Radix Echinaceae

Definition

Radix Echinaceae consists of the fresh or dried roots of *Echinacea angustifolia* D.C. var. *angustifolia* or its variety *strigosa* McGregor, or *E. pallida* (Nutt.) Nutt. (Asteraceae) (*1–3*).

Synonyms

Echinacea angustifolia D.C. var. angustifolia

Brauneria angustifolia Heller, *Echinacea pallida* var. *angustifolia* (D.C.) Cronq. (*4, 5*).

Echinacea pallida (Nutt.) Nutt.

Echinacea angustifolia Hook, *Rudbeckia pallida* Nutt., *Brauneria pallida* Britt., *Echinacea pallida* f. *albida* Steyerm (*4, 5*).

E. angustifolia and *E. pallida* were regarded as varieties of the same species or even identical plants. However, in a revision of the genus *Echinacea* in 1968, McGregor (*4*) classified them as two distinct species with *E. angustifolia* further divided into two varieties (*4, 5*). A considerable amount of commercial "*E. angustifolia*" cultivated in Europe was, in fact, *E. pallida*. Data on *E. angustifolia* published prior to 1987 and based on material of commerce from Europe should be reviewed with caution (*5*).

Current commercial preparations are derived primarily from *E. angustifolia* and *E. pallida* roots; the preparation of a monograph on *E. purpurea* root awaits further data.

Asteraceae are also known as Compositae.

Selected vernacular names

Echinacea angustifolia D.C. var. angustifolia

American coneflower, black sampson, cock up head, coneflower, echinacea root, Igelkopf, Indian head, Kansas snakeroot, Kegelblume, narrow-leaved purple coneflower root, purple coneflower, Sonnenhut, racine d'echinacea (*5–10*).

Echinacea pallida (Nutt.) Nutt.

Blasser Igelkopf, blasse Kegelblume, blasser Sonnenhut, pale coneflower root, pale purple coneflower root, pallida root (*8, 10*).

Description

Echinacea species are hardy, herbaceous perennials with either simple or branched stems. The terminal single flowering heads have fertile disc florets that terminate in spines (paleae). These are surrounded by infertile drooping or spreading ray flowers that have 2 or 3 teeth at each end. The leaf shape varies from lanceolate to ovate, its margin may be dentate and the leaf may be pubescent or smooth. Roots are either single taproot or fibrous in form (*6–11*).

Echinacea angustifolia D.C. var. angustifolia

Stems simple or occasionally branched, 10–50 cm high, smooth or hirsute below, hirsute or tuberculate-hispid above; leaves oblong-lanceolate to elliptical, entire, dark green tuberculate-hirsute to tuberculate-hispid; basal leaves short- to long-petiolate, 5–27 cm long, 1–4 cm broad, lower cauline leaves petiolate, 4–15 cm long, 0.5–3.8 cm broad, upper cauline leaves sessile, acute; heads 1.5–3 cm high, 1.5–2.5 cm broad exclusive of ligules, phyllaries in three or four series, lanceolate, acute, entire, 6–11 mm long, 2–3 mm wide, tuberculate-hirsute or tuberculate-hispid; rays spreading, 2–3.8 cm long, 5–8 mm wide, white, pinkish or purplish; disc corollas 6–8.5 mm long, lobes 1.2–2 mm long; achenes 4–5 mm long, pappus a toothed crown; pollen grains yellow, 19–26 μm in diameter; haploid chromosome number $n = 11$ (*4*).

Echinacea pallida (Nutt.) Nutt.

