
Folium Melissaе

Definition

Folium Melissaе consists of the dried leaves of *Melissa officinalis* L. (Lamiaceae, Labiatae) (1, 2).

Synonyms

Calamintha officinalis Moench. (3), *Melissa graveolens* Host, *Thymus melissa* E.H.L. Krause (4). Lamiaceae is also referred to as Labiatae.

Selected vernacular names

Alahana, appiastro, badarendjabouya, badranjbuyeh, balm, balm mint, bee balm, blue balm, cedronella, citromfülevél, citronelle, citrounado, citrounela, citrounelo, common balm, cure-all, dropsy plant, erva-cidreira-miuda-de-folha, folia citronellae, franjmeshk, garden-balm, Herzkraut, hhashyshat ennahhl, honey plant, lemon balm, limiera, limouna, limounneta, mallisa, melissa, Melisse, Melissenblätter, Melissenkraut, melisso, melliss, ponciarada, pouncinado, sidrunmeliss, sweet balm, toronjil, toronjil-cidrado, touroudjan, turungan, Zitronenkraut, Zitronenmelisse (4–8).

Geographical distribution

Indigenous to western Asia and the eastern Mediterranean region, and is cultivated in central, eastern and western Europe, and the United States of America (4, 7, 8).

Description

An odorous perennial herb, 0.3–0.9 m high, usually with several stems, lemon-scented on bruising. Stems obtusely quadrangular, furrowed pubescent. Leaves 2–9 cm long and 1–5 cm wide, ovate to obovate-oval, base cuneate truncate or cordate at the base, densely pilose on both surfaces, petiole 0.2–3.5 cm long. Corolla white or pinkish; infundibuliform tube 8–12 mm long; stamens inserted deep in the tube; bracteoles oval-oblong, about 1.5 cm long, pubescent; calyx 5–9 mm long, pubescent outside, pubescent inside (with very short hairs), densely pilose in the middle (4, 8, 9).

Plant material of interest: dried leaves

General appearance

Leaves oval, cordate, up to about 8 cm long and 5 cm wide, with more or less long petioles; lamina thin, lower surface has conspicuous, raised, reticulate venation; margins roughly dentate or crenate; upper surface bright green, lower surface lighter in colour (1).

Organoleptic properties

Odour: aromatic, lemon-like; taste: aromatic, lemon-like (1).

Microscopic characteristics

Dorsoventral epidermal cells with sinuous walls and diacytic stomata on lower surface only; very short, conical, unicellular covering trichomes with a finely striated cuticle occur abundantly, especially over the veins on the lower surface; also uniseriate, multicellular (2–5 cells) covering trichomes, wide at the base and narrowing rapidly toward the tip, with slightly thickened, warty walls; secretory trichomes also very abundant, some small with unicellular stalk and unicellular or bicellular head, others large, of laminaceous type, with unicellular stalk and spherical to ovoid head composed of 8 cells (5).

Powdered plant material

Greenish. Fragments of the leaf epidermis with sinuous walls; short, conical, unicellular covering trichomes with a finely striated cuticle; uniseriate, multicellular covering trichomes; 8-celled secretory trichomes of laminaceous type, others with unicellular to tricellular stalks and unicellular or, more rarely, bicellular heads; diacytic stomata, on the lower surface only (1).

General identity tests

Macroscopic and microscopic examinations, and thin-layer chromatography for rosmarinic, chlorogenic and caffeic acids (1).

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 (10).

Foreign organic matter

Not more than 2% total foreign matter and not more than 10% of stem fragments with a diameter greater than 1 mm (1).

Total ash

Not more than 12% (1).

Loss on drying

Not more than 10% (1).

Pesticide residues

The recommended maximum limit of aldrin and dieldrin is not more than 0.05 mg/kg (11). For other pesticides, see the *European pharmacopoeia* (11), and the WHO guidelines on quality control methods for medicinal plants (10) and pesticide residues (12).

Heavy metals

For maximum limits and analysis of heavy metals, consult the WHO guidelines on quality control methods for medicinal plants (10).

