# Echinacea

## Species (Family)

(i) *Echinacea angustifolia* (DC.) Hell. (Asteraceae/Compositae)
(ii) *Echinacea pallida* (Nutt.) Britt.
(iii) *Echinacea purpurea* Moensch.

## Synonym(s)

Black Sampson, Coneflower
(i) *Brauneria angustifolia*
(ii) *Brauneria pallida* (Nutt.) Britt.

## Part(s) Used

Rhizome, root

## Pharmacopoeial and Other Monographs

BHC 1992[G6]
BHP 1996[G9]
Complete German Commission E[G3]
ESCOP 1999[G52]
Martindale 32nd edition[G43]
Mills and Bone[G50]
PDR for Herbal Medicines 2nd edition[G36]
WHO volume 1 1999[G63]

## Legal Category (Licensed Products)

GSL[G37]

## Constituents[1–5,G2,G6,G39,G40,G48,G53,G64]

*Alkaloids* Saturated pyrrolizidine-type. Isotussilagine and tussilagine 0.006% in *Echinacea angustifolia* and *Echinacea purpurea*.[1]

*Amides* Alkylamides, at least 20, especially isobutylamides of $C_{11}$–$C_{16}$ straight-chain fatty acids;[2–6] echinacein, an unsaturated amide reported to be identical with neoherculin and α-sanshool.

*Carbohydrates* High molecular weight polysaccharides, echinacin (polysaccharide component), inulin and sugars (fructose, glucose, pentose).[7–9]

*Glycosides* Caffeic acid derivatives (e.g. echinacoside 0.5–1.0%).[4,10,11] Cynarin (quinic acid derivative) is reported to be specific to *E. angustifolia* and is stated to be the first documented isolation of cynarin from the genus *Echinacea*.

*Polyenes* Polyacetylenes are reported to be specific to *E. pallida*. However, polyacetylenes have also been documented for both *E. angustifolia* and *E. purpurea*.[4,12,13]

*Terpenoids* Sesquiterpene lactone esters (germacrane- or guaiane-type skeleton) isolated from *E. purpurea*[14] have subsequently been attributed to *Parthenium integrifolium*,[15] a known adulterant of *E. purpurea*.

*Other constituents* Betaine (carotenoid), fatty acids, phytosterol, resin and volatile oil (alkylketones main constituents in *E. pallida*).

*Other plant parts* The aerial parts of *E. purpurea* have been reported to contain amides (highly unsaturated), germacrene (a sesquiterpene) alcohol, a labdane derivative, methyl *p*-hydroxycinnamate and vanillin.

## Food Use

Echinacea is not used in foods.

## Herbal Use

Echinacea is stated to possess antiseptic, antiviral and peripheral vasodilator properties. Traditionally, it has been used for furunculosis, septicaemia, nasopharangeal catarrh, pyorrhoea, tonsillitis, and specifically for boils, carbuncles and abscesses.[1,G2,G6,G7,G8,G64] It is under investigation for its immunostimulant action.

## Dosage

*Dried root/rhizome* 1 g or by infusion or decoction three times daily.[G6,G7]

*Liquid extract* 0.25–1.0 mL (1:1 in 45% alcohol) three times daily.[G6,G7]

*Tincture* 1–2 mL (1:5 in 45% alcohol) three times daily.[G6,G7]

## Pharmacological Actions[16–20]

### *In vitro* and animal studies

*In vivo* immunostimulant activity in mice has been documented for echinacea, indicated by phagocytosis enhancement and by an increase in the serum elimination of carbon particles (carbon clearance test).[7,21] Documented *in vitro* immunostimulant activity, indicated by phagocytosis enhancement and by stimulation of TNF (tumour necrosis factor) secretion in human macrophages and lymphocytes, is stated to be indicative of non-specific T cell activation.[7,22]

Immunostimulant activity has been associated with polysaccharide fractions (PSF) and polyacetylene fractions (PCF) in both *in vivo* and *in vitro* studies.[23] However, no direct influence on T lymphocytes and only a moderate induction of B lymphocyte proliferation were reported for a PSF, from *E. purpurea*, that was found to selectively induce macrophage cytotoxicity against tumour targets *in vitro*.