Stems simple, rarely branched, 40–90 cm high, sparsely hirsute below, more densely so above; leaves oblong-lanceolate to long-elliptical, entire, dark green, hirsute on both surfaces, triple-veined; basal leaves 10–35 cm long, 1–4 cm broad, the cauline leaves 10–25 cm long, 1–2.5 cm broad, acute, petiolate below to sessile above; phyllaries lanceolate to narrowly oblong, 8–17 mm long, 2–4 mm broad, hirsute, ciliate, three or four series gradually passing into the echinaceous pales; rays reflexed, 4–9 cm long, 5–8 mm broad, purplish, pink, or white; pales 1–1.3 cm long, body 8–10 mm long, awn 2.5–3.5 mm long; disc floret 8–10 mm long, lobes 2–3 mm long, achenes 3.7–5 mm long, glabrous, pappus a toothed crown, teeth about even, longest 1 mm; pollen grains white, 24–28.5 μm in diameter; haploid chromosome number $n = 22$ (*4*).

Plant material of interest: fresh or dried roots

General appearance

Echinacea angustifolia D.C. var. *angustifolia*

Cylindrical or slightly tapering and sometimes spirally twisted, passing imperceptibly into a rhizome in the upper part; rhizome up to about 15 mm in diameter, roots 4–10 mm in diameter; outer surface pale brown to yellowish brown; rhizomes crowned with remains of the aerial stem and sometimes showing surface annulations; roots longitudinally wrinkled and deeply fur-

rowed; fracture short when dry but becoming tough and pliable on exposure to air (*12*).

***Echinacea pallida* (Nutt.) Nutt.**

Similar in appearance to *E. angustifolia* (*5–7*).

Organoleptic properties

Odour, mild, aromatic; taste, sweet initially but quickly becoming bitter followed by a tingling sensation on the tongue (*12*).

Microscopic characteristics

The roots of the two species are very similar. The transverse section shows a thin outer bark separated by a distinct cambium line from a wide xylem; a small circular pith in the rhizome. Cork composed of several rows of thin-walled cells containing yellowish brown pigment; cortex parenchymatous; rhizome with occasional small groups of thick-walled, lignified fibres in the pericycle; phloem and xylem composed of very narrow strands of vascular tissue separated by wide, non-lignified medullary rays; xylem vessels lignified, 25–75 μm in diameter, usually reticulate thickening but occasionally with spiral or annular thickening; stone cells, occurring singly or in small groups, varying considerably in size and shape from rounded to rectangular to elongated and fibre-like, up to 300 μm long and 20–40 μm wide, with intercellular spaces containing a dense black deposit; schizogenous oleoresin canals; spherocrystalline masses of inulin occur throughout the parenchymatous tissue. In *E. angustifolia* oleoresin canals, 80–150 μm in diameter and containing yellowish orange oleoresin, are present only outside the central cylinder, but in *E. pallida* they are present both inside and outside. In *E. angustifolia* the narrow, 300–800 μm long, lignified fibres are in scattered groups usually surrounded by phytomelanin deposits, while in *E. pallida* they are present only in the periphery of the cortex and they are mostly single, wider, and shorter, 100–300 μm, and phytomelanin is often absent (*9*, *12*).

Powdered plant material

E. angustifolia

Powdered rhizome and roots are brown with a slight aromatic odour and initially a sweet taste, quickly becoming bitter and leaving a tingling sensation on the tongue. Thin-walled polygonal cork cells with red-brown contents; lignified reticulately thickened vessels; abundant stone cells of various shapes; fragments of oleoresin canals with reddish brown contents; abundant thin-walled parenchyma with spherocrystalline masses of inulin (*12*).

E. pallida

Descriptions of powdered *E. pallida* are currently unavailable.

Geographical distribution

Echinacea species are native to the Atlantic drainage area of the United States of America and Canada, but not Mexico. Their distribution centres are in Arkansas, Kansas, Missouri, and Oklahoma in the United States of America (*4*). *E. pallida* was cultivated in Europe for a number of years and was mistaken for *E. angustifolia* (*9*).

General identity tests

Macroscopic and microscopic examinations (*5–7*, *9*, *12*). Chemical finger-prints of lipophilic constituents, echinacosides, and other caffeic acid derivatives in methanol extracts can be obtained by thin-layer chromatography and high-performance liquid chromatography (*5*, *13*, *14*).