Radioactive residues

Where applicable, consult the WHO guidelines on quality control methods for medicinal plants (10) for the analysis of radioactive isotopes.

Other purity tests

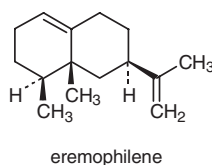
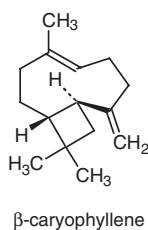
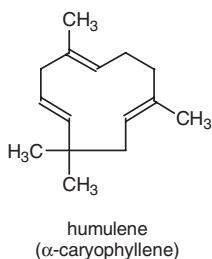
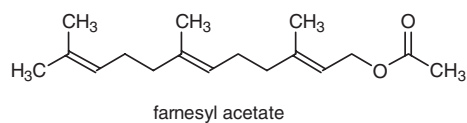
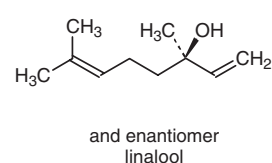
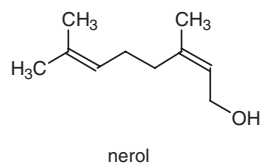
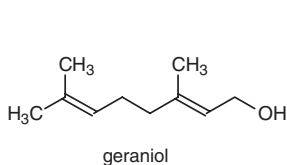
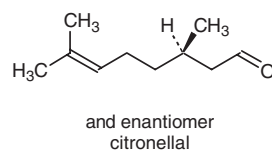
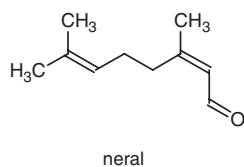
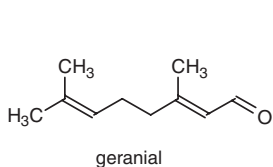
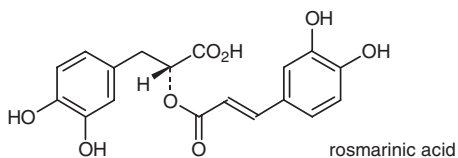
Chemical, acid-insoluble ash, sulfated ash, water-soluble extractive and alcohol-soluble extractive tests to be established in accordance with national requirements.

Chemical assays

Contains not less than 4.0% total hydroxycinnamic acids calculated as rosmarinic acid (1). Quantitative analysis is performed by spectrophotometry at 505 nm (1). Essential oil analysis is carried out according to the method described in the *European pharmacopoeia* (1).

Major chemical constituents

The major characteristic constituents are the hydroxycinnamic acids (rosmarinic [up to 6%], *p*-coumaric, caffeic and chlorogenic acids), and an essential oil (0.02–0.37%) composed of more than 40% monoterpenes and more than 35% sesquiterpenes. The most significant terpenoid components are citral (a mixture of the isomers neral and geranial), citronellal, geraniol, nerol, linalool, farnesyl acetate, humulene (α -caryophyllene), β -caryophyllene and eremophilene. Other constituents include flavonoids, tannins and acidic triterpenes (e.g. ursolic and oleanolic acids) (4, 6, 7, 13–15). The structures of the major compound, rosmarinic acid, and terpenoid components are presented below.



Medicinal uses

Uses supported by clinical data

Externally, for symptomatic treatment of herpes labialis (16–18).

Uses described in pharmacopoeias and in traditional systems of medicine

Orally as a carminative for gastrointestinal disorders, and as a sedative for treatment of nervous disturbances of sleep (5, 15).

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

Treatment of amenorrhoea, asthma, bee stings, coughs, dizziness, dysmenorrhoea, migraine headaches, tachycardia, toothache, tracheobronchitis and urinary incontinence (6, 19).

