Folium et Cortex Hamamelidis

Definition

Folium et Cortex Hamamelidis consists of the dried or fresh leaves and/or the dried bark of *Hamamelis virginiana* L. (Hamamelidaceae).

Folium Hamamelidis consists of the dried (*1*, *2*) or fresh leaves (*3*), and Cortex Hamamelidis consists of the dried bark of the trunk and twigs of *Hamamelis virginiana* L. (*2*, *4*).

Synonyms

Hamamelis androgyna Walt., *H. caroliniana* Walt., *H. corylifolia* Moench., *H. dentata* Moench., *H. dioica* Walt., *H. estivalis* Raf., *H. macrophylla* Pursh., *H. nigra* Raf., *H. parvifolia* Raf., *H. rotundifolia* Raf., *H. virginata* sic, *H. virginiae* L., *H. virginiana* ssp. *parvifolia* Nutt., *H. virginica* L., *Trilopus dentata* Raf., *T. estivalis* Raf., *T. nigra* Raf., *T. parvifolia* Raf., *T. rotundifolia* Raf., *T. virginica* Raf. (*5*, *6*).

Selected vernacular names

Amamelide, Amerikamansaku, cortice de hamamelis, feuilles d'hamamélis, feuilles du noisetier de la sorcière, folhas de hamamelis, hamamelis, hamamélis de virginie, Hexenhasel, magician's rod, noisetier de sorcière, oczar, pistachio nut, snapping hazelnut, spotted alders, striped alder, tobacco wood, varázsdió levél és kéreg, vilin virginsky, virginische Zaubernuss, virginischer Zauberstrauch, white hazel, winter bloom, witch hazel, Zauberhasel, Zaubernuss (*5–8*).

Geographical distribution

Indigenous to the Atlantic coast of North America, found in damp woods ranging from Nova Scotia to Florida and as far west as Texas (*6*, *8*, *9*).

Description

A tall shrub or small tree, up to 4.6 m high. Branches highly branched. Leaves alternate, stipulate, short-petioled, unequilaterally ovate or rhomboid-ovate, with oblique base and sinuate or sinuate-dentate margin. Flowers thread-like, golden-yellow; appear in axillary clusters as leaves fall in autumn and at about the same time as fruits ripen from blossoms of the previous year. Fruit a

2-beaked, 2-celled, woody capsule dehiscing loculicidally from the top, each cell containing a single black seed (*8*, *10*, *11*).

Plant material of interest: dried and fresh leaves, dried bark

General appearance

Folium

Green or greenish-brown, often broken, crumpled and compressed into more or less compact masses. Lamina 5–12 cm long, 3–8 cm wide, broadly ovate to obovate; base oblique and asymmetric; apex acute or, rarely, obtuse; margins of lamina roughly crenate or dentate. Venation pinnate and prominent on the abaxial surface; usually 4–6 pairs of secondary veins attached to main vein, leaving at an acute angle and curving gently to marginal points where there are fine veins often at right angles to secondary veins (*1*).

Cortex

Channelled, seldom quilled or in strips, up to 3 cm wide and 2 mm thick. Outer surface light yellowish-brown or reddish-brown, has thin, whitish or greyish-brown cork with numerous lenticels; inner surface yellowish-brown to reddish-brown, longitudinally striated. Fracture splintery and fibrous (*9*).

Organoleptic properties

Folium

Odour: slight; taste: astringent, slightly aromatic, bitter (*8*).

Cortex

Odourless; taste: strongly astringent, slightly bitter (*2*, *9*).

