Flos Chamomillae

Definition

Flos Chamomillae consists of the dried flowering heads of *Chamomilla recutita* (L.) Rauschert (Asteraceae) (1–4).

Synonyms

Matricaria chamomilla L., M. recutita L., M. suaveolens L. (3).

In most formularies and reference books, *Matricaria chamomilla* L. is regarded as the correct species name. However, according to the International Rules of Botanical Nomenclature, *Chamomilla recutita* (L.) Rauschert is the legitimate name for this species (5). Asteraceae are also known as Compositae.

Selected vernacular names

Baboonig, babuna, babunah camomile, babunj, bunga kamil, camamilla, camomile, chamomile, camomilla, chamomille allemande, campomilla, chamomille commune, camomille sauvage, fleurs de petite camomille, flos chamomillae, german chamomile, hungarian chamomile, Kamille, Kamillen, kamitsure, kamiture, manzanilla, manzanilla chiquita, manzanilla comun, manzanilla dulce, matricaire, matricaria flowers, pin heads, sweet false chamomille, sweet feverfew, wild chamomile (3, 6-9).

Description

Herbaceous annual; 10-30 cm in height, with erect, branching stems and alternate, tripinnately divided leaves below and bipinnately divided leaves above, both types having almost filiform lobes; the capitulum (to 1.5 cm in diameter) comprises 12-20 white ligulate florets surrounding a conical hollow receptacle on which numerous yellow tubular (disk) florets are inserted; the inflorescence is surrounded by a flattened imbricated involucre; fruit small, smooth, yellow-ish (*3*, *7*, *10*).

Plant material of interest: flower heads General appearance

Flos Chamomillae consists of conical flower heads, each bearing a few white ligulate florets and numerous yellowish orange to pale yellow tubular or disk florets on conical, narrow hollow receptacles with a short peduncle; disk florets perfect and without a pappus; ray florets pistillate, white, 3-toothed and 4-veined; involucre hemispherical, composed of 20–30 imbricate, oblanceolate and pubescent scales; peduncles weak brown to dusky greenish yellow, longitudinally furrowed, more or less twisted and up to 2.5 cm long; achenes more or less obovoid and faintly 3- to 5-ribbed; pappus none, or slightly membranous crown (7, 11).

Organoleptic properties

Odour, pleasant, aromatic; taste, aromatic and slightly bitter (1-3).

Microscopic characteristics

Receptacle and bracteoles with schizogenous secretory ducts; vascular bundles with phloem fibres; spiral, annular and reticulate but pitted vessels; lignified cells at the bases of the ovaries absent; nearly all parts of florets bear composite-type glandular hairs with short, biseriate stalk and enlarged head, formed of several tiers, each of two cells; ovary with longitudinal bands of small mucilage cells; stigma with elongated papillae at the apex; pollen grains, spherical or triangular, with numerous short spines (3).

Powdered plant material

Powdered Flos Chamomillae is greenish yellow to yellowish brown; spiny pollen grains numerous, $18-25\,\mu\text{m}$ in diameter; fragments of yellow or white corolla, with polygonal, small epidermal cells having straight or slightly wavy walls, sometimes papillosed, and sometimes bearing glandular hairs of composite type; fragments of the fibrous layer of anther; fragments from ovary, with glandular hairs and rows of small mucilage cells; green fragments of parenchyma of involucre; stigma with papillae; cells of the achenes with sclariform perforations in walls; fragments of fibrovascular bundles with spiral, annular and reticulate vessels and sclerenchyma fibres; fragments of involucral bracts with epidermis having elliptical stomata up to $30\,\mu\text{m}$ in length, also vessels and fibres; occasional fibre from the stems; minute cluster crystals of calcium oxalate, up to $10\,\mu\text{m}$ in diameter; fragments of lignified parenchyma of the filaments and occasional fragments of vessels (*3*, *7*, *10*).

