Monograph

Matricaria chamomilla (German chamomile)

Description

Chamomile is a widely recognized herb in Western culture. Its medicinal usage dates back to antiquity where such notables as Hippocrates, Galen, and Asclepius made written reference to it. A common ingredient today in herbal teas because of its calming, carminative, and spasmolytic properties, it is also a popular ingredient in topical health and beauty products for its soothing and anti-inflammatory effects on skin. Chamomile has a sweet, grassy, and lightly fruity aroma. Its flowers are daisy-like, with yellow centers (approximately 1-1.5 cm in diameter) and white petals (between 12-20 in number). It is from the plant's fresh and dried flower heads that infusions, liquid extracts, and essential oils are made.

Two species of chamomile are generally used in traditional herbalism, *Matricaria chamomilla* (*Chamomilla recutita*; German chamomile; Hungarian chamomile) and *Chamaemelum nobile* (Roman chamomile). Both annual herbs belong to the Asteraceae/Compositae family and are similar in physical appearance, chemical properties, and general applications. German chamomile, however, is the more familiar and more commonly used of the two.

Active Constituents

German chamomile flowers contain 0.24- to 2.0-percent volatile oil that is blue in color. The two key constituents, (-)-alpha-bisabolol and chamazulene, account for 50-65 percent of total volatile oil content. Other components of the oil include (-)-alpha-bisabolol oxide A and B, (-)-alpha-bisabolone oxide A, spiroethers (cis- and trans- en-yn-dicycloether), sesquiterpenes (anthecotulid), cadinene, farnesene, furfural, spathulenol, and proazulene (matricarin and matricin). Chamazulene is formed from matricin during steam distillation of the oil. Yield varies depending on the origin and age of the flowers. European Pharmacopoeia recommends chamomile contain no less than 4 mL/kg of blue essential oil.[1]

Chamomile also contains up to eight-percent flavone glycosides (apigenin 7-glycoside and its 6'-acetylated derivative) and flavonols (luteolin glucosides, quercetin glycosides, and isohamnetin); up to 10-percent mucilage polysaccharides; up to 0.3-percent choline; and approximately 0.1-percent coumarins (umbelliferone and its methyl ether, herniarin). The tannin level in chamomile is less than one percent.

Mechanisms of Action

Several pharmacological actions have been documented for German chamomile, based primarily on *in vitro* and animal studies. Such actions include antibacterial, antifungal, anti-inflammatory, antispasmodic, anti-ulcer, antiviral, and sedative effects.

The constituents of chamomile thought to have antimicrobial properties include alpha-bisabolol, luteolin, quercetin, and apigenin. Herniarin may also have antibacterial and antifungal properties in the presence of ultraviolet light. Preliminary *in vitro* studies on the antimicrobial activity of chamomile have yielded promising results. Chamomile oil, at a concentration of 25 mg/mL, demonstrates antibacterial activity against such gram-positive bacteria as *Bacillus subtilis*, *Staphylococcus aureus*, *Streptococcus mutans*, and *Streptococcus salivarius*, as well as some fungicidal activity against *Candida albicans*.[2-4] Whole plant chamomile extract at 10 mg/mL demonstrates a similar effect, completely inhibiting growth of group B Streptococcus *in vitro*.[3] In addition, chamomile extract blocks aggregation of *Helicobacter pylori* and various strains of *Escherichia coli*.[3,5] Chamomile extract has also been shown to inhibit the growth of poliovirus and herpes virus. German chamomile esters and lactones demonstrate activity against *Mycobacterium tuberculosis* and *Mycobacterium avium*. Chamazulene, alpha-bisabolol, flavonoids, and umbelliferone display antifungal properties against *Trichophyton mentagrophytes* and *Trichophyton rubrum*.[6]

The high alpha-bisabolol content in chamomile oil is credited for providing the majority of antibacterial, antifungal, anti-inflammatory, and anti-ulcer activity, although the precise mechanism of action remains unclear.[7-9]

In vitro, chamomile extract inhibits both cyclooxygenase and lipoxygenase, and consequently prostaglandins and leukotrienes.[10] Other anti-inflammatory effects are thought to occur via the influence of azulenes (chamazulene, prochamazulene, and guaiazulene) on the pituitary and adrenals, increasing cortisone release and reducing histamine release.[2]

Chamomile extracts exhibit antispasmodic properties. Apigenin, alpha-bisabolol, and the cis-spiroethers appear to provide the most significant antispasmodic effects. When tested on spasms of isolated guinea pig ileum induced by barium chloride, 10 mg of apigenin provided the antispasmodic activity roughly equivalent to 1 mg of papaverine (an opioid antispasmodic).[11] Similar results were observed with alpha-bisabolol and the cis-spiroethers.[11-14] Other flavonoids and the small amount of coumarins contribute to smooth muscle relaxation, but to a lesser degree.

In vitro studies demonstrate alpha-bisabolol inhibits gastric ulcer formation induced by indomethacin, ethanol, or stress.[7] Oral administration of chamomile oil to rats at doses ranging from 0.8-80 mg/kg bisabolol demonstrate significant protective effect against gastric toxicity of 200 mg/kg acetylsalicylic acid.[15]

Regarding sedative activity, one study using intraperitoneal administration of chamomile extract in mice concluded that apigenin functions as a ligand for benzodiazepine receptors, resulting in anxiolytic and mild sedative effects, but no muscle relaxant or anticonvulsant effects.[16] In contrast to diazepam, apigenin does not cause memory impairment. A lyophilized infusion of chamomile, also administered intraperitoneally in mice, elicited a depressive effect on the central nervous system.[17]

Research is exploring the antiproliferative and apoptotic effects of chamomile extract in various human cancer cell lines. One preliminary study observed *in vitro* exposure to chamomile results in differential apoptosis in cancer cells but not in normal cells at similar doses; apigenin and apigenin glycosides appear to be the key components responsible for these effects.[18]

Clinical Indications

Although chamomile is a well-known and widely used herb in Western culture, few well designed, randomized, double-blind, placebo-controlled studies are available to fully assess its therapeutic benefit.

