose of standardized horsechestnut extract (600 mg containing 100 mg escin) prevented or significantly reduced the increase in ankle and foot oedema ($p<0.05$) in healthy humans during a 15-hour air flight. The study was of randomized, double-blind design and the oedema was compared to the preflight circumference.[29]

Antioxidant activity

Horsechestnut extract demonstrated strong active oxygen-scavenging activity and protective activity in vitro against cell damage induced by active oxygen.[30] Standardized horsechestnut extract (containing 70% escin) inhibited enzymatic and non-enzymatic lipid peroxidation in vitro and counteracted the deleterious effects of free radical oxidative stress in mice and rats (200–400 mg/kg oral, 25 mg/kg IV, respectively).[22]

Other activity

The inhibitory effects of plant constituents on the activity of the connective tissue enzymes elastase and hyaluronidase was investigated in vitro. Saponin constituents from horsechestnut showed inhibitory effects on hyaluronidase. The activity was mainly linked to escin and, to a lesser extent, its genin, escinol.[31]

Triterpene oligoglycosides from horsechestnut (escin Ia, Ib, IIa and IIb) exhibited an inhibitory effect on ethanol absorption and hypoglycaemic activity on oral glucose tolerance test in rats.[32] Saponins can inhibit absorption of small molecules (see Ch. 2).

The saponin components hippocaesulin and barringtogenol-C 21-angelate have demonstrated cytotoxic activity in vitro.[33] For an aqueous-alcoholic extract of horsechestnut (5% w/w), an antiirritant effect was observed in a cosmetic test for irritancy.[34]

PHARMACOKINETICS

Very high concentrations of escin were measured in skin and muscle tissue underlying the site of topical application of radiolabelled sodium escinate. Low values were measured in internal organs, blood, urine, skin and musculature from other parts of the body. A range of 0.5–1% of the applied dose was excreted in urine within 24 hours of administration. The total elimination (bile and urine) was calculated at 1–2.5% of the dose. Less than one half is excreted as escin, the remainder as metabolites.[35] However, the availability of escin to skin and muscle tissue may not be as high as reported in this study, since the radioactivity detected may have been carried by the metabolites of escin as well as by escin itself.

Studies indicate that escin is eliminated quickly following intravenous injection, with two-thirds excreted via the bile and one-third by renal elimination.[36] Two recent studies of the bioavailability of beta-escin following oral doses of various horsechestnut preparations have been conducted using healthy volunteers. Validated radioimmunosorbent assay (RIA) was used to determine levels of beta-escin in plasma. One study in 18 subjects on two solid-dose preparations found a large variation in absorption parameters for beta-escin. Maximum concentration (C_{max}) after a dose containing 50 mg escin varied from 0.19 to 45.1 ng/ml, time for maximum concentration (T_{max}) varied from 0.73 to 8.5 hours and the area under the curve (AUC, an assessment of concentration over time) varied from 24.6 to 389 ng/h/ml.[37] The second study, also on two solid-dose preparations (one sustained-release), and using 24 volunteers found more consistent results. This may have been because horsechestnut extract containing a defined dose of escin was used, rather than just escin alone. Parameters for the sustained-release tablet were superior. For example, after a dose containing 50 mg escin, C_{max} for the sustained-release tablet was 9.81 ± 8.9 ng/ml, T_{max} was 2.23 ± 0.9 h and AUC averaged 187.1 ng/h/ml.[38] The half-life for both preparations was about 20 hours.

Saponins are large molecules containing highly polar groups and their intact bioavailability can be expected to be low after oral doses. This was confirmed in the above studies, since the pharmacokinetic parameters indicate an absorption of less than 1% of the administered dose. However, saponins can be hydrolysed by intestinal flora, leaving the less polar aglycone or sapogenin available for absorption. These sapogenins, or their hepatic metabolites, may in fact be the main active form of escin following oral doses. More studies are needed to clarify this issue.