Geographical distribution

The plant is indigenous to northern Europe and grows wild in central European countries; it is especially abundant in eastern Europe. Also found in western Asia, the Mediterranean region of northern Africa, and the United States of America. It is cultivated in many countries (3, 7-13).

General identity tests

The drug is identified by its macroscopic and microscopic characteristics, and by thin-layer chromatography (1-3).

Purity tests

Microbiology

The test for *Salmonella* spp. in Flos Chamomillae products should be negative. The maximum acceptable limits of other microorganisms are as follows (1, 14, 15). For preparation of decoction: aerobic bacteria—not more than 10^{7} /g; fungi—not more than 10^{5} /g; *Escherichia coli*—not more than 10^{2} /g. Preparations for internal use: aerobic bacteria—not more than 10^{5} /g or ml; fungi—not more than 10^{4} /g or ml; enterobacteria and certain Gram-negative bacteria—not more than 10^{3} /g or ml; *Escherichia coli*—0/g or ml. Preparations for external use: aerobic bacteria—not more than 10^{2} /g or ml; fungi—not more than 10^{2} /g or ml; enterobacteria and certain Gram-negative bacteria—not more than 10^{2} /g or ml; fungi—not more than 10^{2} /g or ml; enterobacteria and certain Gram-negative bacteria—not more than 10^{2} /g or ml; enterobacteria and certain Gram-negative bacteria—not more than 10^{2} /g or ml; enterobacteria and certain Gram-negative bacteria—not more than 10^{2} /g or ml; fungi—not more than 10^{2} /g or ml; enterobacteria and certain Gram-negative bacteria—not more than 10^{2} /g or ml; enterobacteria and certain Gram-negative bacteria—not more than 10^{2} /g or ml; fungi—not more than 10^{2} /g or ml; enterobacteria and certain Gram-negative bacteria—not more than 10^{2} /g or ml; fungi—not more than 10^{2} /g or ml; enterobacteria and certain Gram-negative bacteria—not more than 10^{2} /g or ml; fungi—not more than 10^{2} /g or ml; fungi—not more than 10^{2} /g or ml; enterobacteria and certain Gram-negative bacteria—not more than 10^{2} /g or ml; fungi—not more than 10^{2} /g or ml; f

Foreign organic matter

Not more than 10% stems and not more than 2% foreign organic matter (3). No flowering heads of *Anthemis cotula* L. or *A. nobilis* L. (7).

Total ash

Not more than 13% (2).

Acid-insoluble ash

Not more than 4% (11).

Moisture

Not more than 12% (12).

Pesticide residues

To be established in accordance with national requirements. Normally, the maximum residue limit of aldrin and dieldrin for Flos Chamomillae is not more than 0.05 mg/kg (1). For other pesticides, see WHO guidelines on quality control methods for medicinal plants (14) and guidelines for predicting dietary intake of pesticide residues (16).

Heavy metals

Recommended lead and cadmium levels are no more than 10 and 0.3 mg/kg, respectively, in the final dosage form of the plant material (14).

Radioactive residues

For analysis of strontium-90, iodine-131, caesium-134, caesium-137, and plutonium-239, see WHO guidelines on quality control methods for medicinal plants (*14*).

Other tests

Chemical, dilute ethanol-soluble extractive, and water-soluble extractive tests to be established in accordance with national requirements.

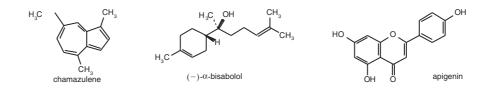
Chemical assays

Contains not less than 0.4% v/w of essential oil (1–3). Total volatile oil content is determined by pharmacopoeial methods (1–3).

Thin-layer (1, 2) and gas–liquid (17) chromatography for volatile oil constituents, and high-performance liquid chromatography for flavonoids (18, 19).

Major chemical constituents

Flos Chamomillae contains an essential oil (0.4–1.5%), which has an intense blue colour owing to its chamazulene content (1–15%). Other major constituents include α -bisabolol and related sesquiterpenes (up to 50% of the oil). Apigenin and related flavonoid glycosides constitute up to 8% (dry weight) of the drug (10, 18).



