Folium Eucalypti

Definition

Folium Eucalypti consists of the dried leaves of *Eucalyptus globulus* Labill (Myrtaceae) (*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

Alcanfor, arbre à la fièvre, Australian fever tree, bach dan xanh, Blaugummibaum, bluegum tree, calibtus, calipso, daun ekaliptus, eucalipus, eucalypto, eucalyptus, Eucalyptusblätter, feuilles d'eucalyptus, fevertree, Fieberbaum, Fieberhilbaum, gigante, gommier bleu, gommier bleu de Tasmania, gum tree, iron bark tree, kalatus, kaphur, khuynh diep, mtiulaya, nkwu-ishi, oykaliptus, Tasmanian bluegum, yukari (*1, 4–8*).

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 (*1, 4, 6, 8–10*).

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 semipersistent and warty. Stamens about 1.5 cm long. Fruit turbinate, angular, 2.0–2.5 cm in diameter (*11, 12*).

Plant material of interest: dried leaves

General appearance

Leaf lanceolate-falcate, bifacial, 8–30 cm long, 2–7 cm wide; petiole twisted, strongly wrinkled, 2–3 cm, occasionally 5 cm, in length; apex, when present, acute or acuminate; base unequal, obtuse or somewhat rounded, margin uneven, revolute; ventral and dorsal surfaces greyish-green to pale yellowish-green, coriaceous, glaucous, glabrous, glandular-punctate, with numerous small, rounded, brown dots of cork; venation pinnate-reticulate, veins of the first order running to a short distance from margin where they are anastomosed and form a vein nearly parallel with the margin (*1–3*, *8*).

Organoleptic properties

Odour: aromatic, camphoric; taste: aromatic, pungent, bitter (*1*, *3*, *8*).

Microscopic characteristics

Upper and lower epidermis composed of clear, polygonal cells with thick cutinized outer walls; both layers possess sunken stomata. Chlorenchyma differentiated into 2 palisade regions: both regions composed of 3–4 (usually 4) rows of cells which face each epidermis; in each region large, subglobular internal glands occur, lined with secretory epithelium and containing yellow oil. Parenchyma spongy, a narrow zone of loosely arranged cells between the 2 palisade regions; its cells contain rosette aggregates or monoclinic prisms of calcium oxalate crystals. Fibrovascular bundles throughout the spongy parenchyma; in midrib and petiole, interrupted arc of slightly lignified pericyclic fibres occurs just outside these bundles (*8*).

Powdered plant material

Greyish-green; fragments of chlorenchyma with numerous embedded, broken, yellow, schizogenous oil glands; calcium oxalate crystals in rosette aggregates or monoclinic prisms; fragments of epidermis with polygonal cells having very thick cuticle, numerous anomocytic stomata of more than 80 µm in diameter, fragments of sclerenchyma fibres; fragments of cork, tracheids, vessels and fibres (*1*, *3*, *8*).

General identity tests

Macroscopic and microscopic examinations, microchemical analysis and thin-layer chromatography for 1,8-cineole (*1–3*, *8*, *13*).

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

Not more than 1% fruits, and not more than 2% stems and other foreign matter (*1*–*3*).

Total ash

Not more than 6% (*2*, *3*).

Acid-insoluble ash

Not more than 0.2% (*8*).

Loss on drying

Not more than 10% (*3*).

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

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

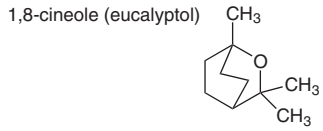
Chemical assays

Contains not less than 2% (v/w) essential oil, consisting of not less than 70% (w/w) 1,8-cineole (also known as cineol, cineole or eucalyptol) (*1*, *3*). A thin-layer chromatography method is available for qualitative determination, using 1,8-cineole as a reference standard (*3*).

Major chemical constituents

Dried leaves contain 1–3% (v/w) essential oil (fresh leaves contain 0.4–1.6%), the major constituent of which is 1,8-cineole (54–95%). In addition, there are moderate amounts of other monoterpenes, including α-pinene (2.6%),

p-cymene (2.7%), aromadendrene, cuminaldehyde, globulol and pinocarveol. Gas chromatography and gas chromatography–mass spectroscopy of the oil indicated the presence of more than 70 components, 48 of which were identified. The concentration of α-terpeneol was estimated to be 28% (*17*). The leaves are rich in tannins and ellagitannins, and also contain 2–4% triterpenes (ursolic acid derivatives), a series of phloroglucinol-sesquiterpene-coupled derivatives (macrocarpals B, C, D, E, H, I and J) and flavonoids (rutin, quercetin, quercitrin and hyperoside) (*5*, *7*, *10*, *12*, *17–19*). The structure of the major monoterpene, 1,8-cineole, is presented below.