CLINICAL TRIALS WITH ESCIN

In a placebo-controlled trial in patients undergoing surgery of the hand, intravenous administration of escin produced a fast reduction in postoperative inflammation and oedema.[39] Escin is mainly used by injection; for example, to treat road accident victims with severe head injury, where it reduced the dangerous rise in intracranial pressure, leading to a more favourable prognosis.[40] Escin has been effective in the treatment of cerebral oedemas following cranial fractures and cranial traumas with or without retrograde amnesia, cerebral tumours, intracranial aneurysms, cerebral sclerosis, subdural haematomas, encephalitis, meningitis and cerebral abscesses. Depending on the seriousness of the condition, disappearance of cephalgia, vertigo and general discomfort were observed within 3–16 days. Cerebral oedemas due to acute vasomotor insufficiency were resolved quickly, while in chronic diseases remission occurred slowly over a long period of administration.[41]

Topical preparations of escin have been successfully used for a variety of applications: treatment of oedema and haematoma in surgical practice,[42] the

prevention and treatment of sports injuries, including acute injuries, blunt injuries (non-penetrating wounds) and oedema.[43–48] It has been used alone and in combination with heparin, buphenin, salicylate or polyunsaturated phosphatidylcholine in venous disorders (inflammation of veins, venous insufficiency, varicose veins);[49–52] in combination with *l*-thyroxine for the treatment of hypertrophic scars, keloid scars, stretch marks and lymphoedema after mastectomy,[53–55] in combination with heparin and phospholipids for the treatment of joint and venous diseases,[56,57] anorectal varicose pathologies, particularly in gynaecology and obstetrics,[58–60] postoperative treatment of episiotomies[61] and in oral and periodontal surgery.[62]

In a randomized, double-blind trial, 81 patients with contused traumas following limb injuries received treatment with an escin gel or placebo gel for 9 days. Compared to placebo, the mobility of the injured extremity increased significantly in comparison to the uninjured extremity in those treated with escin ($p<0.02$). The circumferences of the lower extremities returned to almost normal (compared to the uninjured leg) in the treatment group but remained unchanged in the placebo group. Escin treatment was also superior for reduction in lower leg swelling, subjective complaints and remission frequencies ($p<0.05$).[63]

Topically applied 2% escin gel was compared to placebo in experimentally induced haematoma in a randomized, double-blind trial. Efficacy was measured over 9 hours after a single application of gel. The escin gel significantly reduced tenderness to pressure within 1 hour and then at all other times during the trial.[64]

CLINICAL TRIALS WITH HORSECHESTNUT

Venous insufficiency

Chronic venous insufficiency is an imprecise term which is frequently referred to and not easily defined. It refers to the impairment of venous return usually from the legs, often with oedema and sometimes with stasis ulcers at the ankle. Other terms used are chronic deep vein incompetence and peripheral venous incompetence. In an uncontrolled trial on 35 patients with chronic venous insufficiency, standardized horsechestnut extract was effective against foot oedema. Haematocrit, body weight and serum potassium were unchanged.[65] In another uncontrolled trial on healthy volunteers and patients with varicose veins, administration of standardized horsechestnut extract demonstrated an increase in venous tone (as measured by plethysmography and radioactive blood flow rate) without arterial constriction or change in blood pressure.[66]

Standardized horsechestnut extract (600 mg per day, containing 100 mg escin, for 3 weeks) significantly reduced the subjective symptoms of patients with varicose veins ($p<0.001$) in a double-blind, placebo-controlled trial.[67] In another double-blind, placebo-controlled trial, 40 patients with leg oedema caused by chronic deep venous incompetence received either standardized horsechestnut extract (738–824 mg per day, containing 150 mg escin) or placebo over 7 weeks. Significant reduction in average leg volume was observed for the treated group compared to placebo, both before and after an oedema provocation test ($p<0.01$). Leg pressure at rest was decreased (indicating better venous tone) and pronounced alleviation of symptoms occurred in the treated group.[68]

The efficacy of standardized horsechestnut extract was investigated in a randomized, double-blind, placebo-controlled trial on 22 patients with proven chronic venous insufficiency. Three hours after taking 600 mg of horsechestnut extract (containing 100 mg escin), a significant decrease in the capillary filtration coefficient (22%) was observed in the treated group.[69] In a randomized, double-blind, placebo-controlled trial, treatment with standardized horsechestnut extract (600 mg per day, containing 100 mg escin) in 20 patients over a 4-week period resulted in significant improvement in volume changes of the foot and ankle ($p<0.001$), compared to the 20 patients treated with placebo. Symptoms such as oedema, pain, fatigue, feeling of tension and itching were also significantly improved ($p<0.05$). There were, however, no changes in venous capacity or calf muscle spasm.[70]