Dosage forms

Dried flower-heads, liquid extract (1:1 in 45% alcohol), tinctures and other galenicals (11). Store in well-closed containers, protected from light (1–3).

Medicinal uses

Uses supported by clinical data

Internal use

Symptomatic treatment of digestive ailments such as dyspepsia, epigastric bloating, impaired digestion, and flatulence (3, 7, 8, 10, 11, 20, 21). Infusions of camomile flowers have been used in the treatment of restlessness and in mild cases of insomnia due to nervous disorders (21, 22).

External use

Inflammation and irritations of the skin and mucosa (skin cracks, bruises, frostbite, and insect bites) (10, 23), including irritations and infections of the mouth and gums, and haemorrhoids (10, 11, 20, 21, 23).

Inhalation

Symptomatic relief of irritations of the respiratory tract due to the common cold (24).

Uses described in pharmacopoeias and in traditional systems of medicine

Adjuvant in the treatment of minor inflammatory conditions of the gastrointestinal tract (24).

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

As an antibacterial and antiviral agent, an emetic, and an emmenagogue. It is also used to relieve eye strain, and to treat urinary infections and diarrhoea (13).

Pharmacology

Experimental pharmacology

Both camomile extract and (-)- α -bisabolol demonstrated antipeptic activity *in* vitro (25, 26). A hydroalcoholic extract of camomile inhibited the growth of Staphylococcus aureus, Streptococcus mutans, group B Streptococcus, and Streptococcus salivarius, and it had a bactericidal effect in vitro on Bacillus megatherium and Leptospira icterohaemorrhagiae (27). In vitro, the volatile oil of camomile also inhibited Staphylococcus aureus and Bacillus subtilis (28). In vitro, camomile extracts inhibited both cyclooxygenase and lipoxygenase (29), and thus the production of prostaglandins and leukotrienes, known inducers of inflammation. Both bisabolol and bisabolol oxide have been shown to inhibit 5-lipoxygenase, but bisabolol was the more active of the two compounds (30). Numerous in vivo studies have demonstrated the anti-inflammatory effects of the drug. The antiinflammatory effects of camomile extract, the essential oil, and the isolated constituents have been evaluated in yeast-induced fever in rats and against ultraviolet radiation-induced erythema in guinea-pig models (31). The principal anti-inflammatory and antispasmodic constituents of camomile appear to be the terpene compounds matricin, chamazulene, (-)- α -bisabololoxides A and B, and $(-)-\alpha$ -bisabolol (32–39). While matricin and $(-)-\alpha$ -bisabolol have been isolated from the plant, chamazulene is actually an artefact formed during the heating of the flowers when an infusion or the essential oil is prepared (10). The anti-inflammatory effects of these compounds in various animal models, such as inhibition of carrageenin-induced rat paw oedema, have been demonstrated (30), although their activity was somewhat less than that of salicylamide (39). In the mouse model for croton oil-induced dermatitis, topical application of either the total camomile extract, or the flavonoid fraction only, was very effective in reducing inflammation (34). Apigenin and luteolin were more active than indometacin and phenylbutazone (34). Activity decreased in the following order: apigenin > luteolin > quercetin > myricetin > apigenin-7-glucoside > rutin (34). The spasmolytic activity of camomile has been attributed to apigenin, apigenin-7-O-glucoside (10, 36) and (-)- α -bisabolol, which have activity similar to papaverine (10, 35).

Intradermal application of liposomal apigenin-7-glucoside inhibited, in a dose-dependent manner, skin inflammations induced in rats by xanthine oxidase and cumene hydroperoxide (*38*).

Intraperitoneal administration to mice of a lyophilized infusion of camomile decreased basal motility, exploratory and motor activities, and potentiated hexobarbital-induced sleep (40). These results demonstrated that in mice camomile depresses the central nervous system (40).