Microscopic characteristics

Folium

Upper epidermis of leaf composed of slightly elongated cells with straight to slightly sinuous walls; walls moderately and sometimes unevenly thickened; no stomata; underlying palisade cells fairly small and distinct. Lower epidermis composed of polygonal cells with very sinuous outline; walls thinner and more uniform than those of upper epidermis; paracytic stomata fairly numerous but rather faint and indistinct; underlying cells of spongy mesophyll frequently brown, appear as clearly defined honeycomb network. Covering trichomes characteristic, stellate, found fragmented, occasionally entire, composed of 4–12 elongated, conical cells united at their bases to form a radiating structure; each cell has moderately and slightly unevenly thickened wall which is slightly lignified. Linear idioblasts, composed of lignified cells, found scattered across

entire thickness of lamina. Prismatic calcium oxalate crystals scattered, occasionally found in clusters, as well as forming a sheath (*12*).

Cortex

Sclereids abundant, vary considerably in size, are of 2 types: rounded to oval, or subrectangular; heavily thickened, usually in groups of just 2 or 3 cells, but smaller cells often form larger groups; walls have numerous, conspicuous branched pits and striations, particularly in the larger cells; other type of sclereids more regular in size and form, frequently found associated with the cork, occurring as a layer of small, polygonal cells with no intercellular spaces. Fibres occur in groups surrounded by a sheath of prismatic calcium oxalate crystals; individual fibres very thick-walled and lignified with indistinct lumen with calcium oxalate prismatic crystals scattered as well as in the parenchyma surrounding the fibres. Crystals also occasionally found associated with thicker-walled sclereids; crystals fairly uniform in size, although a few very large prisms may occur. Parenchyma cells thin-walled, several filled with dark brown contents. Medullary rays uniseriate, composed of rounded cells with slightly thickened walls. Cork cells thin-walled and polygonal. Fragments of lignified xylem tissue from adherent wood infrequent and consist of narrow tracheids with conspicuous bordered pits, accompanied by thin-walled fibres and pitted medullary ray cells. Starch grains rare; a few small, spherical grains may be found in some parenchymatous cells (*12*).

Powdered plant material

Folium

Brownish-green; fragments of adaxial epidermis with wavy anticlinal walls; abaxial epidermis with stomata, some paracytic, others atypical; covering trichomes, stellate, either entire or broken, composed of 4–12 cells united at their bases; cells elongated and conical, usually up to 250 µm long, thick-walled with clearly visible lumen with often brown contents. Fibres lignified and thick-walled, isolated or in groups; accompanied by sheath of prismatic calcium oxalate crystals. Parenchymatous palisade cells small and cylindrical; irregular-shaped cells of spongy mesophyll; sclereids, frequently enlarged at one or both ends, 150–180 µm long, whole or fragmented; fragments of annular or spiral vessels; isolated prismatic calcium oxalate crystals (*1*).

Cortex

Masses of brownish or yellowish cork cells, some lignified; groups of parenchyma cells with tannin or small starch grains; strands of lignified bast; tracheae with bordered pores; strongly lignified wood fibres with slit-like or bordered pores; crystal fibres containing monoclinic prismatic calcium oxalate crystals (up to 40 µm in length) (*13*).

General identity tests

Macroscopic and microscopic examinations (*1*), thin-layer chromatography (*1*, *2*) and high-performance liquid chromatography (*5*) for characteristic tannin constituents.

Purity tests

Microbiological

Tests for specific microorganisms and microbial contamination limits are as described in the WHO guidelines on quality control methods for medicinal plants (*14*).

Foreign organic matter

Folium

Not more than 7% stems, and not more than 2% other foreign matter (*1*).

Cortex

Not more than 2% foreign matter (*2*, *4*).

Total ash

Folium

Not more than 7% (*1*).

Cortex

Not more than 6% (*2*).

Acid-insoluble ash

Folium

Not more than 2% (*1*).

Cortex

Not more than 1.5% (*2*).

Alcohol-soluble extractive

Folium

To be established in accordance with national requirements.

Cortex

Not less than 20% using 45% alcohol (*2*).

Loss on drying

Folium

Not more than 10% (*1*).

Cortex

Not more than 12% (*4*).