Seventy-four patients with chronic venous insufficiency and lower leg oedema participated in a randomized, double-blind, placebo-controlled trial. An antioedema effect was observed for those treated with standardized horsechestnut extract (600 mg per day, containing 100 mg escin) for 8 weeks. Leg volume was reduced, while in the placebo group it was increased. The progress of the oedema was slowed in the treatment group, as were the subjective symptoms.[71] In a randomized, double-blind, placebo-controlled, crossover trial on 20 women with pregnancy-induced varicose veins or chronic venous insufficiency, treatment with standardized horsechestnut extract for 4 weeks resulted in significant reduction in leg volume ($p<0.01$).[72] The influence of standardized horsechestnut extract (approximately 600 mg per day, standardized to 100 mg escin for 4 weeks) was tested in a randomized, placebo-controlled trial involving 30 patients with peripheral venous incompetence. Horsechestnut effected a reduction in leg circumference and improvement in subjective symptoms.[73] In a double-blind trial using the same

dosage over 20 days involving 30 outdoor patients suffering from chronic venous incompetence, a significant reduction of leg circumference was shown ($p<0.05$).[74]

One hundred and eighteen patients with varicose veins or chronic venous insufficiency were treated for 40 days with 60 mg per day of standardized horsechestnut extract (containing 70% escin) or placebo. The trial was double-blinded. Significant improvement in symptoms (oedema, cramps, pain, fatigue, sensation of heaviness) was observed in the treated group ($p<0.05$).[75] The dosage quoted for this trial is a low dose in comparison to the majority of trials conducted. Similar results were observed in a double-blind, placebo-controlled, crossover trial for those treated with horsechestnut. Improvement was observed for: oedema and pain ($p<0.01$), itchiness, fatigue and sensation of heaviness ($p<0.05$). Calf cramping, however, was not significantly improved.[76]

Treatment with standardized horsechestnut extract (600 mg per day, containing 100 mg escin) for 2 weeks was superior to placebo in pregnant women with oedema due to venous insufficiency. Reduction in oedema and symptoms such as pain, fatigue and itching were observed in the treatment group and these patients also showed a greater resistance to oedema provocation. The trial was double-blinded and crossover in design.[77]

In a randomized, partially blinded, placebo-controlled parallel study published in *The Lancet*, 240 patients with chronic venous insufficiency took part in a comparison of the efficacy of compression stockings class II and standardized horsechestnut extract (600 mg per day, containing 100 mg escin) over 12 weeks. Lower leg volume decreased by a similar amount (43–47 ml) for both horsechestnut and compression therapy compared to placebo. A significant reduction in oedema was observed for horsechestnut ($p=0.005$) and compression ($p=0.002$) compared to placebo and the two therapies were shown to be equivalent ($p=0.001$). Compression achieved high oedema reductions at the beginning of the study, while horsechestnut gradually decreased oedema volume, reaching a maximum by the end of the trial. (Patients allocated to compression treatment received a diuretic once daily during the first week of the trial to ensure the best possible stocking fit. Class II stockings provide a certain pressure.) Compliance was better for the herbal therapy.[78]

In a case observation study involving more than 800 German general practitioners, more than 5000 patients with chronic venous insufficiency were treated with standardized horsechestnut extract and followed up at regular intervals. All the symptoms investigated (pain, tiredness, tension, swelling in the leg, itching, tendency towards oedema) improved markedly or completely disappeared. Horsechestnut extract was considered an economical, practice-relevant therapeutic tool which, in comparison with compression therapy, has the additional advantage of better compliance.[79] In a postmarketing surveillance study, 1183 patients with chronic venous insufficiency received the recommended dosage of horsechestnut extract over a 5-month period. A clear reduction in the objective and subjective symptoms was proven.[80]

A review of oedema-protective agents (diosmin, beta-hydroxyethyl rutosides and horsechestnut extract) used in double-blind, placebo-controlled clinical trials for the treatment of chronic venous insufficiency indicates they combine proven therapeutic efficacy with excellent safety of use and have a favourable benefit:risk ratio. The extent of oedema reduction in patients is equivalent to that achieved by compression therapy with elastic stockings. Combined treatment with oedema-protective agents and compression therapy has a better clinical benefit compared to either treatment alone.[81] A review of medicines used in the treatment of chronic venous diseases of the lower limb found horsechestnut extract moderates the development of tissue oedema.[36]