Purity tests

Microbiology

The test for *Salmonella* spp. in Radix Echinaceae products should be negative. The maximum acceptable limits of other microorganisms are as follows (*15–17*). For preparation of decoction: aerobic bacteria—not more than 10^7/g; fungi—not more than 10^5/g; *Escherichia coli*—not more than 10^2/g. Preparations for internal use: aerobic bacteria—not more than 10^5/g or ml; fungi—not more than 10^4/g or ml; enterobacteria and certain Gram-negative bacteria—not more than 10^3/g or ml; *Escherichia coli*—0/g or ml.

Foreign organic matter

Not more than 3% (*2*, *3*, *12*). Does not contain roots of *Parthenium integrifolium* L., commonly known as "American feverfew", which have been found to be adulterants of or substitutes for Radix Echinaceae (*5*, *6*, *9*, *13*).

Total ash

Not more than 9% (*12*).

Acid-insoluble ash

Not more than 3% (*12*).

Water-soluble extractive

Not less than 15% (*12*).

Moisture

Not more than 10% (*3*).

Pesticide residues

To be established in accordance with national requirements. Normally, the maximum residue limit of aldrin and dieldrin in Radix Echinaceae is not more

than 0.05 mg/kg (*17*). For other pesticides, see WHO guidelines on quality control methods for medicinal plants (*15*) and guidelines for predicting dietary intake of pesticide residues (*18*).

Heavy metals

Recommended lead and cadmium levels are no more than 10 and 0.3 mg/kg, respectively, in the final dosage form of the plant material (*15*).

Radioactive residues

For analysis of strontium-90, iodine-131, caesium-134, caesium-137, and plutonium-239, see WHO guidelines on quality control methods for medicinal plants (*15*).

Other purity tests

Chemical tests and tests of dilute ethanol-soluble extractive to be established in accordance with national requirements.

Chemical assays

Essential oil (0.2–2%) and echinacoside (0.4–1.7%) in both *E. angustifolia* and *E. pallida* roots (*5*).

Quantitative analysis of echinacoside, cynarin, chicoric acid, chlorogenic acid derivatives, and other constituents by high-performance liquid chromatography (*5, 19*).

Major chemical constituents

A number of chemical entities have been identified and reported to be biologically active, including a volatile oil, alkamides, polyalkenes, polyalkynes, caffeic acid derivatives, and polysaccharides (*5–7, 9–11*).

The volatile oil contains, among other compounds, pentadeca-(1,8-*Z*)-diene (44%), 1-pentadecene, ketoalkynes and ketoalkenes.

More than 20 alkamides, mostly isobutylamides of C_{11}–C_{16} straight-chain fatty acids with olefinic or acetylenic bonds, or both, are found in the roots; the highest concentration is in *E. angustifolia*, followed by *E. purpurea*, and the lowest is in *E. pallida.* The main alkamide is a mixture of isomeric dodeca-2,4,8,10-tetraenoic acid isobutylamides.

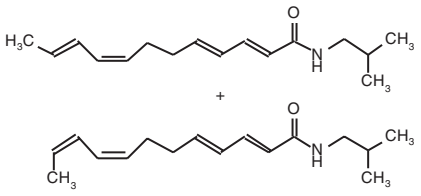
Caffeic acid ester derivatives present include echinacoside, cynarin, and chicoric acid. Cynarin is present only in *E. angustifolia*, thus distinguishing it from the closely related *E. pallida*.

Polysaccharide constituents are of two types: a heteroxylan of relative molecular mass about 35 000 and an arabinorhamnogalactan of relative molecular mass about 45 000.

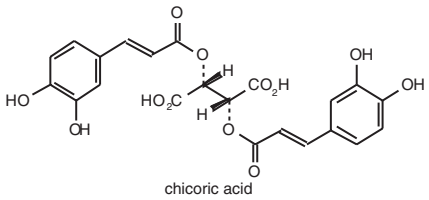
Other constituents include trace amounts of pyrrolizidine alkaloids (tussilagine (0.006%) and isotussilagine). At these concentrations, the alkaloids

are considered to be non-toxic (*7*, *20*), and since they lack the 1,2-unsaturated necine ring of alkaloids such as senecionine (structure in box) from *Senecio* species, they are considered to have no hepatotoxic potential (*5*).

