Aetheroleum Rosmarini

Definition
Aetheroleum Rosmarini consists of the essential oil, obtained by steam distillation, from the flowering aerial parts of *Rosmarinus officinalis* L. (Lamiaceae) (*1*).

Synonyms
No information was found.

Selected vernacular names
Alecrim, azir, biberine, biberye, boithran, common rosemary, echter Rosmarin, encensier, garden rosemary, gusmarino, hasalban, hatsa louban, hhassâ lubân, iklil, iklil el jabal, iklil kuhi, kusdilli, mannenrou, old man, romani, romarin, romero, romero blanco, rosmariin, rosmarina, Rosmarin, rosmarini, rosmarino, rosemary, tresmarino (*2–4*).

Geographical distribution
Native to Mediterranean region of Europe, and cultivated worldwide (*4–7*).

Description
A bushy, low, much branched, perennial sub-shrub attaining a height of about 1 m. Leaves leathery with fringed margin, 1.0–2.5 cm long, aromatic, evergreen, opposite, sessile, linear and coriaceous. Old branches brown in colour. Spiciform inflorescences of pale blue or light lilac flowers spotted with purple, with the two stamens projecting far beyond the corolla (*4*, *5*, *7*).

Plant material of interest: essential oil
General appearance
Clear, mobile, colourless to pale yellow liquid (*1*).

Organoleptic properties
Odour: characteristic (*1*).

Microscopic characteristics
Not applicable.

Powdered plant material
Not applicable.

General identity tests
Physicochemical properties, thin-layer and gas chromatography (*1*).

Purity tests
Microbiological
Not applicable.

Foreign organic matter
To be established in accordance with national requirements.

Total ash
Not applicable.

Acid-insoluble ash
Not applicable.

Water-soluble extractive
Not applicable.

Loss on drying
Not applicable.

Pesticide residues
The recommended maximum limit of aldrin and dieldrin is not more than 0.05 mg/kg (*1*). For other pesticides, see the *European pharmacopoeia* (*1*) and the WHO guidelines for assessing quality of herbal medicines with reference to contaminants and residues (*8*) and pesticide residues (*9*).

Heavy metals
For maximum limits and analysis of heavy metals, consult the WHO guidelines for assessing quality of herbal medicines with reference to contaminants and residues (*8*).

Radioactive residues
Where applicable, consult the WHO guidelines for assessing quality of herbal medicines with reference to contaminants and residues (*8*).

Other purity tests

Relative density: 0.895–0.920 (*1*).
Refractive index: 1.464–1.473 (*1*).
Optical rotation: -5° to + 8° (*1*).
Acid value: not more than 1.0 (*1*).

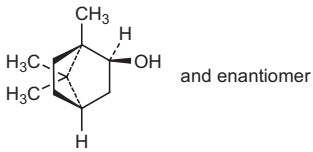
Chemical assays

Gas chromatographic analysis of Spanish type rosemary oil: α-pinene (18–26%), camphene (8–12%), β-pinene (2.0–6.0%), β-myrcene (1.5–5.0%), limonene (2.5–5.0%), 1,8-cineol (16.0–25.0%), *p*-cymene (1.0–2.2%), camphor (13.0–21.0%), bornyl acetate (0.5–2.5%), α-terpineol (1.0–3.5%), borneol (2.0–4.5%) and verbenone (0.7–2.5%) (*1*).

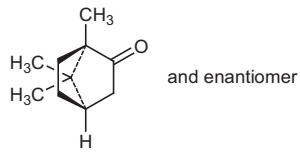
The oil of rosemary from Morocco and Tunisia contains: α-pinene (9–14%), camphene (2.5–6.0%), β-pinene (4.0–9.0%), β-myrcene (1.0–2.0%), limonene (1.5–4.0%), 1,8-cineol (38.0–55.0%), *p*-cymene (0.8–2.5%), camphor (5.0–15.0%), bornyl acetate (0.1–1.5%), α-terpineol (1.0–2.6%), borneol (1.5–5.0%) and verbenone (0.4%) (*1*).