Medicinal uses

Uses supported by clinical data

None.

Uses described in pharmacopoeias and in traditional systems of medicine

As an expectorant for symptomatic treatment of mild inflammation of the respiratory tract and bronchitis (*20*). Also for symptomatic treatment of asthma, fever and inflammation of the throat (*1*).

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

Treatment of cystitis, diabetes, gastritis, kidney disease (unspecified), laryngitis, leukorrhoea, malaria, pimples, ringworm, wounds, ulcers of the skin, urethritis and vaginitis (*5*).

Pharmacology

Experimental pharmacology

Antibacterial and antifungal activity

An ethanol–water extract of Folium Eucalypti inhibited the growth in vitro of *Staphylococcus aureus* at a concentration of 25 µg/ml (*21*). An aqueous leaf extract inhibited the growth in vitro of *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis* and *Enterococcus faecalis* (MIC 0.07–1.30 mg/ml) (*22*). A methanol extract of the leaves inhibited the growth in vitro of *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Candida albicans* (MIC 1.25–10.00 mg/ml) (*23*). A

fluidextract of the leaves inhibited the growth in vitro of *Mycobacterium tuberculosis* (MIC 6.25 mg/ml) (*24*). A methanol–water extract of the leaves inhibited the growth in vitro of *Candida albicans* (*25*).

Antiviral activity

An aqueous leaf extract inhibited the replication of influenza virus A_2 (Mannheim 57), vaccinia virus and herpes simplex virus type 2 in vitro at a concentration of 0.1% (*26*).

Antimalarial activity

Intragastric administration of a hexane leaf extract to mice (100 mg/kg body weight) did not inhibit the growth of *Plasmodium berghei* (*27*). Furthermore, administration of an aqueous (3.48 g/kg body weight) or chloroform (264 mg/kg body weight) leaf extract to chickens by gastric lavage did not inhibit the growth of *P. gallinaceum* (*28*). An ethanol–water extract of the leaves inhibited the growth in vitro of *P. falciparum* at a concentration of 75 µg/ml (*21*).

Antidiabetes activity

A hot aqueous extract of the leaves suppressed streptozocin-induced hyperglycaemia in mice when added to the diet (6.25%) and drinking-water (0.25%). The same extract did not stimulate insulin production by the pancreas (*29*). However, intragastric administration of aqueous or ethanol extracts of the leaves at a dose of 1 g/kg body weight did not suppress alloxan-induced hyperglycaemia in mice and rabbits (*30*, *31*).

Clinical pharmacology

None.

Contraindications

Preparations of Folium Eucalypti should not be administered internally to children or patients with inflammation of the gastrointestinal tract, gall bladder disease or impaired liver function (*4*, *20*).

Warnings

Folium Eucalypti preparations should not be applied to the face, especially the nose, of infants or young children (*20*). Keep out of reach of children.

Precautions

Drug interactions

Although no published drug interactions were found, a number of animal studies indicate possible concern that the leaf essential oil may induce liver

enzymes involved in drug metabolism. Therefore, the effects of other drugs may be decreased following concomitant administration (*20*, *32*).

Carcinogenesis, mutagenesis, impairment of fertility

A tincture of the leaves was not mutagenic in the *Salmonella*/microsome assay using *S. typhimurium* strains TA100 and TA98 (*33*).

Pregnancy: teratogenic effects

The leaf essential oil was not teratogenic when administered subcutaneously to pregnant mice (135 mg/kg body weight) daily on days 6–15 of gestation (*34*).

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 (*35*). Therefore, Folium Eucalypti should not be administered during pregnancy without medical supervision.

Paediatric use

See Contraindications and Warnings.

Other precautions

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

Adverse reactions

Excessive ingestion of Folium Eucalypti can cause nausea, vomiting and diarrhoea (*20*). Several cases of urticaria, contact dermatitis and skin irritation have been reported after therapeutic doses (*36*).

Dosage forms

Crude drug (*1*, *20*). Store in a tightly closed container, protected from light (*3*).

Posology

(Unless otherwise indicated)

Daily dosage: 4–6 g crude drug or equivalent preparations. Infusion: pour 150 ml of hot water over a half teaspoon of the leaves, allow them to stand for 10 minutes, then remove the leaves with a strainer (*10*, *20*). One cup (240 ml) of the freshly prepared infusion is drunk slowly three times daily. The vapour of the hot infusion is inhaled deeply (*10*).

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