Aetheroleum Eucalypti

Definition

Aetheroleum Eucalypti is the essential oil obtained by steam distillation and rectification of the fresh leaves or terminal branchlets of *Eucalyptus globulus* Labill (Myrtaceae) or other *Eucalyptus* species rich in 1,8-cineole (*1–3*).

Synonyms

Eucalyptus cordata Miq., *E. diversifolia* Miq., *E. gigantea* Dehnh., *E. glauca* D.C., *E. globulus* St Lag., *E. pulverulenta* Link (*4*).

Selected vernacular names

Aceite de eucalipto, esencia de eucalipto, essence d'eucalyptus rectifiée, eucalipto essenza, eucalyptus oil, eucalyptus olie, Eucalyptusöl, huile essentielle d'eucalyptus, klei de eucalipt, minyak ekaliptus, oleo de eucalipto, Oleum eucalypti, tinh dâu Bach dan (*1–7*).

Geographical distribution

Indigenous to Australia, cultivated in subtropical regions of the world including Africa, South America (e.g. Argentina, Brazil and Paraguay), Asia (e.g. China, India and Indonesia), southern Europe and the United States of America (*4, 7–11*).

Description

A large tree with smooth bark, very pale or ash-grey, up to 3–20 m high. Branchlets quadrangular, glaucous. Leaves of young trees and first leaves of young shoots opposite, sessile, oval-oblong, with a cordate base, farinaceous-glaucous; older leaves dangling, spirally arranged, lanceolate-falcate, up to 30 cm long. Flowers with very short pedicels, mostly umbellate, sometimes 2–3 in a fascicle. Calyx-tube double: outer tube drops early, smooth, inner tube semi-persistent and warty. Stamens about 1.5 cm long; fruit turbinate, angular, 2.0–2.5 cm in diameter (*12, 13*).

Plant material of interest: essential oil

General appearance

A colourless or pale yellow liquid that darkens slightly on long storage (*1*, *2*).

Organoleptic properties

Odour: aromatic, camphoric; taste: pungent, camphoric, followed by a sensation of cold (*1*–*3*).

Microscopic characteristics

Not applicable.

Powdered plant material

Not applicable.

General identity tests

Thin-layer and gas chromatography (*1*–*3*).

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*).

Chemical

Refractive index: 1.458–1.470 (*1*–*3*); specific gravity: 0.906–0.925 (*2*); optical rotation: 0° to +10° (*2*); solubility in ethanol: soluble in 5 volumes of 70% ethanol (*2*, *5*). Methods to detect the presence of aldehyde and phellendrene are available (*2*).

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.

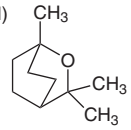
Chemical assays

Contains not less than 70% (w/w) 1,8-cineole (also known as cineol, cineole or eucalyptol) (*1*, *2*). Quantitative analysis according to the method described for 1,8-cineole (*1*–*3*).

Major chemical constituents

The major constituent is 1,8-cineole (54–95%). In addition, there are moderate amounts of α-pinene (2.6%), *p*-cymene (2.7%), aromadendrene, cuminaldehyde, globulol and pinocarveol (*11*, *13*). The structure of 1,8-cineole is presented below.

1,8-cineole (eucalyptol)



Medicinal uses

Uses supported by clinical data

None.

Uses described in pharmacopoeias and in traditional systems of medicine

Symptomatic treatment of catarrh and coughs (*17, 18*). As a component of certain dental root canal sealers; topically as a rubefacient for treatment of rheumatic complaints (*18*, *19*).

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

Treatment of cystitis, diabetes, gastritis, kidney disease (unspecified), neuralgia, laryngitis, leukorrhoea, malaria, pimples, ringworm, sinusitis, wounds, ulcers of the skin, urethritis and vaginitis (*4*, *6*).

Pharmacology

Experimental pharmacology

Antimicrobial activity

Aetheroleum Eucalypti inhibited the growth in vitro of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Enterococcus faecalis* and *Escherichia coli* (*20*–*25*), but not of *Bacillus cereus*, *Penicillium cyclopium* or *Aspergillus aegyptiacus* (*22*, *25*). Intramuscular injection of the essential oil (500 mg/kg body weight) inhibited the growth of *Mycobacterium tuberculosis* in guinea-pigs, and enhanced the efficacy of streptomycin and isoniazid (*26*).

Anti-inflammatory activity

The essential oil inhibited prostaglandin biosynthesis in vitro at a concentration of 37 µmol/l (*27*).

Respiratory tract effects

Intragastric administration of the essential oil increased respiratory tract secretions in cats (100 mg/kg body weight), guinea-pigs (50 mg/kg body weight), rabbits (100 mg/kg body weight) and rats (100 mg/kg body weight) (*28*). Administration of non-lethal doses of the essential oil by steam inhalation to urethane-treated rabbits did not enhance the output of respiratory tract fluid (*29*).