Major chemical constituents

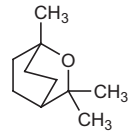
The chief constituents of rosemary oil are camphor (5–31%), 1,8-cineol (15–55%), α-pinene (9–26%), borneol (1.5–5.0%), camphene (2.5–12.0%), β-pinene (2.0–9.0%), limonene (1.5–5.0%), verbenone (2.2–11.1%), β-caryophyllene (1.8–5.1%) and myrcene (0.9–4.5%) (*1*, *10*, *11*). The structures of 1,8-cineole, borneol and camphor are presented below.



Borneol



Camphor



1,8-Cineole

Medicinal uses

Uses supported by clinical data

None.

Uses described in pharmacopoeias and well established documents

Used orally for the treatment of dyspeptic complaints, and in external applications for supportive management of rheumatic complaints and circulatory disorders (*12*, *13*). Although one pilot study has indicated that the

crude drug may enhance cognition (*13*), further data from randomized controlled clinical trials are required before any therapeutic recommendations can be made.

Uses described in traditional medicine

Used as a cholagogue, diaphoretic, digestant, diuretic, emmenagogue, laxative and a tonic (*3*, *5*, *6*). Also used in the management of headache, menstrual disorders, nervous menstrual complaints, tiredness, defective memory, sprains and bruises (*14*).

Pharmacology

Experimental pharmacology

Antihepatotoxic activity

The hepatoprotective and antimutagenic effects of the essential oil were compared to those of ethanol leaf extracts in vivo using carbon tetrachloride (CCl_4) and cyclophosphamide as the hepatotoxic and mutagenic compounds. The results of the study showed that intragastric administration of 1.5 g/kg body weight (bw) of the essential oil or the leaf extract to rats for 3 weeks protected the animals against CCl_4-induced hepatotoxicity. The results were similar to those obtained using the control compound, silymarin (*15*). The results showed amelioration of most of the serum and liver parameters studied, and were confirmed by histopathological examination of the liver tissue. The hepatoprotectant activity of essential oil was not as great as that of the leaf extract. However, intragastric pretreatment of mice for 7 days with the essential oil (1.1 mg/g bw), reduced cyclophosphamide-induced mitodepression in bone marrow cells (*15*).

Antimicrobial activity

The essential oil weakly inhibited the growth of *Acinetobacter iwoffi*, *Bacillus subtilis*, *Erwinia carotovora*, *Shigella flexneri*, *Staphylococcus aureus*, *Streptococcus pyogenes and Yersinia enterocolitica* when added undiluted or in a 1:1 dilution to the agar medium (*16*).

Antispasmodic effects

The essential oil inhibited electrically stimulated muscular contractions in isolated guinea-pig ileum, but the effect of the lowest spasmolytic dose is preceded by an initial increase in the electrically stimulated contractile response. Pinene, which had weak spasmogenic properties, was considered to be the active constituent (*17*). In guinea-pig ileum, addition of the essential oil to the bath medium inhibited acetyl choline-induced contrac-

tions, with a median inhibitory concentration (IC_{50}) of 465 nl/ml of the oil and 41 nl/ml of 1,8-cineole (*18*).

Osteoclastic effects

The essential oil, and its individual constituents, camphor, borneol, thymol, α-pinene, β-pinene and bornyl acetate, inhibited bone resorption when added to the food of rats. The monoterpenes borneol, thymol and camphor, were directly inhibitory in the osteoclast resorption pit assay. Within 30 minutes, borneol inhibited the formation of actin rings, a characteristic of resorbing osteoclasts indicating cell polarization. Both the in vitro and the in vivo effects of borneol were reversible (*19*).

