# Chamomile, German

## Species (Family)

*Matricaria recutita* L. (Asteraceae/Compositae)

## Synonym(s)

*Chamomilla recutita* (L.) Rauschert, Hungarian Chamomile, *Matricaria chamomilla* L., Matricaria Flowers, Sweet False Chamomile, Wild Chamomile

## Part(s) Used

Flowerhead

## Pharmacopoeial and Other Monographs

BHC 1992[G6]
BHP 1996[G9]
BP 2001[G15]
Complete German Commission E[G3]
ESCOP 1999[G52]
Martindale 32nd edition[G43]
Mills and Bone[G50]
PDR for Herbal Medicines 2nd edition[G36]
Ph Eur 2002[G28]
USP24/NF19[G61]
WHO volume 1 1999[G63]

## Legal Category (Licensed Products)

GSL[G37]

## Constituents[G2,G6,G22,G38,G41,G48,G52,G64]

*Coumarins* Umbelliferone and its methyl ether, heniarin.

*Flavonoids* Apigenin, apigetrin, apiin, luteolin, quercetin, quercimeritrin and rutin.

*Volatile oils* 0.24–1.9%. Pharmacopoeial standard not less than 4 mg/kg blue oil.[G15,G28] Main components are (−)-α-bisabolol (up to 50%)[1] and chamazulene (1–15%).[2] Others include (−)-α-bisabolol oxide A and B, (−)-α-bisabolone oxide A, spiroethers (e.g. *cis*- and *trans*-en-yn-dicycloether), sesquiterpenes (e.g. anthecotulid), cadinene, farnesene, furfural, spanthulenol and proazulenes (e.g. matricarin and matricin).

Chamazulene is formed from matricin during steam distillation of the oil. It varies in yield depending on the origin and age of the flowers.[2]

*Other constituents* Amino acids, anthemic acid (bitter), choline, polysaccharide, plant and fatty acids, tannin and triterpene hydrocarbons (e.g. triacontane).

## Food Use

German chamomile is listed by the Council of Europe as a natural source of food flavouring (category N2). This category indicates that chamomile can be added to foodstuffs in small quantities, with a possible limitation of an active principle (as yet unspecified) in the final product.[G16] German chamomile is commonly used in herbal teas. In the USA, German chamomile is listed as GRAS (Generally Recognised As Safe).[G41]

## Herbal Use[G2,G4,G6,G7,G8,G43,G52,G64]

German chamomile is stated to possess carminative, antispasmodic, mild sedative, anti-inflammatory, antiseptic and anticatarrhal properties. It has been used for flatulent nervous dyspepsia, travel sickness, nasal catarrh, nervous diarrhoea, restlessness and specifically for gastrointestinal disturbance with associated nervous irritability in children. It has been used topically for haemorrhoids, mastitis and leg ulcers. German Commission E approved use for gastrointestinal spasms and inflammatory diseases of the gastrointestinal tract and externally for skin and mucous membrane inflammation and bacterial skin diseases including oral cavity and gums. It is also approved for inflammations and irritations of the respiratory tract (by inhalation) and ano-genital inflammation (baths and irrigation).[G3]

## Dosage

*Dried flowerheads* 2–8 g or by infusion three times daily.[G7]

*Liquid extract* 1–4 mL (1 : 1 in 45% alcohol) three times daily.[G7]

## Pharmacological Actions

### *In vitro* and animal studies

A wide range of pharmacological activities have been documented for German chamomile, including antibacterial, anti-inflammatory, antispasmodic, anti-ulcer, antiviral and hypouraemic activities.