Both standardized horsechestnut extract (720–824 mg per day, containing 150 mg escin) and beta-hydroxyethyl rutosides (2000 mg per day) demonstrated an oedema-protective effect in a randomized, double-blind trial on 40 patients with chronic venous insufficiency and peripheral venous oedema.[82] In a multicentre, randomized, double-blind trial, the comparative efficacy of oxerutins (hydroxylethyl derivatives of rutin) and horsechestnut extract was investigated in 137 postmenopausal patients with grade II chronic venous insufficiency. Patients received either 600 mg per day of standardized horsechestnut extract (containing 100 mg escin), 1000 mg per day of oxerutins for 12 weeks or 1000 mg per day of oxerutins for 4 weeks followed by 500 mg per day (of oxerutins) for 8 weeks. All treatments achieved a mean leg volume reduction of about 100 ml after 12 weeks of treatment, comparable to that achieved in compression therapy. The 6-week follow-up period without treatment indicated that both treatments also exhibit a substantial carry-over effect.[83]

Deep vein thrombosis

Over a 3-year period, a controlled trial of 4176 patients with thrombosis, lung infarction or lung embolism investigated prophylactic treatment for thrombosis and embolism arising from surgery. Patients received an intravenous injection of horsechestnut extract (10 ml per day), strophanthin or digitalis, vitamin B

complex and vitamin C or a similar injection without the horsechestnut extract for 4 days prior to surgery and continuing for up to 7 days after the operation. Horsechestnut significantly reduced the incidence of deep venous thrombosis following surgery compared to the control group (lung embolism patients: $p<0.01$; other patients: $p<0.001$).[84]

Topical use

A gel containing horsechestnut extract and heparin was found to be effective in the treatment of acute and chronic traumas and venopathies in an uncontrolled study. In particular, the gel quickly broke down haematomas.[85] The tolerance and efficacy of a topical horsechestnut preparation were assessed in 15 patients with first and second-degree chronic venous insufficiency. The horsechestnut preparation contained 1.4% triterpene glycosides calculated as escin and was compared with a preparation containing heparin. Efficacy was assessed via the change in circumference of the lower, middle and upper leg and by changes in symptoms. Both treatments were well tolerated and the horsechestnut preparation showed a higher tendency to improvement than the heparin.[86]

TOXICOLOGY

Oral administration of sodium salt of escin to rats (10 mg/kg, 70 mg/kg) did not induce any substantial changes in carbohydrate and lipid metabolism and steatosis did not develop.[87] Intraperitoneal administration of 10 mg/kg escin to juvenile male rats did not affect fertility or produce any nephrotoxic activity.[88]

Horsechestnut seeds have low acute and chronic toxicities and the therapeutic index is high.[4] Escin also has a high therapeutic index.[89] The LD_{50} of the water-soluble portion of horsechestnut extract after single oral dose in chicks was 10.6 g/kg body weight and for dried, powdered seed after two consecutive daily doses was 6.5 g/kg.[90] The LD_{50} of horsechestnut seed by oral administration was 990 mg/kg in mice, 2150 mg/kg in rats, 1530 mg/kg in rabbits and 130 mg/kg in dogs. No toxicity was observed in rats administered oral doses of 400 mg/kg of horsechestnut.[91]

CONTRAINDICATIONS

Horsechestnut should not be applied to broken or ulcerated skin.

SPECIAL WARNINGS AND PRECAUTIONS

None required.

INTERACTIONS

None known.

USE IN PREGNANCY AND LACTATION

No adverse effects expected.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No adverse effects expected.

SIDE EFFECTS

As with all saponin-containing herbs, oral use may cause irritation of the gastric mucous membranes and reflux. However, the gastric irritation and reflux can be avoided by the use of enteric-coated preparations. Because of the irritant effect of the saponins, horsechestnut should not be applied to broken or ulcerated skin. Saponins and sapogenins in the bloodstream cause haemolysis but this effect is negligible at the oral doses used. From 1968 until 1989 nearly 900 million individual doses of one brand of standardized horsechestnut extract (Venostasin) were prescribed. In that time, only 15 patients reported significant side effects.[92]

OVERDOSE

Very high doses will result in gastrointestinal irritation. If sufficient quantities of escin are absorbed through damaged or irritated gastrointestinal mucous membranes, haemolysis with associated kidney damage could result.

CURRENT REGULATORY STATUS IN SELECTED COUNTRIES

A draft monograph of horsechestnut is being prepared and may appear in the *European Pharmacopoeia* subsequent to the 1997 edition.