Pesticide residues

The recommended maximum limit of aldrin and dieldrin is not more than 0.05 mg/kg (*15*). For other pesticides, see the *European pharmacopoeia* (*15*), and the WHO guidelines on quality control methods for medicinal plants (*14*) and pesticide residues (*16*).

Heavy metals

For maximum limits and analysis of heavy metals, consult the WHO guidelines on quality control methods for medicinal plants (*14*).

Radioactive residues

Where applicable, consult the WHO guidelines on quality control methods for medicinal plants (*14*) for the analysis of radioactive isotopes.

Other purity tests

Folium and Cortex

Chemical, sulfated ash and water-soluble extractive tests to be established in accordance with national requirements.

Folium

Alcohol-soluble extractive test to be established in accordance with national requirements.

Chemical assays

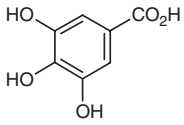
Folium: contains not less than 3% tannins (*1*). Cortex: contains not less than 4% tannins (*4*). Thin-layer chromatography is used for qualitative and quantitative analysis of tannins (*1*). A high-performance liquid chromatography method for quantitative analysis of condensed and hydrolysable tannins has been developed (*17*, *18*).

Major chemical constituents

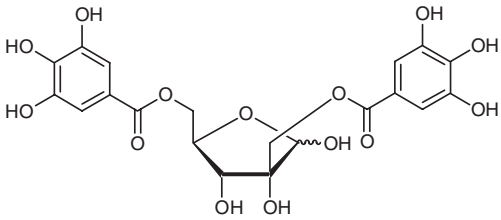
The major constituents of the dried leaf and bark are tannins (up to 10%). Both hydrolysable and condensed tannins are present, with the latter predominating (*9*, *11*, *19*). Folium tannins are a mixture of gallic acid (10%), hydrolysable

hamamelitannin (1.5%) and condensed proanthocyanidins (88.5%) (*17*). Cortex tannins are similar qualitatively, but have a much higher hamamelitannin level (up to 65% of a hydroalcoholic extract) (*11*).

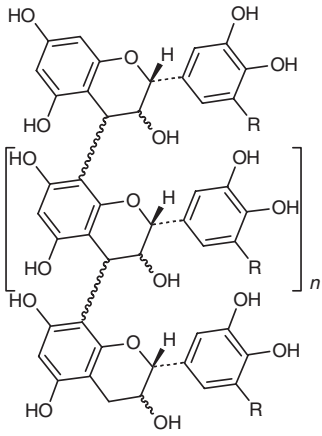
The structures of gallic acid, hamamelitannin and condensed proanthocyanidins are presented below.



gallic acid



hamamelitannin



proanthocyanidins
procyanidin $n = 0$, R = H
prodelphinidin $n = 0$, R = OH

Medicinal uses

Uses supported by clinical data

Topically for minor skin lesions, bruises and sprains (*3*, *5*, *20*), local inflammation of the skin and mucous membranes (*3*, *5*, *20–24*), haemorrhoids (*3*, *5*, *20*, *25–28*) and varicose veins (*3*).

Uses described in pharmacopoeias and in traditional systems of medicine

Topically as a haemostat (*27*).

Uses described in folk medicine, not supported by experimental or clinical data

Treatment of colitis, diarrhoea, dysentery, dysmenorrhoea, eye inflammations, haematuria, kidney pains, neuralgia, nosebleeds and excessive menstruation. Also as a tonic (*6*, *7*, *19*).

Pharmacology

Experimental pharmacology

Astringent activity

The phenolic constituents of Folium et Cortex Hamamelidis, particularly the tannins (e.g. hamamelitannin), aldehydes and oligomeric proanthocyanidins, are responsible for its astringent activity (*6*, *18*, *29*, *30*). Similar to other astringent drugs, application of Hamamelidis[1] preparations to the skin and mucosa in low concentrations sealed cell membranes and reduced capillary permeability (*6*, *30*). Higher concentrations precipitated proteins and thickened colloidal tissue, forming a thin membrane in the wound region, and slightly compressed the skin tissue beneath it (*6*). Alcohol extracts of Hamamelidis had strong astringent action, with the bark extract being slightly superior to the leaf extract (*31*).