Phagocytosis enhancement *in vitro* has also been reported for non-volatile sesquiterpene esters isolated from *E. purpurea*,[14] and tissue culture experiments have yielded immunologically active polysaccharides.[24]

*In vitro* antiviral activity has been described for alcoholic and aqueous echinacea extracts.[25] Incubation of mouse cells with the extracts was stated to result in 24 hour resistance to influenza, herpes and vesicular (pox) viruses.[25] Documented immunostimulant and antiviral properties are thought to be partly mediated via the binding of the PSF to carbohydrate receptors on the cell surface of T cell lymphocytes, resulting in non-specific T cell activation (e.g. interferon production, lymphokine (TNF) secretion).[26,27]

*In vivo* anti-inflammatory activity has been reported for the PSF in the carrageenan rat paw oedema test and in the croton oil mouse ear test, with the PSF administered intravenously and topically, respectively.[8] The isolated PSF was stated to be twice as active as the total aqueous extract in the carrageenan test, and to be about half as active as indomethacin in the croton oil test.

In addition, an aqueous echinacea extract was reported to be more effective in the croton oil test than benzydamine, a topical non-steroidal anti-inflammatory drug. When an echinacea leaf extract was administered orally to rats, it was stated to be devoid of anti-inflammatory activity in the carrageenan test.[28]

A long-chain alkene from *E. angustifolia* is stated to possess significant antitumour activity *in vivo*, inhibiting the growth of Walker tumours in rats and lymphocytic leukaemia (P388) in mice.[29]

Antibacterial activity against *Escherichia coli*, *Proteus mirabilis*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* has been demonstrated for a multi-herbal preparation containing echinacea and other herbal ingredients, with slight activity against *Staphylococcus aureus* and *Proteus mirabilis* attributed to echinacea.[30]

The same preparation exhibited *in vitro* antispasmodic activity against acetylcholine-induced spasm of the isolated guinea-pig ileum. Echinacea was one of two components to which the main antispasmodic activity was attributed.[30]

Echinacin, a polysaccharide extract, has been used experimentally as an antagonist of hyaluronidase.[31] The wound-healing properties documented for echinacea have been attributed to echinacin (polysaccharide extract), which is said to inhibit the action of hyaluronidase via formation of a stable hyaluronic acid–polysaccharide complex and to stimulate fibroblast cell growth.[G2]

Echinacea is stated to have some cortisone-like activity.[31]

### Clinical studies

Echinacea has been used for its non-specific action on cell-mediated immunity. A single 2-mL subcutaneous injection (stated as equivalent to 0.1 g of press sap) followed by a free interval of one week was reported to stimulate cell-mediated immunity, whereas daily administration of the injection was stated to have a depressant effect on cell-mediated immunity.[30]

A multi-herbal preparation containing echinacea as one of the ingredients was reported to have a favourable effect on the symptoms of irritable bladder associated with functional and neurohormonal disorders, and on bacterial bladder infections. Contributions of the individual ingredients to the overall efficacy of the preparations were assessed in animal experiments (*see In vitro* and animal studies).[30]

Numerous trials have been undertaken with the commercial preparations Echinacin (fresh juice of the aerial parts) and Esberitox (a mixture of *Echinacea purpurea*, *Echinacea angustifolia*, *Baptista tinctoria* and *Thuja occidentalis*). The majority of these trials, which utilised intravenous injections and small groups of patients, were not randomised and controlled double-blind trials. The clinical conditions studied have included infections and wound-healing, polyarthritis, influenza, colds, upper respiratory tract infections, eczema, psoriasis, urogenital infections, allergies, candidiasis, gynaecological infections, chronic osteomyelitis and chronic skin ulcers.[18]

## Side-effects, Toxicity

Echinacea is stated to have produced positive patch test reactions in four patients with a previous history of plant dermatitis.[G51] Trace amounts of echinacin (polysaccharide extract) placed on the tongue are stated to produce excessive salivation and an intense burning paralytic effect on the tongue and on the mucous membranes of the lips and mouth. The roots are stated to produce a similar but milder effect.[G39]

Pyrrolizidine alkaloids with an unsaturated pyrrolizidine nucleus are reported to be hepatotoxic in both animals and humans (*see* Comfrey). The alkaloids isotussilagine and tussilagine have been documented for echinacea; they possess a saturated pyrrolizidine nucleus and are not thought to be toxic.