Horsechestnut seed is covered by a positive Commission E monograph and can be used to treat symptoms of venous disorders and chronic venous insufficiency, such as pain and a feeling of heaviness in the legs, night cramps, itching and swelling.

Horsechestnut (unspecified) is on the UK General Sale List.

Horsechestnut does not have GRAS status. However, it is freely available as a 'dietary supplement' in the USA under DSHEA legislation (1994 Dietary Supplement Health and Education Act).

Horsechestnut is not included in Part 4 of Schedule 4 of the Therapeutic Goods Act Regulations of Australia.

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Daily Dosage: The average daily dose is 4.5 g of the drug; 30 to 60 mL pressed juice.

The infusion dosage is 1 to 2 g of the drug taken up to 3 times daily. The liquid extract dosage is 2 to 4 mL 3 times daily.

Homeopathic Dosage: 5 drops, 1 tablet, or 10 globules every 30 to 60 minutes (acute) or 1 to 3 times daily (chronic); parenterally: 1 to 2 mL sc acute, 3 times daily; chronic: once a day (HAB1).

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Horse Chestnut

Aesculus hippocastanum

TRADE NAMES

Horse Chestnut (available from numerous manufacturers), Horse Chestnut-Power, Venastat, Standardized Horsechestnut Extract

DESCRIPTION

Medicinal Parts: The medicinal parts are the dried Horse Chestnut leaves, the oil extracted from the peeled fruit capsules (seeds) and dried chestnut seeds.

Flower and Fruit: The white flowers are in stiffly upright panicles gradually thickening near the distal end. Most of the flowers are male, but a few are female or androgynous. The calyx is fused and bell-shaped with 5 irregular tips. The petals are 10 to 15 mm long with a yellow spot, which turns red. There are 3 upward petals and 2 downward, which are folded at the edge. The flower is ciliate and cordate (heart shaped) at the base and contains 7 S-shaped, bending stamens with red anthers that are longer than the petals. The ovary is trivalved, superior, and velvety. The fruit capsules are green and globular with soft spines and fine hairs. There are 1 to 3 red-brown seeds (Chestnuts) within the capsules, which are shiny brown with a yellowish gray-brown navel and a tough shell.

Leaves, Stem, and Root: The seasonal tree is up to 35 m high; it includes a large regular crown and widely spread roots. The trunk is initially smooth but later has thinly scaled, peeling, and fissured bark. The young twigs are yellowish to red-brown and are initially covered with brown hairs. The buds gradually thicken near the distal end and are extremely sticky with dark red bud scales to protect the seed plant bud. The leaves are long, 5 to 7 palmate, with a 20-cm long grooved petiole. The leaflets are initially red-haired, 20 cm long, cuneate-obovate, acute, and dentate. The leaflets are rich green above and beneath are light green.

Habitat: Although the herb is indigenous to the mountains of Greece, Bulgaria, the Caucasus, northern Iran and the Himalayas, it is cultivated elsewhere, especially in northern Europe, including the British Isles, Denmark, Scandinavia, and Russia (Narva and St. Petersburg).

Production: Horse Chestnut leaf consists of the fresh or dried leaf of *Aesculus hippocastanum*. A dry extract is manufactured from Horse Chestnut seeds standardized to a content of 16-20% triterpene glycosides (calculated as anhydrous aescin).

Not to be Confused With: The leaves of the Horse Chestnut are commonly confused with those of Sweet Chestnut.

Other Names: Buckeye, Common Horse Chestnut, Conqueror Tree, Spanish Chestnut

ACTIONS AND PHARMACOLOGY

COMPOUNDS: HORSE CHESTNUT LEAF

Triterpene saponins

Hydroxycoumarins: chief component is aesculin, in addition fraxin and scopolin

Flavonoids: including rutin, quercitrin, and isoquercitrin

Tannins

EFFECTS: HORSE CHESTNUT LEAF

The main active principles of the anti-exudative effect and improvement of venous tone are hydroxycoumarins (aesculin and fraxin), triterpene saponins in the petioles and leaf veins, flavonoids, and a rich supply of tannins. Although the drug is said to have an anti-exudative effect and improve venous tone, there is a lack of clinical data to support the efficacy.