Antitussive effects

The antitussive effect of the essential oil was compared to that of codeine in guinea-pigs in which coughs were induced by mechanical stimulation. Inhalation of the essential oil (5% emulsified in normal saline) had a significant antitussive effect relative to codeine (15 mg/kg body weight) of 0.68 ($P < 0.05$). When the essential oil was administered by intraperitoneal injection (50 mg/kg body weight), the antitussive effect relative to codeine was 0.57, which was also significant ($P < 0.001$) (*30*).

Clinical pharmacology

Nasal decongestant activity

A clinical trial without controls assessed the effects of Aetheroleum Eucalypti as a nasal decongestant in 31 healthy volunteers. Inhalation of the essential oil (10 ml) over a period of 5 minutes had no effect on nasal resistance to airflow. However, the oil had a stimulant or sensitizing effect on nasal cold receptors, and the majority of subjects reported a sensation of increased airflow (*31*). A single-blind, parallel clinical trial assessed the efficacy of vaporized essential oil, camphor, menthol or steam in reducing nasal congestion in 234 patients with acute respiratory tract infections. The essential oil was significantly more effective in reducing nasal congestion only during the first hour following treatment ($P < 0.02$) (*32*). In other clinical studies of patients with acute common colds, no significant differences in nasal decongestant activity were reported between the essential oil (1.3%) in petrolatum and a petrolatum placebo (*32*).

Analgesic activity

A randomized, double-blind, placebo-controlled, crossover study assessed the efficacy of a combination product of the essential oil (eucalyptus oil) and Aetheroleum Menthae Piperitae (peppermint oil) for headache relief in 32 patients. Five different preparations were used (all in 90% ethanol, to a final weight of 100 g): 10 g peppermint oil and 5 g eucalyptus oil; 10 g peppermint oil and traces of eucalyptus oil; traces of peppermint oil and 5 g eucalyptus oil; traces of both peppermint oil and eucalyptus oil; or a placebo. The test

preparations or placebo were applied topically to large areas of the forehead and temples, and the effects on neurophysiological, psychological and experimental algesimetric parameters were measured. All test preparations improved cognitive performance, and induced muscle and mental relaxation compared to the placebo, but had no effect on sensitivity to headache (*33*).

Contraindications

Preparations of Aetheroleum Eucalypti should not be administered internally to children (*34*), or patients with inflammation of the gastrointestinal tract, gall bladder disease or impaired liver function (*4*, *17*, *34*). Aetheroleum Eucalypti should not be taken internally during pregnancy (*35*), see Precautions.

Warnings

Aetheroleum Eucalypti preparations should not be applied to the face, especially the nose, of infants or young children (*17*). Keep out of reach of children.

Precautions

General

Oily vehicles for the essential oil are unsuitable for use in nasal sprays as the vehicle inhibits ciliary movement and may cause lipid pneumonia (*19*).

Drug interactions

Although no published drug interactions were found, a number of animal studies indicate possible concern that the essential oil may induce liver enzymes involved in drug metabolism. Therefore, the effects of other drugs may be decreased following concomitant administration (*17*, *36*).

Carcinogenesis, mutagenesis, impairment of fertility

The essential oil was a weak promoter of papilloma formation by 9, 10-dimethyl-12-benzanthracene in mice. However, the development of tumours in mice after intragastric administration of 8 or 32 mg 1,8-cineole per kg body weight daily for 80 weeks was similar to that in mice treated with vehicle controls (*37*).

Pregnancy: teratogenic effects

The essential oil was not teratogenic when administered subcutaneously to pregnant mice (135 mg/kg body weight) daily on days 6–15 of gestation (*38*).

Pregnancy: non-teratogenic effects

Eucalyptol (500 mg/kg body weight, administered subcutaneously) has been reported to penetrate the placenta in rodents and reach concentrations in the

fetal blood which are sufficient to stimulate hepatic enzyme activity (*39*). Therefore, Aetheroleum Eucalypti should not be taken internally during pregnancy (*35*).

Paediatric use

See Contraindications and Warnings.

Other precautions

No information available on precautions concerning drug and laboratory test interactions or nursing mothers. Therefore, Aetheroleum Eucalypti should not be administered during lactation without medical supervision.

Adverse reactions

Topical applications of Aetheroleum Eucalypti are generally non-irritating, non-sensitizing and non-phototoxic (*40*). However, one case of systemic toxicity in a 6-year-old girl (*41*), and several cases of urticaria, contact dermatitis and skin irritation (*42*) have been reported.