*In vivo* antitumour activity and *in vitro* stimulation of TNF secretion have been reported for echinacea. TNF is one of a group of polypeptide inflammatory mediators which have been collectively termed cytokines (produced by various cell types) or lymphokines (produced by lymphocytes).[G45] TNF is stated to be produced mainly by lymphocytes and macrophages. In addition to its antitumour effects, TNF is stated to be a mediator of cachexia and the manifestations of endotoxic shock. Concern has been expressed over the possible toxicity of TNF.[G45]

## Contra-indications, Warnings

None documented. Echinacea may interfere with immunosuppressive therapy.

*Pregnancy and lactation* The safety of echinacea has not been established. In view of the lack of toxicity data, excessive use of echinacea during pregnancy should be avoided.

## Pharmaceutical Comment

The chemistry of echinacea is well documented.[1–20] *E. angustifolia* and *E. pallida* are described under the same monograph heading in the BHP 1983, although it has been proposed that the two species are in fact chemically dissimilar. *E. purpurea* and *E. angustifolia* both contain amides as their major lipophilic constituents, but of differing structural types.[4,5] By contrast, the lipophilic fraction of *E. pallida* is characterised by polyacetylenes and contains only very low concentrations, if any, of amides.[4,5]

Commercial echinacea samples may contain one or more of the three *Echinacea* species mentioned above, and the reported presence of polyenes in commercial samples of *E. angustifolia* is thought to result from sample contamination with *E. pallida*.[4]

The polyene components are stated to be susceptible to auto-oxidation resulting in the formation of artefacts during storage. It has therefore been recommended that the roots should be stored full-size and that extracts should be kept in solution.[4,G2]

Documented scientific evidence from animal studies supports some of the uses for echinacea as well as the more recent interest in immunostimulant properties.[16–20] Reported pharmacological activities seem to be mainly associated with polyene and high molecular weight polysaccharide constituents. Further well-designed clinical studies using standardised preparations and larger numbers of patients are required in order to verify the efficacy of echinacea.

In view of the lack of toxicity data, excessive use of echinacea should be avoided.

## References

*See also* General References G2, G3, G5, G6, G7, G8, G9, G18, G30, G31, G32, G34, G36, G37, G39, G40, G43, G45, G48, G50, G52, G53, G56 and G64.


1 Bauer R *et al.* Alkamides from the roots of *Echinacea angustifolia*. *Phytochemistry* 1989; 28: 505–508.

2 Wagner H *et al.* Immunostimulating polysaccharides (heteroglycans) of higher plants. *Arzneimittelforschung* 1985; 35: 1069–1075.

3 Tubaro A *et al.* Anti-inflammatory activity of a polysaccharide fraction of *Echinacea angustifolia*. *J Pharm Pharmacol* 1987; 39: 567–569.

4 Protsch A, Wagner H. Structural analysis of a 4-O-methylgluconoarabinoxylan with immunostimulating activity from *Echinacea purpurea*. *Phytochemistry* 1987; 26: 1989–1993.

5 Becker H *et al.* Structure of echinoside. *Z Naturforsch* 1982; 37c: 351–353.

6 Becker H, Hsieh WC. Cichoric acid and its derivatives from Echinacea species. *Z Naturforsch* 1985; 40c: 585–587.

7 Schulte KE *et al.* Das Vorkommen von Polyacetylen-Verbindungen in *Echinacea purpurea* Mnch. und *Echinacea angustifolia* DC. *Arzneimittelforschung* 1967; 17: 825–829.