The healing effect of Hamamelidis distillate was compared with hydrogen peroxide on skin damaged by application of dichlorodiethyl sulfide (mustard gas) in various animal models. The distillate was more effective than hydrogen peroxide in reducing the occurrence of pus in the affected skin areas. Furthermore, subsequent treatment of the purulent skin areas with a 20% Hamamelidis ointment reduced the incidence of suppuration as compared with hydrogen peroxide treatment (*6*, *32*).

Venotonic activity

The venotonic effects of leaf preparations (steam distillate, tincture or alcohol extract) were tested by measuring the blood supply to the rear paw of rabbits (*33*). A decrease in blood supply was observed after intra-arterial administration of the distillate. This effect was not influenced by concomitant administration of adrenergic, adrenolytic or myotonic drugs (*33–35*).

Antibacterial activity

An aqueous extract of the leaves inhibited the growth in vitro of *Escherichia coli* (MIC 0.4 mg/ml), *Staphylococcus aureus* (MIC 0.4 mg/ml), *Bacillus subtilis* (MIC 1.1 mg/ml) and *Enterococcus faecalis* (MIC 3.0 mg/ml). Aqueous extracts of the bark inhibited the growth in vitro of *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis* and *Enterococcus faecalis* (MIC for all 10.0 mg/ml) (*36*).

Antioxidant activity

Hamamelitannin inhibited the production of superoxide anion radicals (IC_{50} 1.38 µmol/l) and hydroxyl radicals (IC_{50} 5.46 µmol/l), as measured by electron spin resonance spectrometry (*37*, *38*). Hamamelitannin also suppressed the depolymerization of hyaluronic acid and protected human dermal fibroblasts against damage induced by superoxide anion radicals (at concentrations of

[1] Refers to Folium et Cortex Hamamelidis.

1 mmol/l and 10 mmol/l, respectively) (*37*). Hamamelitannin and gallic acid protected murine dermal fibroblasts against damage induced by superoxide anion radicals (IC_{50} 1.31 µmol/l and 1.01 µmol/l, respectively) (*38*). Both tannins had free radical scavenging activity. For superoxide anion scavenging, the IC_{50} was 1.31 µmol/l for hamamelitannin and 1.01 µmol/l for gallic acid, compared with 23.31 µmol/l for ascorbic acid. For hydroxyl radical scavenging, the IC_{50} was 5.46 µmol/l for hamamelitannin and 78.04 µmol/l for gallic acid. For singlet oxygen scavenging, the IC_{50} was 45.51 µmol/l for hamamelitannin and 69.81 µmol/l for gallic acid (*39*).

Anti-inflammatory activity

Hamamelidis extracts and isolated chemical constituents have anti-inflammatory activity both in vitro and in vivo. Intraperitoneal administration of a 70% ethanol extract of the leaves (200 mg/kg body weight) significantly inhibited the chronic phase of carrageenan-induced rat footpad oedema (*40*). Hamamelitannin and galloylated proanthocyanidins isolated from Hamamelidis are potent inhibitors of 5-lipoxygenase (IC_{50} range 1.0–18.7 µg/ml). Topical application of a hydroalcoholic extract of the bark (250 µg/ml) inhibited croton oil-induced ear oedema in mice. In addition to anti-inflammatory activity, this study demonstrated that the proanthocyanidin fraction of the hydroalcoholic extract was active against herpes simplex virus type 1 (ED_{50} 11 µg/ml), and also inhibited α-glucosidase (ED_{50} 0.35 µg/ml) and human leukocyte elastase (ED_{50} 1.4 µg/ml) (*41*).