Clinical pharmacology

A double-blind study of the therapeutic effects of a camomile extract on reepithelialization and drying of wound weeping after dermabrasion demonstrated a statistically significant decrease in the wound size and drying tendency (41).

In clinical trials, topical application of a camomile extract in a cream base was found to be superior to hydrocortisone 0.25% for reducing skin inflammation (42). In an international multicentre trial camomile cream was compared with hydrocortisone 0.25%, fluocortin butyl ester 0.75% and bufexamac 5% in the treatment of eczema of the extremities (42). The camomile cream was shown to be as effective as hydrocortisone and superior to the other two treatments, but no statistical analysis was performed. Camomile preparations have also been found to be beneficial in the treatment of radiation mucositis owing to head and neck radiation and systemic chemotherapy (43).

Contraindications

Camomile is contraindicated in patients with a known sensitivity or allergy to plants of the Asteraceae (Compositae) such as ragweed, asters, and chrysanthemums (21).

Warnings

No information available.

Precautions

Carcinogenesis, mutagenesis, impairment of fertility

No mutagenic effects were found in *Salmonella typhimurium* strains TA 97a, TA 98, TA 100 and TA 104, with or without metabolic activation (44).

Pregnancy: teratogenic effects

No adverse effects reported in vivo (45).

Other precautions

No information available concerning general precautions, drug interactions, drug and laboratory test interactions, non-teratogenic effects on pregnancy, nursing mothers, or paediatric use.

Adverse reactions

The presence of lactones in Flos Chamomillae-based preparations may cause allergic reactions in sensitive individuals and there have been reports of contact dermatitis due to camomile preparations (46-48). It should be noted that very few cases of allergy were specifically attributed to German camomile (49). A few cases of anaphylactic reactions to the ingestion of Flos Chamomillae have also been reported (50-52).

Posology

Internal use

Adult dose of flower head: average daily dose 2–8g, 3 times a day (7, 8, 11); of fluid extract 1:1 in 45% ethanol: dose 1–4ml, 3 times a day (6, 11). Child dose of flower head: 2g, 3 times daily; of fluid extract (ethanol 45–60%): single dose 0.6-2 ml (11). Should not be used by children under 3 years old.

External use

For compresses, rinses or gargles: 3-10% (30-100g/l) infusion or 1% fluid extract or 5% tincture (11). For baths: 5g/l of water or 0.8g/l of alcoholic extract. For semisolid preparations: hydroalcoholic extracts corresponding to 3-10% (30–100 g/kg) of the drug. For vapour inhalation: 6g of the drug or 0.8g of alcoholic extract per litre of hot water (11).

References

- 1. European pharmacopoeia, 3rd ed. Strasbourg, Council of Europe, 1997.
- 2. Pharmacopée française. Paris, Adrapharm, 1996.
- 3. African pharmacopoeia, 1st ed. Lagos, Organization of African Unity, Scientific, Technical & Research Commission, 1985.
- 4. Estra farmakope Indonesia. Jakarta, Cetakan Kedua, Hal 152, Departemen Kesehatan, Republik Indonesia, 1974.
- 5. Rauschert S. Nomenklatorische Probleme in der Gattung Matricaria L. Folia geobotanica phytotaxonomica, 1990, 9:249–260.
- 6. Farnsworth NR, ed. NAPRALERT database. Chicago, University of Illinois at Chicago, IL, August 8, 1995 production (an on-line database available directly through the University of Illinois at Chicago or through the Scientific and Technical Network (STN) of Chemical Abstracts Services).
- Youngken HW. Textbook of pharmacognosy, 6th ed. Philadelphia, Blakiston, 1950.
 The Indian Pharmaceutical Codex. Vol. I. Indigenous drugs. New Delhi, Council of Scientific & Industrial Research, 1953.
- 9. Leung A, Foster S. Encyclopedia of common natural ingredients used in food, drugs, and cosmetics, 2nd ed. New York, John Wiley, 1996.