Between 1981 and 1992, the clinical effects of poisoning were observed in 59% of 109 children after accidental ingestion of the essential oil (2–10 ml) (*43*, *44*). The symptoms included depression of conscious state (28% of cases), drowsiness (25% of cases) and unconsciousness (3% of cases), and were dose-dependent (*43*). Other reported symptoms included epigastric burning, nausea, vomiting, dizziness, muscular weakness, miosis, a feeling of suffocation, cyanosis, delirium and convulsions (*8*, *18*, *45*). Allergic reactions have been reported after ingestion of 20 lozenges containing the essential oil (*46*).

Between 1889 and 1922, 17 cases of fatal poisoning due to ingestion of the essential oil were reported (*36*). A dose of as little as 3.5 ml was fatal (*47*). However, these data are old and the purity of the oil used is unknown.

Dosage forms

Essential oil in solid, semisolid or liquid preparations (*1*) and galenical preparations (*17*). Store in a well-filled, tightly closed container, protected from heat and light (*1*, *2*).

Posology

(Unless otherwise indicated)

Internal use

Daily dosage: 0.3–0.6 ml essential oil or equivalent preparations (*17*). Capsules: 1 capsule of 100–200 mg, 2–5 times daily (*48*, *49*). Lozenges: 1 lozenge of 0.2–15.0 mg dissolved slowly in the mouth, every 30–60 minutes (*32*). Mouth-

wash: 20 ml of a 0.91 mg/ml solution, gargled twice daily (*32*). Inhalation: 12 drops/150 ml boiling water (*49*).

External use

Daily dosage: several drops (*17*) or 30 ml essential oil in 500 ml lukewarm water (*35*) rubbed into the skin for local application; 5–20% essential oil in liquid and semisolid preparations; 5–10% in hydroalcoholic preparations.

References

1. *Pharmacopoeia of the People's Republic of China* (English ed.). Guangzhou, Guangdong Science and Technology Press, 1997.
2. *European pharmacopoeia*, 3rd ed., Suppl. 2000. Strasbourg, Council of Europe, 1999.
3. *The Japanese pharmacopoeia*, 13th ed. (English ed.). Tokyo, Ministry of Health and Welfare, 1996.
4. Blaschek W et al., eds. *Hagers Handbuch der pharmazeutischen Praxis. Folgeband 2: Drogen A–K*, 5th ed. Berlin, Springer-Verlag, 1998.
5. *Ekstra Farmakope Indonesia*. Jakarta, Departemen Kesehatan, Republik Indonesia, 1974.
6. Farnsworth NR, ed. *NAPRALERT database*. Chicago, University of Illinois at Chicago, IL, August 8, 1998 production (an online database available directly through the University of Illinois at Chicago or through the Scientific and Technical Network [STN] of Chemical Abstracts Services).
7. Youngken HW. *Textbook of pharmacognosy*, 6th ed. Philadelphia, PA, Blakiston, 1950.
8. *African pharmacopoeia. Vol. 1*, 1st ed. Lagos, Organization of African Unity, Scientific, Technical & Research Commission, 1985.
9. Heyne K. *De nuttige planten van Indonesie*, 3rd ed. Wageningen, H. Veenman & Konen, 1950.
10. Iwu MM. *Handbook of African medicinal plants*. Boca Raton, FL, CRC Press, 1993.
11. Bisset NG. *Herbal drugs and phytopharmaceuticals*. Boca Raton, FL, CRC Press, 1994.
12. Backer CA, van den Brink B. *Flora of Java. Vol. 2*. Groningen, Netherlands, NVP Noordhof, 1965.
13. Bruneton J. *Pharmacognosy, phytochemistry, medicinal plants*. Paris, Lavoisier, 1995.
14. *Quality control methods for medicinal plant materials*. Geneva, World Health Organization, 1998.
15. *European pharmacopoeia*, 3rd ed. Strasbourg, Council of Europe, 1996.
16. *Guidelines for predicting dietary intake of pesticide residues*, 2nd rev. ed. Geneva, World Health Organization, 1997 (document WHO/FSF/FOS/97.7).
17. Blumenthal M et al., eds. *The complete German Commission E monographs*. Austin, TX, American Botanical Council, 1998.
18. Reynolds JEF, Prasad AB. *Martindale, the extra pharmacopoeia*, 30th ed. London, Pharmaceutical Press, 1996.
19. Leung AY, Foster S. *Encyclopedia of common natural ingredients used in food, drugs, and cosmetics*, 2nd ed. New York, NY, John Wiley & Sons, 1996.
20. Benouda A et al. Les propriétés antiséptiques des huiles essentielles in vitro, testées contre des germes pathogènes hospitaliers. *Fitoterapia*, 1988, 59:115–119.
21. Brantner A, Grein E. Antibacterial activity of plant extracts used externally in traditional medicine. *Journal of Ethnopharmacology*, 1994, 44:35–40.
22. El-Keltawi NEM et al. Antimicrobial activity of some Egyptian aromatic plants. *Herba Polonica*, 1980, 26:245–250.