Clinical pharmacology

Anorectal complaints

The astringent properties of Hamamelidis extracts have led to their use in ointments and suppositories for the treatment of anorectal complaints, such as haemorrhoids (*25–27*). In a clinical study without controls of 75 patients with acute stage 1 haemorrhoidal symptoms, the efficacy of rectal ointments containing either a Hamamelidis fluidextract or bismuth subgallate was assessed. After application of either ointment twice daily for 3 days, significant improvement was observed in pruritus, burning sensation and pain ($P < 0.001$). Marked recovery was noted after 3 weeks of therapy (*25*). A randomized, double-blind trial compared the efficacy of rectal ointments containing either a Hamamelidis fluidextract, bismuth subgallate or a local anaesthetic in the treatment of 90 patients with acute stage 1 haemorrhoidal symptoms. The local anaesthetic was present in two control ointments which also contained either policresulen or fluocinolone acetonide. After 21 days of treatment, all four ointments were equally effective in improving pruritus, bleeding, burning sensation and pain (*26*).

The efficacy of a Hamamelidis ointment containing 25 g aqueous distillate/100 g ointment base (equivalent to about 4 g drug) was compared to a Hamamelidis reference preparation in a study without controls of 70 patients

with various anorectal complaints. Preparations were applied to the affected skin or transitional mucosa three times daily either alone or in combination with sclerotherapy. After 4 weeks of treatment, symptoms such as pruritus, burning sensation and pain were eliminated in 60% of the patients treated with the Hamamelidis ointment (*28*).

Anti-inflammatory activity

The anti-inflammatory efficacy of an aftersun lotion containing 10% Aqua Hamamelidis was compared with that of two Hamamelidis-free aftersun lotions in 30 healthy volunteers. Each volunteer received four doses of ultraviolet B in a modified ultraviolet B erythema test. Chromametry and visual scoring were used to determine the degree of erythema at 7, 24 and 48 hours after irradiation. The lotion containing Hamamelidis suppressed erythema by 20% at 7 hours and by 27% at 48 hours, whereas the degree of suppression seen with the Hamamelidis-free lotions was 11% and 15%, respectively (*42*).

A randomized, double-blind study of 48 patients assessed the anti-inflammatory efficacy of topical application of a Hamamelidis distillate in a phospholipid-containing vehicle, hydrocortisone, camomile and four drug-free vehicle-based preparations. Erythema induced by ultraviolet light or repeated stripping of the skin with adhesive tape was suppressed only by the Hamamelidis preparation (0.64 mg or 2.5 mg Hamamelidis ketone per 100 g vehicle) and hydrocortisone cream (1%). However, the hydrocortisone cream was superior to all other preparations tested (*21*).

Vasoconstriction

A randomized, placebo-controlled study assessed the vasoconstrictive effects of an aqueous propylene glycol extract of Hamamelidis in 30 healthy volunteers. The extract produced a reduction in skin temperature as compared with the placebo (*6*, *43*). The anti-inflammatory effects of a Hamamelidis ointment containing 25 g aqueous distillate/100 g ointment base (about 4 g drug) were analysed in five patients with dermatoses and 22 healthy volunteers. Fluvography measurements indicated that in both groups the ointment reduced the thermal conductivity of the skin due to vasoconstriction, suggesting a mild anti-inflammatory activity. These data were confirmed by transcutaneous oxygen measurements (*44*).

Eczema

A randomized, double-blind, placebo-controlled trial compared the efficacy of three creams containing either a Hamamelidis distillate, 0.5% hydrocortisone or a drug-free vehicle in the symptomatic treatment of 72 patients with moderately severe atopic eczema. All treatments reduced the incidence of itching, scaling and erythema after 1 week of treatment: the cream containing Hamamelidis distillate was no more effective than that containing the placebo (*45*).