*Anti-inflammatory and anti-allergic activity* Anti-allergic and anti-inflammatory activities[2,3] are well documented for German chamomile. The azulene components of the volatile oil are thought to contribute by inhibiting histamine release and they have been reported to prevent allergic seizures in guinea-pigs.[2] Aqueous alcoholic extracts inhibited 5-lipoxygenase and cyclooxygenase activity, and oxidation of arachidonic acid, and a supercritical carbon dioxide extract had $IC_{50}$ values of 6–25 μg/mL for these three activities.[G52] The active compounds identified included apigenin, chamazulene, *cis*-en-yn spiroether and (−)-α-bisabolol.[G52] Matricin, the precursor to chamazulene, is reported to be a more effective anti-inflammatory agent than chamazulene.[2,4] Anti-inflammatory activity has also been documented for the sesquiterpene bisabolol compounds, with greatest activity reported for (−)-α-bisabolol,[2,5] and for *cis*-spiroether.[2] Anti-inflammatory activity (rat paw carrageenan test) has also been documented for a *cis*-spiroether against dextran induced oedema; no activity was observed against oedema induced by serotonin, histamine or bradykinin.[6] In addition, flavonoids are known to possess anti-inflammatory activity.

*Sedative activity* Apigenin competitively inhibited binding of flunitrazepam to the central benzodiazepine receptor, but lacked activity at other receptors, including muscarinic, $\alpha_1$-adrenoreceptor and $GABA_A$.[G52] High-performance liquid chromatography (HPLC) fractions of a methanol extract displaced flunitrazepam from its receptors in rat cerebellum membranes and muscimol from GABA receptors in rat cortical membranes, due to the presence of GABA in the fractions. Prolongation of hexobarbital-induced sleeping time and reduction in activity of mice have been documented.[G52]

*Anti-ulcerogenic activity* Anti-ulcerogenic activity in rats has been reported for (−)-α-bisabolol; the development of ulcers induced by indomethacin, stress or ethanol was inhibited.[2,7]

*Antimicrobial and antiviral activities* German chamomile oil has been reported to have antifungal activity and antibacterial activity against Gram-positive bacteria.[G52] The coumarin herniarin has antibacterial and antifungal activities in the presence of UV light. Antibacterial activity has been documented for the coumarin constituents.[2] An ethanolic extract of the entire plant has been reported to inhibit the growth of poliovirus and herpesvirus.[8]

*Antispasmodic activity* Antispasmodic activity on the isolated guinea-pig ileum has been documented for the flavonoid and bisabolol constituents.[2,9] Greatest activity was exhibited by the flavonoids, especially apigenin which was found to be more than three times as potent as papaverine.[2] (−)-α-Bisabolol activity was found to be comparable to that of papaverine, while the total volatile oil was considerably less active.[2] Smooth muscle relaxant properties have also been documented for a *cis*-spiroether.[2,6,10]

Enhancement of uterine tone in the guinea-pig and rabbit has been reported for an aqueous extract at a concentration of 1–2 mg extract/$cm^3$.[11]

*Other activities* High molecular weight polysaccharides with immunostimulating activity have been isolated from German chamomile.[12] The oil has been reported to increase bile secretion and concentration of cholesterol in the bile, following the administration of 0.1 mL/kg by mouth to cats and dogs.[13] A dose of 0.2 mL/kg was stated to exhibit hypotensive, and cardiac and respiratory depressant properties.[13]

The ability of the volatile oil to regenerate liver tissue in partially hepatectomised rats has been attributed to the azulene constituents.[2]

The volatile oil has been documented to reduce the serum concentration of urea in rabbits with experimentally induced uraemic conditions.[14]

### Clinical studies

German chamomile extracts have been reported to exhibit anti-inflammatory, antipeptic and antispasmodic activities on the human stomach and duodenum.[2]

*Anti-inflammatory and wound-healing effects* Clinical studies investigating the anti-inflammatory effects and wound-healing properties of German chamomile preparations have been reviewed.[G52] A summary of this information is given below.

A cream containing German chamomile extract was reported to have effects equivalent to 0.25% hydrocortisone, and superior effects to 0.1% diflucortolone and 5% bufexamax in inflammatory dermatoses, as assessed in 161 patients. Studies involving healthy volunteers who received German

chamomile preparations have reported that German chamomile ointment was superior to 0.1% hydrocortisone acetate in dermatitis, and German chamomile cream (20 mg/g) reduced visual sores and redness of skin in an adhesive-tape stripping test. A randomised, double-blind trial involving 25 participants indicated that a cream containing an aqueous alcoholic extract of German chamomile was more effective than hydrocortisone against UVB-induced erythema.