Pharmacology

Experimental pharmacology

Antiviral activity

Aqueous extracts of Folium Melissae inhibited the replication in vitro of herpes simplex virus type 2, influenza virus A₂ (Mannheim 57) and vaccinia virus at a concentration of 10% (20). A dried aqueous extract of the leaves inhibited the replication of herpes simplex viruses in vitro at a concentration of 200 µg/ml (18). A condensed tannin isolated from an aqueous extract of the leaves inhibited haemagglutination induced by Newcastle disease virus or mumps virus; protected eggs and chick cell cultures from infection by Newcastle disease virus; and prevented haemagglutination by Newcastle disease, mumps and parainfluenza viruses 1, 2 and 3, but not by influenza viruses A and B (21). A tannin-free polyphenol fraction of an aqueous extract of the leaves was active against herpes simplex and vaccinia viruses in egg and cell culture systems (22). Aqueous extracts of the leaves have also been reported to have activity against Semliki Forest virus, influenza viruses and myxoviruses in vitro (23, 24).

Antispasmodic activity

An ethanol extract of the leaves inhibited histamine- and barium-induced contractions of guinea-pig ileum in vitro (200 µg/ml), while an aqueous extract was inactive (25). A 30% ethanol extract did not inhibit acetylcholine- and histamine-induced contractions in guinea-pig ileum in vitro at concentrations up to 10 µl/ml (26). The essential oil inhibited contractions in guinea-pig ileum, rat duodenum and vas deferens, and rabbit jejunum and aorta in vitro (27, 28). The essential oil also exhibited smooth muscle relaxant activity in guinea-pig tracheal muscle (ED₅₀ 22 µg/ml) and in an electrically stimulated ileum myenteric plexus/longitudinal muscle preparation (ED₅₀ 7.8 µg/ml) (29).

Behavioural effects

Inhalation of the essential oil had a weak tranquillizing effect in mice (30).

Clinical pharmacology

An open multicentre study of 115 patients with herpes simplex infections of the skin and transitional mucosa demonstrated that external applications of a 1% lyophilized aqueous extract of Folium Melissae in a cream base reduced

the healing time of herpetic lesions from 10–14 days to 6–8 days (18). Treatment with the cream also prolonged the recidivation-free intervals, as compared with other topical virustatic preparations containing idoxuridine and tromantidine hydrochloride (16, 18). A subsequent randomized, double-blind, placebo-controlled study of 116 patients with herpes simplex infections of the skin and transitional mucosa demonstrated a significant reduction in the size of herpetic lesions within 5 days in patients treated with the same cream ($P = 0.01$), as compared with placebo treatment (17, 18).

Contraindications

External use: none. Internal use: see Precautions.

Warnings

No information available.

Precautions

Carcinogenesis, mutagenesis, impairment of fertility

A tincture of *Folium Melissa* was not mutagenic in vitro (31) and alcohol extracts had antimutagenic activity in vitro (32).

Pregnancy: teratogenic effects

Internal use: no information available. Therefore, *Folium Melissa* should not be administered internally during pregnancy without medical supervision.

Pregnancy: non-teratogenic effects

Internal use: no information available. Therefore, *Folium Melissa* should not be administered internally during pregnancy without medical supervision.

Nursing mothers

Internal use: no information available. Therefore, *Folium Melissa* should not be administered internally during lactation without medical supervision.

Paediatric use

Internal use: no information available. Therefore, *Folium Melissa* should not be administered internally to children without medical supervision.

Other precautions

No information available on general precautions or precautions concerning drug interactions; or drug and laboratory test interactions; pregnancy.

Adverse reactions

No information available.

Dosage forms

Comminuted crude drug; powder, tea bags, dried and fluidextracts for infusions and other galenical preparations (7, 14, 15). Store in a tightly closed container, protected from light (1). Do not store in plastic containers (7).

Posology

(Unless otherwise indicated)

Daily dosage for oral administration (for gastrointestinal disorders and as a sedative for nervous disturbances of sleep).

Infusion: 1.5–4.5 g crude drug per cup several times daily as needed (15); 45% alcohol extract (1:1): 2–4 ml three times daily (5); tincture (1:5 in 45% alcohol): 2–6 ml three times daily (14).

Daily dosage for topical application (for herpes labialis).

Cream containing 1% of a lyophilized aqueous extract applied 2–4 times daily from the appearance of prodromal signs to a few days after the healing of the lesions, for a maximum of 14 days (14, 18).

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