The efficacy of two Hamamelidis ointments (differing only in the ointment base), containing 25 g aqueous distillate/100 g ointment base (equivalent to about 4 g drug), for the treatment of endogenous eczema (neurodermatitis) and toxic degenerative eczema (attrition eczema) was compared in a placebo-controlled, double-blind study (the placebo was not described). Symptomatic improvements in itching, redness, burning sensation and desquamation of the skin were observed in the 36 patients with endogenous eczema (neurodermatitis) with both Hamamelidis preparations after treatment for 39 days. Eighty patients with toxic degenerative eczema (attrition eczema) treated with the Hamamelidis ointments showed improvements in rough skin, redness, burning sensation and desquamation of the skin after 28 days of treatment (*23*).

A randomized, double-blind comparison study assessed the efficacy of ointments containing either a standardized extract of the dried leaves or bufexamac in the treatment of 22 patients with bilateral, moderately severe endogenous eczema (neurodermatitis). Patients were treated three times daily for an average of 17 days. Comparison of the patients' forearms showed that both treatments reduced the severity of symptoms such as desquamation of the skin, redness, itching and lichenification, with desquamation showing the highest reduction (55%). No differences were observed in the global assessment of the therapy or the severity of symptoms between treatments (*24*).

In a pilot study of 37 patients with endogenous eczema (neurodermatitis), a cream containing a Hamamelidis leaf extract was applied twice daily for 2 weeks. Following treatment, considerable improvement in symptoms such as inflammation and itching was noted in 24 patients (*46*).

Analgesic activity

In a randomized clinical trial involving 266 patients undergoing episiotomy, the efficacy of three analgesic treatments was investigated to determine their effects on pain, bruising and oedematous swelling. The treatments tested were local application of: a cream containing Hamamelidis water BPC 1973; a reference cream containing 1% hydrocortisone and a local anaesthetic; and ice packs. Oral paracetamol and salt baths were also used as needed. The efficacy of all three analgesic treatments appeared to be equal (*22*).

Antiviral activity

The efficacy and safety of an ointment prepared with a special extract from the bark was assessed in a randomized, double-blind, placebo-controlled study for the treatment of herpes labialis infection. Thirty-four patients were treated within 48 hours of recurrence of symptoms, and treatment (daily) lasted for 8 days. By the end of the therapy, the size of the inflamed area was significantly reduced in patients treated with the Cortex Hamamelidis ointment as compared with placebo treatment ($P = 0.022$) (*47*).

Contraindications

No information available.

Warnings

No information available.

Precautions

Carcinogenesis, mutagenesis, impairment of fertility

Aqueous extracts of the dried leaves were not carcinogenic when administered subcutaneously to rodents (10 mg/animal) (*48*).

Other precautions

No information available on general precautions or precautions concerning drug interactions; drug and laboratory test interactions; teratogenic and non-teratogenic effects in pregnancy; nursing mothers; or paediatric use. Therefore, Folium et Cortex Hamamelidis should not be administered during pregnancy or lactation or to children without medical supervision.

Adverse reactions

Allergic contact dermatitis may occur in sensitive individuals (*49*, *50*).

Dosage forms

Dried leaves and bark for decoctions; steam distillate, ointment and suppositories (*3*, *9*). Fresh leaves and twigs are collected in the spring and early summer to make a steam distillate (*3*). Store in a well-closed container, protected from light (*19*).

Posology

(Unless otherwise indicated)
External use: steam distillate, undiluted or diluted 1 : 3 with water to make poultices; 20–30% in semisolid preparations (*3*). Extracts: in semisolid and liquid preparations corresponding to 5–10% of the crude drug (*3*, *5*). Crude drug: decoctions from 5–10 g to 1 cup (250 ml) water for poultices and wound irrigation (*3*, *5*). Rectal suppositories: 1–3 times daily the quantity of a preparation corresponding to 0.1–1.0 g crude drug, use Hamamelidis water undiluted or diluted 1 : 3 with water (*3*, *5*). Other preparations: several times daily, corresponding to 0.1–1.0 g drug in preparations, or witch hazel water undiluted or diluted with water (*3*).

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