In an open study involving 98 patients with cancer, an extract preparation (containing 50 mg α-bisabolol and 150–300 mg apigenin-7-glucoside/100 g) used three times daily was reported to reduce oral mucositis caused either by irradiation or chemotherapy. However, a double-blind, placebo-controlled trial involving 164 patients showed that a mouthwash containing German chamomile did not decrease 5-fluorouracil-induced stomatitis.

German chamomile has been reported to be an effective treatment for mucosal infections. Diluted extracts administered as a mouthwash 5 or 6 times daily provided cooling and astringent effects.[2]

A cream containing German chamomile has produced additional anti-inflammatory, slight anaesthetic, cooling and deodorant effects in patients with cutaneous leg infections, when used in conjunction with existing treatment.[2]

The healing effects of German chamomile ointment and dexapanthenol 5% cream administered for six days were reported to have comparable effects in a study involving 147 female patients who underwent episiotomy during childbirth. A standardised extract (50 mg α-bisabolol and 3 mg chamazulene/100 g) significantly decreased weeping wound area and drying of wound in 14 patients following removal of tattoos. An ointment preparation improved haemorrhage, itching, burning and oozing due to haemorrhoids in a study involving 120 patients.

*Sedative effects* Sedative effects have been documented for German chamomile. Oral administration of a German chamomile extract was reported to induce a deep sleep in 10 of 12 patients undergoing cardiac catheterisation.[2]

## Side-effects, Toxicity

Reports of allergic reactions to chamomile are common, although in the majority of cases the plant species is not specified.[15] Two reports of anaphylactic reactions to chamomile (species unspecified) have been documented[16,17] and in both cases the individuals concerned had an existing hypersensitivity to ragweed (member of Asteraceae/Compositae). The symptoms they experienced included abdominal cramps, thickness of the tongue and a tight sensation in the throat,[17] angioedema of the lips and eyes, diffuse pruritus, a full sensation of the ears, generalised urticaria, upper airway obstruction, and pharyngeal oedema.[16] Both patients made a full recovery following medical treatment. Patients with an existing hypersensitivity to German chamomile have demonstrated cross-sensitivities to other members of the family Asteraceae/Compositae[18,G51], and also to celery (family Umbelliferae).[G51]

Allergic skin reactions have been documented following external contact with German chamomile.[2,19,G51] Consumption of chamomile tea may exacerbate existing allergic conditions and the use of a chamomile enema has been documented to cause asthma and urticaria.[G51]

The allergenic properties documented for chamomile have been attributed to anthecotulid, a sesquiterpene lactone present in low concentrations,[15] and to matricarin, a proazulene which has produced positive patch tests in patients with an existing sesquiterpene lactone hypersensitivity.[G51]

Sesquiterpene lactones have been implicated in the allergenic activity of many plants, especially those belonging to the Asteraceae/Compositae family (*see* Feverfew). The prerequisite for allergenic activity is thought to be an exocyclic α-methylene group.[20]

The flowerheads contain anthemic acid, which is reported to act as an emetic in large doses.[G22]

The acute toxicity of chamomile oil (German and Roman) is reported to be low.[21] Oral and dermal $LD_{50}$ values in rabbits have been documented as greater than 5 g/kg,[21] and the application of undiluted oil to the hairless backs of mice, to rabbit skin, and to human skin was not found to produce any observable irritation.[21] An $LD_{50}$ value (mouse, by mouth) for German chamomile oil has been documented as 2.5 mL/kg.[13] The acute oral toxicity of (−)-α-bisabolol in mice and rats is reported to be low at approximately 15 mL/kg.[22] The subacute oral toxicity of (−)-α-bisabolol has been estimated to be between 1.0 and 2.0 mL/kg in rats and dogs.[22] An $LD_{50}$ value (mouse, intraperitoneal injection) for *cis*-spiroether has been stated as 670 mg/kg.[6]

## Contra-indications, Warnings

In view of the documented allergic reactions and cross-sensitivities, German chamomile should be avoided by individuals with a known hypersensitivity to any members of the Asteraceae/Compositae family. In addition, German chamomile may precipitate an allergic reaction or exacerbate existing symptoms in susceptible individuals (e.g. asthmatics).