Enzyme induction

Modulation of cytochrome P450 isozymes and detoxification enzymes was compared after oral administration of the dried leaves, a dried dichloromethane leaf extract or the essential oil to rats. The animals received the leaves, extracts or essential oil in their rations at a concentration of 0.5% (w/w) for 2 weeks. The effects of the treatments were evaluated in assays for cytochrome P450 isozymes 1A, 2B, 2E1, glutathione S-transferase, nicotinamide adenine dinucleotide phosphate (NAD(P)H), quinone reductase and uridine diphosphate (UDP)-glucuronosyltransferase activities and on protein levels (immunoblot analyses). The results demonstrated that the essential oil selectively induced cytochrome P450, particularly isozyme 2B. The leaf extract enhanced both cytochrome P450 and detoxification enzymes. A dichloromethane extract of the leaves acted as a monofunctional inducer, inducing glutathione S-transferase, quinone reductase and UDP-glucuronosyltransferase, in particular UDP-glucuronosyltransferase 1A6 (*20*).

Toxicology

The embryotoxic effects of d-camphor were investigated in rats and rabbits after intragastric administration for the treatment of hypotonic circulatory dysregulations. No evidence of teratogenicity was observed when d-camphor was administered orally to pregnant rats during the fetal period of organogenesis, at doses up to 1 g/kg bw per day, and to pregnant rabbits at doses up to 681 mg/kg bw per day. For rats, the no-observed-effect level for the fetal organism was above 1 mg/kg bw, and for rabbits, above 681 mg/kg bw. In rat dams a dose-dependent reduction in food intake and salivation was noted at doses of 464 mg/kg bw and higher. The high dose of 1 mg/kg bw per day resulted in pronounced signs of toxicity such as clonic convulsion, pilo-erection, reduced motility and body weight gain. In rabbit dams, intragastric administration of a high dose (681 mg/kg

bw per day) resulted in reduced body weight gain and food consumption. No increased incidence of variations, retardations or malformations was observed in any of the offspring at any of the doses, not even at the highest dose tested (rat: 1000 mg/kg bw per day; rabbit: 681 mg/kg bw per day). The daily maximum dose of camphor for human therapeutic use is approximately 1.43 mg/kg bw. Hence, under the present test conditions the therapeutic ratio is above 450 for the end-point of embryotoxicity, reflecting a wide margin of safety (*21*). Since d-camphor is only one of the chemical constituents of the essential oil, the relevance of these data to the toxicology of the essential oil needs to be investigated.

Clinical pharmacology

A clinical study to assess the olfactory impact of the essential oils of lavender (*Lavandula angustifolia*) and rosemary (*Rosmarinus officinalis*) on cognitive performance and mood in healthy volunteers was performed (*13*). One hundred and forty-four participants were randomly assigned to one of three independent groups. Each of the subjects was asked to take the Cognitive Drug Research (CDR) computerized cognitive assessment battery in a cubicle containing one of the two odours or no odour (control). Visual analogue mood questionnaires were completed before exposure to the odour and after completion of the test battery. The participants were misled as to the genuine aim of the study until the completion of testing to prevent expectancy effects from possibly influencing the data. The outcome variables from the nine tasks that constitute the CDR core battery feed into six factors that represent different aspects of cognitive functioning. Analysis of performance revealed that lavender produced a significant decrement in performance of working memory, and impaired reaction times for both memory and attention-based tasks compared to the performance of the controls. In contrast, rosemary produced a significant enhancement of performance for overall quality of memory and secondary memory factors, but also impaired speed of memory compared to controls. With regard to mood, comparisons of the change in ratings from baseline to post-test revealed that following the completion of the cognitive assessment battery, both the control group and the group exposed to lavender were significantly less alert than the subjects exposed to rosemary; however, subjects in the control group were significantly less content than subjects who received the rosemary and lavender treatments (*13*).