COMPOUNDS: HORSE CHESTNUT SEEDS

Triterpene saponins (3-5%): The triterpene saponine mixture known as aescin (also escin) consists of diacylated tetra-and pentahydroxy-beta-amyrin compounds.The compounds bear a glucuronic acid remnant substituted with 2 monosaccharide remnants in position 3 at the OH-group. Aglycones, protoes-

OVERDOSAGE

HORSE CHESTNUT SEEDS

The intake of larger quantities of Horse Chestnut seeds (in one case of a child with 5 seeds) can bring about vomiting, diarrhea, severe thirst, reddening of the face, enlargement of pupils, vision and consciousness disorders. Following stomach and intestinal emptying (gastric lavage, sodium sulfate) and the administration of activated charcoal, therapy for poisonings consists of diazepam for spasms, atropine for colic, electrolyte replenishment, and sodium bicarbonate infusions for any acidosis that may arise. Intubation and oxygen respiration may also be necessary.

DOSAGE

HORSE CHESTNUT LEAF

Mode of Administration: Extracts of the drug are contained in "vein teas" or "hemorrhoid teas," as well as in pharmaceutical preparations for the treatment of venous symptoms.

Preparation: One ampule corresponds to 4 mg flavones in 0.9% NaCl.

Daily Dosage:

Infusion (as a tea)—Pour boiling water over 1 tsp. of finely cut drug and strain after 5 to 10 minutes (1 tsp = 1 g drug).

Intravenously—1 to 2 ampules daily.

Intramuscularly—1 ampule daily.

HORSE CHESTNUT SEEDS

Mode of Administration: Available in liquid and solid preparations for internal use; semi-solid preparations for external use; and parenterally for homeopathic use.

How Supplied:

Ampules

Capsules — 250 mg, 300 mg, 375 mg, 485 mg

Drops

Liquid extract

Ointment/Gels

Tablets

Tincture

Preparation: Stabilized extract of Horse Chestnut (5:1) is standardized for aescin; tincture of Horse Chestnut 1:1 with 75% ethanol; isolated aescin.

Daily Dosage:

Intravenous—Doses of 5 mg once or twice daily of aescin as the sodium salt has been used for treatment or prevention of post-traumatic edema and potoperative edema. The maximum daily dose is 20 mg.

Oral—Aescin from encapsulated standardized extracts are initially given at doses of 10 mg. The encapsulated standardized extract has been used for the treatment of postoperative or traumatic edema, hemorrhoids or symptoms due to varicose veins in doses providing 40 to 120 mg of aescin per day. Aescin (escin) 100 mg corresponding to 250-312.5 mg extract may be administered twice daily in delayed-release form.

Tincture—For the treatment of painful hemorrhoids, a dose of 1:10 tincture is 0.6 ml.

Topical—A 1 to 2% gel is applied topically several times daily for soft tissue injuries, bruises and symptomatic relief of varicose veins.

Homeopathic Dosage: 5 drops, 1 tablet, or 10 globules every 30 to 60 minutes (acute) and 1 to 3 times daily (chronic); parenterally: 1 to 2 mL 3 times daily sc; ointment 1 to 2 times daily (HAB1).

Storage: The herb should be stored in a dry and dark place.

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cigenin and barringtogenol C, are bonded like esters onto the OH-group at position 21 with either angelic or tiglic acid, or with either alpha-methyl butyric or isobutyric acid remnants. The OH-group in position 22 (beta-escin) or 28 (cryptoescin) is acetylated, and both positional isomeric compounds remain in equilibrium though migration of the acetyl remnant.

Flavonoids: in particular biosides and triosides of the quercetins

Oligosaccharides: including 1-kestose, 2-kestose, stachyose

Polysaccharides: starch (50%)

Oligomeric proanthocyanidins, condensed tannins: (only in the seed-coat)

Fatty oil (2-3%)

EFFECTS: HORSE CHESTNUT SEEDS

As found in different animal tests and preclincal investigations, the principal ingredient of Horse Chestnut seed extract, triterpene glycoside mixture (aescin), has an anti-exudative, vascular tightening effect, and reduction of vascular permeability which result in an antiedemic effect. The vein-toning properties of the Horse Chestnut extract also demonstrated improvement of venous return flow. A significant reduction of transcapillary filtration was seen in a placebo-controlled human pharmacological trial (Bisler, 1986). Significant improvement in the symptoms of chronic venous insufficiency was demonstrated in diverse, randomized, double-blind and cross-over studies (Calabrese, 1993; Steiner, 1990).