Excessive doses may interfere with existing anticoagulant therapy, because of the coumarin constituents.

The use of chamomile preparations for teething babies is not recommended.

*Pregnancy and lactation* German chamomile is reputed to affect the menstrual cycle[G30] and extracts are reported to be uterotonic.[2,11] Teratogenicity studies in rats, rabbits and dogs have been documented for (−)-α-bisabolol, with the oral toxic dose stated as 1–3 mL/kg.[22] A dose of 3 mL/kg was found to increase the number of fetuses reabsorbed and reduce the body weight of live offspring.[22] (−)-α-Bisabolol administered orally (250 and 500 mg/kg) to pregnant rats has been reported to have no effect on the fetus.[1] In view of the documented information, the excessive use of chamomile during pregnancy and lactation should be avoided.

## Pharmaceutical Comment

The chemistry of German chamomile, especially of the volatile oil component, is well documented and is similar to that of Roman chamomile.[24] Pharmacological activity is associated with the flavonoid and volatile oil fractions. A wide range of pharmacological actions have been documented (e.g. anti-inflammatory and antispasmodic activities) and many of these support the reputed herbal uses[23,24]. A small number of studies in patients and healthy volunteers have reported anti-inflammatory, wound healing and sedative effects. Toxicity studies to date have indicated chamomile to be of low toxicity, although allergic reactions are documented.

## References

*See also* General References G2, G3, G5, G6, G9, G11, G15, G16, G18, G19, G22, G28, G30, G31, G32, G36, G37, G38, G41, G43, G48, G50, G51, G52, G56, G63 and G64.


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24 Berry M. The chamomiles. *Pharm J* 1995; 254: 191–193.

# Chamomile, Roman

## Species (Family)

*Chamaemelum nobile* (L.) All. (Asteraceae/Compositae)

## Synonym(s)

*Anthemis nobilis* L.

## Part(s) Used

Flowerhead

## Pharmacopoeial and Other Monographs

BHC 1992[G6]
BHP 1996[G9]
BP 2001[G15]
Martindale 32nd edition[G43]
PDR for Herbal Medicines 2nd edition (English Chamomile)[G36]
Ph Eur 2002[G28]
USP24/NF19[G61]

## Legal Category (Licensed Products)

GSL[G37]

## Constituents[G2,G6,G22,G41,G48,G64]

*Coumarins* Scopoletin-7-glucoside.

*Flavonoids* Apigenin, luteolin, constituents in, quercetin and their glycosides (e.g. apiin, luteolin-7-glucoside, and rutin).

*Volatile oils* 0.4–1.75%. Angelic and tiglic acid esters (85%);[1] others include 1,8-cineole, *l-trans*-pinocarveol, *l-trans*-pinocarvone, chamazulene, farnesol, nerolidol; germacranolide-type sesquiterpene lactones (0.6%),[2] including nobilin, 3-epinobilin, 1,10-epoxynobilin, 3-dehydronobilin; various alcohols including amyl and isobutyl alcohols, anthemol.[1–4] Chamazulene is formed from a natural precursor during steam distillation of the oil, and varies in yield depending on the origin and the age of flowers.[1]

*Other constituents* Anthemic acid (bitter), phenolic and fatty acids, phytosterol, choline and inositol.