8 Bauer R *et al.* Two acetylenic compounds from *Echinacea pallida* roots. *Phytochemistry* 1987; 26: 1198–1200.

9 Bauer R *et al.* Structure and stereochemistry of new sesquiterpene esters from *Echinacea purpurea*. *Helv Chim Acta* 1985; 68: 2355–2358.

10 Bauer R *et al.* Nachweis einer Verfälschung von *Echinacea purpurea* (L.) Moench mit *Parthenium integrifolium* L. *Dtsch Apoth Ztg* 1987; 127: 1325.

11 Bauer R, Wagner H. *Echinacea. Ein Handbuch für*

*Ärzte, Apotheker und andere Naturwissenschaftler*. Stuttgart: Wissenschaftliche Verlagsgesellschaft, 1990: 182.

12 Bauer R, Wagner H. Echinacea – Der Sonnenhut – Stand der Forschung. *Z Phytother* 1988; 9: 151–159.

13 Hobbs C. In: Miovich M, ed. *The Echinacea Handbook*, Portland, Oregon: Eclectic Medical Publications, 1989: 118.

14 Hobbs C. Echinacea – a literature review. *Herbalgram* 1994; 30: 33–47.

15 Houghton PJ. Echinacea. *Pharm J* 1994; 253: 342–343.

16 Röder E *et al.* Pyrrolizidine in *Echinacea angustifolia* DC und *Echinacea purpurea* M. *Arzneimittelforschung* 1984; 124: 2316–2317.

17 Jacobson M. The structure of echinacein, the insecticidal component of American coneflower roots. *J Org Chem* 1967; 32: 1646–1647.

18 Bohlman F, Hoffmann M. Further amides from *Echinacea purpurea*. *Phytochemistry* 1983; 22: 1173–1175.

19 Bauer R *et al.* Analysis of *Echinacea pallida* and *E. angustifolia* roots. *Planta Med* 1988; 54: 426–430.

20 Bauer R, Remiger P. TLC and HPLC analysis of alkamides in *Echinacea* drugs. *Planta Med* 1989; 55: 367–371.

21 Bauer R *et al.* Immunologische *in-vivo* und *in-vitro* Untersuchungen mit *Echinacea* Extracten. *Arzneimittelforschung* 1988; 38: 276–281.

22 Vömel T. Der einfluss eines pflanzelischen Immunostimulans auf die Phagozytose von Erythozyten durch das retikulohistozytäre System der isoliert perfundierten Rattenleber. *Arzneimittelforschung* 1985; 35: 1437–1439.

23 Stimpel M *et al.* Macrophage activation and induction of macrophage cytotoxicity by purified polysaccharide fractions from the plant *Echinacea purpurea*. *Infect Immun* 1984; 46: 845–849.

24 Wagner H *et al.* Immunologically active polysaccharides of *Echinacea purpurea* cell cultures. *Phytochemistry* 1988; 27: 119–126.

25 Wacker A, Hilbig W. Virus inhibition by *Echinacea purpurea*. *Planta Med* 1978; 33: 89–102.

26 Mose J. Effect of echinacin on phagocytosis and natural killer cells. *Med Welt* 1983; 34: 1463–1467.

27 Wagner H *et al.* Immunostimulating polysaccharides (heteroglycans) of higher plants – preliminary communications. *Arzneimittelforschung* 1984; 34: 659–660.

28 Tragni E *et al.* Evidence from two classical irritation tests for an anti-inflammatory action of a natural extract, echinacea B. *Food Chem Toxic* 1985; 23: 317–319.

29 Voaden DJ, Jacobson M. Tumour inhibitors. 3. Identification and synthesis of an oncolytic hydrocarbon from American coneflower roots. *J Med Chem* 1972; 15: 619–623.

30 Westendorf J. Carito® – *in-vitro* Untersuchungen zum Nachweiss spasmolytischer und kontraktiler Einflüsse. *Therapiewoche* 1982; 32: 6291–6297.

31 Busing K. Hyaluronidasehemmung durch echinacin. *Arzneimittelforschung* 1952; 2: 467–469.