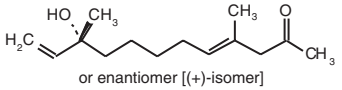
Structures of representative constituents are presented below.



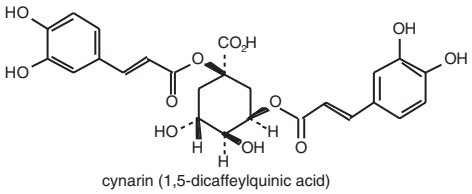
(2*E*,4*E*,8*Z*,10*E*)- and (2*E*,4*E*,8*Z*,10*Z*)-dodeca-2,4,8,10-tetraenoic acid isobutylamides



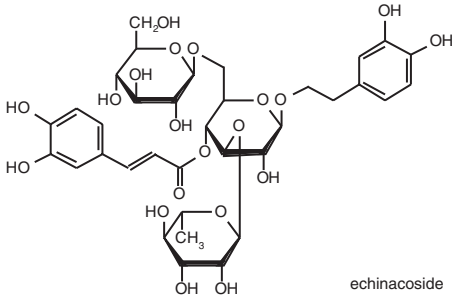
chicoric acid



or enantiomer [(+)-isomer] echinolone

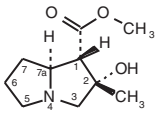


cynarin (1,5-dicaffeylquinic acid)

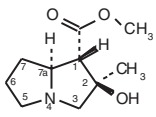


echinacoside

Necine ring pyrrolizidine alkaloids :

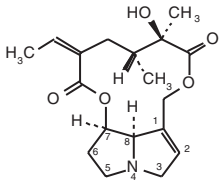


tussilagine



isotussilagine

1,2-saturated



senecionine

1,2-unsaturated

Dosage forms

Powdered roots, and galenics and preparations thereof for internal use (*9*).

Medicinal uses

Uses supported by clinical data

Preparations of Radix Echinaceae are administered orally in supportive therapy for colds and infections of the respiratory and urinary tract (*1*, *5–7*, *9*, *11*, *21–23*). Beneficial effects in the treatment of these infections are generally thought to be brought about by stimulation of the immune response (*5*, *6*, *9*, *10*).

Uses described in pharmacopoeias and in traditional systems of medicine

None.

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

Treatment of yeast infections, side-effects of radiation therapy, rheumatoid arthritis, and food poisoning (*1*, *5*, *6*, *9*, *24*).

Pharmacology

Experimental pharmacology

Current claims for the effectiveness of Radix Echinaceae as a stimulator of the immune system are based on over 350 scientific studies in the past 50 years. Numerous *in vitro* and *in vivo* studies have documented the activation of an immune response after treatment with Radix Echinaceae extracts. The immunostimulant effect is brought about by three mechanisms: activation of phagocytosis and stimulation of fibroblasts; increasing respiratory activity; and causing increased mobility of the leukocytes (*5*, *9*, *11*). Chemically standardized extracts, derived from roots and aerial parts from the three *Echinacea* species, have been assessed for their phagocytotic potential. All ethanolic root extracts increased phagocytosis *in vitro* (*25*). Inhibition of hyaluronidase activity, stimulation of the activity of the adrenal cortex, stimulation of the production of properdin (a serum protein which can neutralize bacteria and viruses), and stimulation of interferon production have also been reported after *Echinacea* treatments (*26*). The pharmacological activity of *Echinacea* spp. has been attributed to five component fractions in addition to the essential oil, namely the alkylamides, caffeic acid derivatives, polyalkynes, polyalkenes and polysaccharides (*6*). The lipophilic amides, alkamides and caffeic acid derivatives appear to contribute to the immunostimulant activity of the alcoholic *Echinacea* extracts by stimulating phagocytosis of polymorphonuclear neutrophil granulocytes (*5*, *23*, *27*). High molecular weight polysaccharides, including heteroxylan, which activates phagocytosis, and arabinogalactan, which promotes the release of tumour necrosis factor and the production of interleukin-1 and interferon beta (*24*, *26*), have also been implicated in the activity of the aqueous extracts and the powdered drug when taken orally. The overall immunostimulant activity of