Frontal electroencephalogram asymmetry shifting from baseline was examined in adults and infants exposed to lavender and rosemary oils by re-analysing previously published data from two studies. The results from 39 adults revealed significant electroencephalogram shifting in the lavender-treated group, with greater relative left frontal electroencephalogram

activation (associated with greater approach behaviour and less depressed affect). The participants in the two groups exposed to the two aromas were further grouped by those with greater baseline, relative to left frontal electroencephalogram activation versus those with a greater baseline relative to right frontal activation. Collapsing across aroma groups, those with greater baseline, relative to right frontal activation, shifted left during exposure to the aroma. Those with greater baseline relative to left frontal activation did not change. In the group subjected to the rosemary aroma, those with greater baseline relative to right frontal electroencephalogram activation shifted left during exposure to the aroma, while those with greater baselines relative to left frontal electroencephalogram activation shifted right. The second study, involving 27 full-term newborns revealed no significant shifts in asymmetry in response to either aroma. However, when the aroma groups were collapsed, the right frontal electroencephalogram group exhibited significant shifting relative to left frontal electroencephalogram activation. This finding was similar to the findings in adults, suggesting that both lavender and rosemary may induce left frontal electroencephalogram shifting in adults and infants who show greater baselines relative to right frontal electroencephalogram activation (*22*).

The effects of lavender and rosemary oils on electroencephalogram activity, alertness and mood were assessed in 40 adults given 3 minutes of aromatherapy. Participants were also given simple mathematical computations to do before and after the therapy. The lavender-treated group showed increased beta power, suggesting increased drowsiness; they also had less depressed mood and reported feeling more relaxed and performed the mathematical computations faster and more accurately following aromatherapy. The rosemary-treated group, on the other hand, showed decreased frontal alpha and beta power, suggesting increased alertness. They also had lower anxiety scores, reported feeling more relaxed and alert and they were only faster, not more accurate, at completing the mathematical computations after the aromatherapy session (*23*).

Adverse reactions

Following oral use gastrointestinal complaints and hypersensitivity reactions may occur rarely. Inhalation can occasionally cause irritation and very rarely laryngospasm (*24*).

External use may worsen bronchospasm. Rarely hypersensitivity reactions of the skin may occur. Photoaggravated allergic contact dermatitis (*25*, *26*) and cheilitis (*27*) have been reported.

Contraindications

Aetheroleum Rosmarini is contraindicated in cases of hypersensitivity or allergy to the plant material. It should not be used in patients suffering from bronchial asthma or bronchitis or on damaged skin, such as in cases of burns, lesions or skin rashes.

Warnings

Due to its irritant properties, the essential oil should not be used on the face or mucosa, and contact with the eyes should be avoided. After application of the essential oil, wash hands to avoid accidental contact with the face and eyes. As with all essential oils, do not exceed the recommended dose.

If there is persistence or worsening of rheumatic symptoms, e.g. in cases of redness, swelling or over-heating of joints, patients should seek advice from a health care practitioner.

Precautions

Drug interactions

Although drug interactions have not been reported, cineole, the main constituent of the oil is known to induce liver metabolic enzymes in animals. Therefore, the oil may interact with other prescription medications.

Carcinogenesis, mutagenesis, impairment of fertility

The crude drug is anti-mutagenic in rats treated with cyclophosphamide (*15*).

Pregnancy: teratogenic effects

See Toxicology.

Pregnancy: non-teratogenic effects

See Toxicology.

Nursing mothers

Due to the lack of safety data, the use of the crude drug during breastfeeding is not recommended.

Paediatric use

Due to the lack of safety data, administration of the crude drug to children under the age of 12 years is not recommended.

Other precautions

No information was found.

Dosage forms

Essential oil for oral and external use (*24*) and aromatherapy (*13*, *22*). Store in a cool place in an airtight container, protected from light (*28*).

Posology

(Unless otherwise indicated)
Daily dosage for oral administration: 1 ml of essential oil (*24*).
External use: 6–10% essential oil in semi-solid and liquid preparations (*24*).

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