There are indications that Horse Chestnut seed extract reduces the activity of lysosomal enzymes, which increases in chronic pathological conditions of the veins. The enzymes will break down glycoacalyx (mucopolysaccharides) in the region of the capillary walls, allowing proteins to leak into the interstitium. The activity of the enzymes is reduced by the aescin and so the breakdown of glycoacalyx is also inhibited. The transcapillary filtration of low-molecular proteins, electrolytes, and water into the interstitium is inhibited through a reduction of vascular permeability by the aescin.

CLINICAL TRIALS

The efficacy and safety of Horse Chestnut seed extract, given as Venostasin retard (50 mg aescin) twice daily, was compared to mechanical compression involving bandages and stockings in a randomized, placebo-controlled clinical study. The study consisted of 240 patients with chronic venous insufficiency over a 12-week period. The results determined a similar decrease of lower leg volume of approximately 25% and noted compression treatment is uncomfortable, not convenient and subject to poor compliance (Diehm, 1996).

Venostasin retard was administered to 52 pregnant women with edema due to venous insufficiency in a placebo-controlled, double-blind, crossover study. A significant reduction of edema and greater resistance to edema provocation was demonstrated in the Venostasin retard group. There were also less severe symptoms of pain, fatigue, swelling, and itching with patients receiving Venostasin retard therapy (Steiner, 1990).

A randomized, placebo-controlled, double-blind study was conducted on 40 patients with venous edema in chronic deep vein incompetence to determine the edema-reducing effect of Horse Chestnut seed extract. The edema reduction effect and reduction of leg volume with edema provocation of the Horse Chestnut seed extract were both statistically significant (Diehm, 1992).

INDICATIONS AND USAGE

HORSE CHESTNUT LEAF

Unproven Uses: Eczema, superficial and deep varicose veins, leg pains, phlebitis, hemorrhoids, pains before and during menstruation. In folk medicine, the leaves are used as a cough remedy, as well as for arthritis and rheumatism.

HORSE CHESTNUT SEEDS

Approved by Commission E:

■ Venous conditions (chronic venous insufficiency)

Treatment of symptoms found in pathological conditions of the veins of the legs (chronic venous insufficiency), for example pain and a sensation of heaviness in the legs, nocturnal cramps in the calves, pruritis, and swelling of the legs.

Unproven uses: Horse Chestnut seeds are used for symptoms of post-traumatic and post-operative soft tissue swelling. Further indications are painful injuries, sprains, bruising, pain syndrome of the spine, edema, rheumatic disease, and varicose veins.

Homeopathic Uses: Homeopathic treatments include hemorrhoids, lumbar and low back pain, venous back pressure.

PRECAUTIONS AND ADVERSE REACTIONS

HORSE CHESTNUT LEAF

General: Health risks or side effects following the proper administration of designated therapeutic dosages are not recorded. One case of liver damage following intramuscular administration of an extract of the drug (origin details of the drug uncertain) is known.

Drug Interactions: Horse Chestnut leaf has a coumarin component and may interact with warfarin, salicylates, and other drugs with anti-coagulant properties.

HORSE CHESTNUT SEEDS

Health risks following the proper administration of designated therapeutic dosages are not recorded. Susceptible patients may nevertheless experience mucous membrane irritations of the gastrointestinal tract (e.g. nausea) following intake of the drug; decrease in kidney function with pre-existing renal insufficiency and acute nephrotoxicity. Hepatotoxicity and urticaria have also been observed. I.V administration of aescin can lead to anaphylactic reactions.

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Horsemint

Monarda Punctata

DESCRIPTION

Medicinal Parts: The medicinal part is the herb.

Flower and Fruit: The flowers grow in axillary whorls. They are bilabiate. The corolla is yellow with red spots. The 2 stamens and the sessile bracts are yellow and purple.

Leaves, Stem, and Root: The plant is a perennial and grows up to 90 cm high with a branched, round stem. The leaves are opposite, lanceolate, and downy.

Characteristics: The taste is pungent and bitter; the odor reminiscent of thyme.

Habitat: The plant is indigenous to the eastern and central U.S.

Other Names: Spotted Monarda, Monarda Lutea, Wild Bergamot

ACTIONS AND PHARMACOLOGY

COMPOUNDS

Volatile oils including among others thymol (20%), thymol methyl ether, thymol hydroquinone; in Monarda punctata varieties, mentha including also gamma-terpinene, geranyl-formate, neryl-formate

EFFECTS

The drug has carminative, stimulant and emmenagogic effects.

CONTRAINDICATIONS

The drug is not to be used during pregnancy.