- 10. Bruneton J. Pharmacognosy, phytochemistry, medicinal plants. Paris, Lavoisier, 1995.
- 11. British herbal pharmacopoeia. London, British Herbal Medicine Association, 1990.
- 12. Polish pharmacopoeia. Warsaw, 1965.
- 13. Tyler VE, Brady LR, Robbers JE, eds. *Pharmacognosy*, 9th ed. Philadelphia, Lea & Febiger, 1988.
- 14. Quality control methods for medicinal plant materials. Geneva, World Health Organization, 1998.
- 15. Deutsches Arzneibuch 1996. Vol. 2. Methoden der Biologie. Stuttgart, Deutscher Apotheker Verlag, 1996.
- 16. Guidelines for predicting dietary intake of pesticide residues, 2nd rev. ed. Geneva, World Health Organization, 1997 (unpublished document WHO/FSF/FOS/97.7; available from Food Safety, WHO, 1211 Geneva 27, Switzerland).
- 17. Carle R, Fleischhauer I, Fehr D. Qualitätsbeurteilung von Kamillenölen. Deutsche Apotheker Zeitung, 1987, 127:2451–2457.
- Dölle B, Carle R, Müller W. Flavonoidbestimmung in Kamillenextraktpräparaten. Deutsche Apotheker Zeitung, 1985, 125(Suppl. I):14–19.
- 19. Redaelli C, Formentini L, Santaniello E. Reversed-phase high-performance liquid chromatography analysis of apigenin and its glucosides in flowers of *Matricaria chamomilla* and chamomille extracts. *Planta medica*, 1981, 42:288–292.
- Carle R, Isaac O. Die Kamille-Wirkung and Wirksamkeit. Zeitschrift für Phytotherapie, 1987, 8:67–77.
- Carle R, Gomaa K. Chamomile: a pharmacological and clinical profile. *Drugs of today*, 1992, 28:559–565.
- 22. Gould L, Reddy CVR, Gomprecht RF. Cardiac effect of chamomile tea. *Journal of clinical pharmacology*, 1973, 13:475-479.
- Hormann HP, Korting HC. Evidence for the efficacy and safety of topical herbal drugs in dermatology. Part 1. Anti-inflammatory agents. *Phytomedicine*, 1994, 1:161– 171.
- 24. Weiß RF. Kamille-"Heilpflanze 1987". Kneipp-Blätter, 1987, 1:4-8.
- 25. Thiemer VK, Stadler R, Isaac O. Biochemische Untersuchungen von Kamilleninhaltsstoffen. Arzneimittel-Forschung, 1972, 22:1086–1087.
- Isaac O, Thiemer K. Biochemische Untersuchungen von Kamilleninhaltsstoffen. Arzneimittel-Forschung, 1975, 25:1086–1087.
- 27. Cinco M et al. A microbiological survey on the activity of a hydroalcoholic extract of chamomile. *International journal of crude drug research*, 1983, 21:145–151.
- 28. Aggag ME, Yousef RT. Study of antimicrobial activity of chamomile oil. *Planta medica*, 1972, 22:140–144.
- 29. Wagner H, Wierer M, Bauer R. *In vitro* inhibition of prostaglandin biosynthesis by essential oils and phenolic compounds. *Planta medica*, 1986:184–187.
- 30. Ammon HPT, Kaul R. Pharmakologie der Kamille und ihrer Inhaltsstoffe. *Deutsche Apotheker Zeitung*, 1992, 132(Suppl. 27):3–26.
- 31. Jakovlev V et al. Pharmacological investigations with compounds of chamomile. II. New investigations on the antiphlogistic effects of (-)- α -bisabolol and bisabolol oxides. *Planta medica*, 1979, 35:125–240.
- Jakovlev V, Isaac O, Flaskamp E. Pharmakologische Untersuchungen von Kamilleninhaltsstoffen. VI. Untersuchungen zur antiphlogistischen Wirkung von Chamazulen und Matricin. *Planta medica*, 1983, 49:67–73.
- 33. Tubaro A et al. Evaluation of anti-inflammatory activity of chamomile extract after topical application. *Planta medica*, 1984, 51:359.
- 34. Della Loggia R. Lokale antiphlogistische Wirkung der Kamillen-Flavone. Deutsche Apotheker Zeitung, 1985, 125(Suppl. 1):9–11.
- 35. Della Loggia R et al. Evaluation of the anti-inflammatory activity of chamomile preparations. *Planta medica*, 1990, 56:657–658.