23. Janssen AM et al. Screening for antibacterial activity of some essential oils by the agar overlay technique. *Pharmaceutisch Weekblad*, 1986, 8:289–292.
24. Ontengco DC et al. Screening for the antibacterial activity of essential oils from some Philippine plants. *Acta Manilana*, 1995, 43:19–23.
25. Ross SA et al. Antimicrobial activity of some Egyptian plants. *Fitoterapia*, 1980, 51: 201–205.
26. Kufferath F, Mundualdo GM. The activity of some preparations containing essential oils in tuberculosis. *Fitoterapia*, 1954, 25:483–485.
27. Wagner H et al. In vitro inhibition of prostaglandin biosynthesis by essential oils and phenolic compounds. *Planta Medica*, 1986, 3:184–187.
28. Boyd EM, Pearson GL. On the expectorant action of volatile oils. *American Journal of Medical Science*, 1946, 211:602–610.
29. Boyd EM, Sheppard EP. The effect of steam inhalation of volatile oils on the output and composition of respiratory tract fluid. *Journal of Pharmaceutical and Experiential Practice*, 1968, 163:250–256.
30. Misawa M , Kizawa M. Antitussive effects of several volatile oils especially of cedar leaf oil in guinea pigs. *Pharmacometrics*, 1990, 39:81–87.
31. Burrows A et al. The effects of camphor, eucalyptus and menthol vapour on nasal resistance to airflow and nasal sensation. *Acta Otolaryngology*, 1983, 96: 157–161.
32. Food and Drug Administration. Over-the-counter drugs. Final monograph for OTC nasal decongestant drug products. *Federal Register*, 1994, 41:38408–38409.
33. Göbel H et al. Essential plant oils and headache mechanisms. *Phytomedicine*, 1995, 2:93–102.
34. Eucalyptol preparation (paediatric)—suspended. *WHO Pharmaceuticals Newsletter*, 1994, 10:2.
35. Newell CA, Anderson LA, Phillipson JD. *Herbal medicines: a guide for healthcare professionals*. London, Pharmaceutical Press, 1996.
36. Corrigan D. *Eucalyptus* species. In: DeSmet PAGM et al., eds. *Adverse reactions of herbal drugs*. Berlin, Springer-Verlag, 1992:125–133.
37. Roe FCJ, Field WEH. Chronic toxicity of essential oils and certain other products of natural origin. *Food, Cosmetics and Toxicology*, 1965, 3:311–342.
38. Pages N et al. Les huiles essentielles et leurs propriétés tératogènes potentielles: exemple de l'huile essentielle d'*Eucalyptus globulus*, étude préliminaire chez la souris. *Plantes médicinales et Phytotherapie*, 1990, 24:21–26.
39. Jori A, Briatico G. Effects of eucalyptol on microsomal enzyme activity of foetal and newborn rats. *Biochemical Pharmacology*, 1973, 22:543–544.
40. Opdyke DLJ. Eucalyptus oil. *Food, Cosmetics and Toxicology*, 1975, 13:107–108.
41. Darben T et al. Topical eucalyptus oil poisoning. *Australas Journal of Dermatology*, 1998, 39:265–267.
42. Mitchell J, Rook A. *Botanical dermatology*. Vancouver, Greengrass, 1979.
43. Tibballs J. Clinical effects and management of eucalyptus oil ingestion in infants and young children. *Medical Journal of Australia*, 1995, 163:177–180.
44. Day LM et al. Eucalyptus oil poisoning among young children: mechanisms of access and potential for prevention. *Australian and New Zealand Journal of Public Health*, 1997, 21:297–301.
45. Hindle RC. Eucalyptus oil ingestion. *New Zealand Medical Journal*, 1994, 107: 185.
46. Oppenheim M. Exanthema produced by eucalyptus cough drops. *Zentralblatt für Biochemie und Biophysik*, 1912, 13:128.
47. MacPherson J. The toxicology of eucalyptus oil. *Medical Journal of Australia*, 1925, 2:108–110.

48. *ESCOP Monographs on the medicinal uses of plant drugs*. Fascicule 6. Devon, European Scientific Cooperative on Phytotherapy, 1999.
49. Van Hellemont J. In: *Fytotherapeutisch Compendium*, 2nd ed. Utrecht, Scheltema & Holkema, 1988:232.