## Food Use

Roman chamomile is listed by the Council of Europe as a natural source of food flavouring (category N2). This category indicates that Roman chamomile can be added to foodstuffs in small quantities, with a possible limitation of an active principle (as yet unspecified) in the final product.[G16] Chamomile is commonly used as an ingredient of herbal teas. In the USA, Roman chamomile is listed as GRAS (Generally Recognised As Safe).[G41]

## Herbal Use

Roman chamomile is stated to possess carminative, anti-emetic, antispasmodic, and sedative properties. It has been used for dyspepsia, nausea and vomiting, anorexia, vomiting of pregnancy, dysmenorrhoea, and specifically for flatulent dyspepsia associated with mental stress.[G2,G6,G7,G8,G64]

## Dosage

*Dried flowerheads* 1–4 g or by infusion three times daily.[G7]

*Liquid extract* 1–4 mL (1 : 1 in 70% alcohol) three times daily.[G7]

## Pharmacological Actions

German and Roman chamomile possess similar pharmacological activities (*see* Chamomile, German for a fuller description of documented pharmacological actions).

### *In vitro* and animal studies

Few studies have been documented specifically for Roman chamomile. The azulene compounds are reported to possess anti-allergic and anti-inflammatory properties; their mechanism of action is thought to involve inhibition of histamine release (*see* Chamomile, German). The volatile oil has been documented as having anti-inflammatory activity (carrageenan rat paw oedema test), and antidiuretic and sedative effects following intraperitoneal administration of doses up to 350 mg/kg body weight to rats.[5]

The azulenes have been reported to stimulate liver regeneration following oral, but not subcutaneous, administration.

The sesquiterpenoids nobilin, 1,10-epoxynobilin and 3-dehydronobilin have demonstrated *in vitro* antitumour activity against human cells.[1] The concentration of hydroxyisonobilin required for cytotoxic activity is reported to be low enough to warrant further investigations ($ED_{50}$ 0.56 µg/mL versus HeLa; $ED_{50}$ 1.23 µg/mL versus KB; arbitrary acceptable test level 4 µg/mL).

## Side-effects, Toxicity

Instances of allergic and anaphylactic reactions to chamomile have been documented (*see* Chamomile, German) The allergenic principles in chamomile are thought to be the sesquiterpene lactones.[1] Roman chamomile yields nobilin, a sesquiterpene lactone that is reported to be potentially allergenic.[1] However, Roman chamomile oil has also been reported to be non-irritant and non-sensitising to human skin.[2] Animal studies have indicated the oil to be either mildly or non-irritant, and to lack any phototoxic effects.[2]

Large doses of Roman chamomile are stated to act as an emetic[G44] and this has been attributed to the anthemic acid content.[6]

The acute toxicity of Roman chamomile in animals is reported to be relatively low.[1] Acute $LD_{50}$ values in rabbits (dermal) and rats (by mouth) have been stated to exceed 5 g/kg.[2]

## Contra-indications, Warnings

In view of the documented allergic reactions and cross-sensitivities (*see* Chamomile, German), Roman chamomile should be avoided by individuals with a known hypersensitivity to any members of the Asteraceae/Compositae family. In addition, Roman chamomile may precipitate an allergic reaction or exacerbate existing symptoms in susceptible individuals (e.g. asthmatics). Excessive doses may interfere with anticoagulant therapy because of the coumarin constituents.

The use of chamomile preparations in teething babies is not recommended.

*Pregnancy and lactation* Roman chamomile is reputed to be an abortifacient and to affect the menstrual cycle.[G30] In view of this and the potential for allergic reactions, the excessive use of chamomile during pregnancy and lactation should be avoided.

## Pharmaceutical Comment

The chemistry of Roman chamomile, particularly of the volatile oil, is well documented and is similar to that of German chamomile.[7] Limited pharmacological data are available for Roman chamomile, although many actions have been reported for German chamomile. In view of the similar chemical compositions, many of the activities described for German chamomile are thought to be applicable to Roman chamomile and thus support the traditional herbal uses[8]. Roman chamomile is stated to be of low toxicity, although allergic reactions (mainly contact dermatitis) have been reported.[G51]

## References

*See also* General References G2, G6, G9, G15, G16, G18, G22, G25, G29, G30, G31, G32, G36, G37, G41, G43, G48, G51, G56, G61 and G64.


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