- Lang W, Schwandt K. Untersuchung über die glykosidischen Bestandteile der Kamille. Deutsche Apotheker Zeitung, 1957, 97:149–151.
- Mann C, Staba J. The chemistry, pharmacology, and commercial formulations of chamomile. In: Craker LE, Simon JE, eds., *Herbs, spices, and medicinal plants: recent advances in botany, horticulture and pharmacology*, Vol. I. Phoenix, AZ, Oryx Press, 1986:233-280.
- Fuchs J, Milbradt R. Skin anti-inflammatory activity of apigenin-7-glucoside in rats. *Arzneimittel-Forschung*, 1993, 43:370–372.
- 39. Albring M et al. The measuring of the anti-inflammatory effect of a compound on the skin of volunteers. *Methods and findings in experimental and clinical pharmacology*, 1983, 5:75–77.
- 40. Della Loggia R et al. Depressive effects of *Chamomilla recutita* (L.) Rausch. tubular flowers, on central nervous system in mice. *Pharmacological research communications*, 1982, 14:153–162.
- Glowania HJ, Raulin C, Svoboda M. The effect of chamomile on wound healing a controlled clinical-experimental double-blind study. *Zeitschrift f
 ür Hautkrankheiten*, 1986, 62:1262–1271.
- Aertgeerts P et al. Vergleichende Prüfung von Kamillosan® Creme gegenüber steroidalen (0.25% Hydrocortison, 0.75% Fluocortinbutylester) und nichtsteroidalen (5% Bufexamac) Externa in der Erhaltungstherapie von Ekzemerkrankungen. Zeitschrift für Hautkrankheiten, 1985, 60:270–277.
- Carl W, Emrich LS. Management of oral mucositis during local radiation and systemic chemotherapy: a study of 98 patients. *Journal of prosthetic dentistry*, 1991, 66:361–369.
- 44. Rivera IG et al. Genotoxicity assessment through the Ames test of medicinal plants commonly used in Brazil. *Environmental toxicology and water quality*, 1994, 9:87–93.
- 45. Leslie GB, Salmon G. Repeated dose toxicity studies and reproductive studies on nine Bio-Strath herbal remedies. *Swiss medicine*, 1979, 1:1–3.
- Dstychova E, Zahejsky J. Contact hypersensitivity to camomile. Ceskoslovenska dermatologie, 1992, 67:14–18.
- 47. Subiza J et al. Allergic conjunctivitis to chamomile tea. Annals of allergy, 1990, 65:127–132.
- Paulsen E, Andersen KE, Hausen BM. Compositae dermatitis in a Danish dermatology department in one year. *Contact dermatitis*, 1993, 29:6–10.
- Hausen BM, Busker E, Carle R. Über das Sensibilisierungsvermögen von Compositenarten. VII. Experimentelle Untersuchungen mit Auszügen und Inhaltsstoffen von *Chamomilla recutita* (L.) Rauschert und *Anthemis cotula* L. *Planta medica*, 1984:229–234.
- 50. Benner MH, Lee HJ. Anaphylactic reaction to chamomile tea. *Journal of allergy and clinical immunology*, 1973, 52:307–308.
- 51. Casterline CL. Allergy to chamomile tea. *Journal of the American Medical Association*, 1980, 244:330–331.
- 52. Subiza J et al. Anaphylactic reaction after the ingestion of chamomile tea: a study of cross-reactivity with other composite pollens. *Journal of allergy and clinical immunology*, 1989, 84:353–358.