the alcoholic and aqueous *Echinacea* extracts appears to depend on the combined effects of several constituents (*5*, *9*, *27*).

Echinacea extracts inhibit streptococcal and tissue hyaluronidase (*28*). Inhibition of tissue and bacterial hyaluronidase is thought to localize the infection and prevent the spread of causative agents to other parts of the body. In addition to the direct antihyaluronidase activity, an indirect effect on the hyaluronic acid–hyaluronidase system has been reported (*29*, *30*). Stimulation of new tissue production by increasing the activity of fibroblasts, and stimulation of both blood- and tissue-produced phagocytosis, appear to be involved in this mechanism (*29*).

Echinacea extracts have anti-inflammatory activity. An alkylamide fraction from *Echinacea* roots markedly inhibited activity *in vitro* in the 5-lipoxygenase model (porcine leukocytes) (*31*). Topical application of a crude polysaccharide extract from *E. angustifolia* has been reported to reduce inflammation in the rat paw oedema model (*32*, *33*).

Clinical pharmacology

One placebo-controlled clinical study of 160 patients with infections of the upper respiratory tract has been performed (*34*). Significant improvement was observed after patients were treated with an aqueous-alcoholic tincture (1:5) at 90 drops/day (900 mg roots). The duration of the illness decreased from 13 to 9.8 days for bacterial infections, and from 12.9 to 9.1 days for viral infections (*34*).

Contraindications

External use

Allergy to plants in the Asteraceae.

Internal use

Should not be used in serious conditions such as tuberculosis, leukosis, collagenosis, multiple sclerosis, AIDS, HIV infection and autoimmune disorders. *Echinacea* preparations should not be administered to people with a known allergy to any plant of the Asteraceae (*1*). Parenteral administration is rarely indicated owing to potential adverse side-effects (see Adverse reactions).

Warnings

None.

Precautions

General

Internal use should not exceed a period of 8 successive weeks (*1*).

Carcinogenesis, mutagenesis, impairment of fertility

Mutagenicity and carcinogenicity tests were negative (*5*, *9*, *35*). Doses up to a polysaccharide concentration of 500 µg/ml caused no increase in sister chromatid exchange or structural chromosome aberrations (*35*).

Pregnancy: teratogenic effects

There are no reliable studies on this subject. Therefore, administration of Radix Echinaceae during pregnancy is not generally recommended (*1*).

Nursing mothers

There are no reliable studies on this subject. Therefore, nursing mothers should not take Radix Echinaceae without consulting a physician (*1*).

Paediatric use

Oral administration of *Echinacea* preparations is not recommended for children, except on the advice of a physician.

Other precautions

No information was available concerning drug interactions, drug and laboratory test interactions, and non-teratogenic effects on pregnancy.

Adverse reactions

External use

Allergic reactions.

Internal use

Allergic reactions, shivering, fever, and headache.

Posology

E. angustifolia root

Unless otherwise prescribed, hot water (about 150 ml) is poured over about 0.5 teaspoon (about 1 g) of powdered plant material, allowed to steep for 10 minutes, passed through a strainer, and taken orally three times a day between meals (*7*).

Liquid extract (1:5, 45% ethanol), 0.5–1 ml three times daily (*7*). Tincture (1:5, 45% ethanol), 2–5 ml three times daily (*7*).

E. pallida root

Unless otherwise prescribed: daily dose, tincture (1:5 with 50% ethanol by volume) from original dry extract (50% ethanol), corresponding to 900 mg of root (*9*).

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