Sleep Enhancement

In an open case study to examine the cardiac effects of two cups of chamomile tea on patients undergoing cardiac catheterization, the authors observed that 10 of 12 patients in the study achieved deep sleep within 10 minutes of drinking the tea.[19] The patients had a small but significant increase in mean brachial artery pressure. No other significant hemodynamic changes were observed.

Diarrhea

In a prospective, randomized, multicenter, double-blind, parallel group trial, 79 children (ages six months to five years) with acute, noncomplicated diarrhea received either a commercial preparation of apple pectin and chamomile extract or placebo for three days,

in addition to a typical rehydration and re-alimentation diet. At the end of three days, significantly more children in the pectin/chamomile group (85%) experienced diarrhea alleviation compared to the placebo group (58%) ($p<0.05$). The children on the pectin/chamomile combination experienced a significant 5.2-hour shorter duration of symptoms compared to the placebo group.[20]

Colic

A double-blind study observed the efficacy of an herbal decoction consisting of German chamomile, vervain, licorice, fennel, and balm mint on 68 healthy infants with colic. For seven days the infants (ages 2-8 weeks) received 150 mL of the herbal preparation or placebo with each colic episode, but no more than three times daily. After seven days, 57 percent of the infants receiving the herbal preparation experienced colic relief compared to 26 percent in the placebo group ($p<0.01$).[21]

Wound Healing

A double-blind trial examined the therapeutic efficacy of a topical chamomile extract on 14 patients with weeping dermabrasions from tattoo applications. Those using chamomile noted a statistically significant decrease in the weeping wound area and increased drying compared to the placebo group.[22]

In a double-blind, randomized, placebo-controlled study, 48 women receiving radiation therapy for breast cancer were treated topically with either chamomile cream or placebo (almond oil) to protect the radiation-treated area. While there were no significant differences between the two groups in objective scores of skin irritation, the patients preferred the chamomile-containing cream to the placebo for its rapid absorption and stainlessness.[23]

Mucositis

Mucositis, characterized by inflammation and ulceration of the gastrointestinal tract (including the mouth), is a dose-limiting consequence of some radiation and chemotherapy treatments. If severe, the patient is unable to eat solid food (grade 3) or even liquids (grade 4). A case series examined the effect of 15 drops of Kamillosan Liquidum, a German chamomile mouthwash preparation, in 100 mL of water taken three times daily, for radiation and/or chemotherapy-induced mucositis. Cancer patients (n=98) were divided into two groups. One group of 66 patients (20 undergoing radiation therapy, 46 undergoing chemotherapy) participated in prophylactic oral care with the mouthwash. The remaining 32 patients underwent chemotherapy and were treated therapeutically after mucositis had developed. Of the 20 patients undergoing radiation, only one developed high-grade (grade 3) mucositis in the final week of treatment, 65 percent developed intermediate-grade mucositis, and 30 percent developed low-grade mucositis. Of the 46 patients concurrently receiving chemotherapy and the mouthwash, 36 remained free of any clinically significant mucositis. Of the 32 patients with existing mucositis, all noted immediate relief from mouth discomfort, and within seven days almost all patients had no clinical sign of mucositis.[24]

A randomized, double-blind study was conducted with 164 cancer patients taking 5-fluorouracil (5-FU) chemotherapy. The patients rinsed three times daily with either a chamomile mouthwash or placebo. After 14 days, no difference was observed between the two groups in the incidence of stomatitis induced by 5-FU.[25]

Eczema

In an open, bilateral comparative trial, 161 patients with eczema on their hands, forearms, and lower legs initially treated with 0.1-percent diflucortolone valerate received one of four treatments: chamomile cream (Kamillosan), 0.25-percent hydrocortisone, 0.75-percent fluocortin butyl ester (a glucocorticoid), or 5.0-percent bufexamac (a nonsteroidal anti-inflammatory). After 3-4 weeks, the chamomile cream was found to be as effective as hydrocortisone and demonstrated superior activity to bufexamac and fluocortin butyl ester.[26]

Drug-Botanical Interactions

Only one report of a possible chamomile-drug interaction has been documented. A 70-year-old woman on warfarin was admitted to the hospital with multiple internal hemorrhages after using chamomile products (tea and body lotion) to alleviate upper respiratory tract

symptoms.[27] That chamomile contributed to the hemorrhaging is doubtful since the coumarin compounds in German chamomile lack the chemical configuration necessary for human anticoagulant activity.[28]

Side Effects and Toxicity

Chamomile use has a high level of safety, as confirmed by numerous animal models.[12,29-31] One particular toxicity study using rabbit models determined the acute oral LD_{50} and acute dermal LD_{50} to be greater than 5 g/kg body weight.[32] The U. S. Food and Drug Administration (FDA) has classified the oil and extract of both German and Roman chamomile as substances Generally Regarded As Safe (GRAS).[33]

A few reports indicate that individuals allergic to the Asteraceae/Compositae family (ragweed, chrysanthemum, marigold, daisy, etc.), can experience cross-over hypersensitivity reactions to chamomile. One report involved an eight-year-old boy with a history of atopy who ingested a chamomile tea infusion that precipitated an anaphylactic reaction.[34] In another report, a 20-year-old woman with confirmed sensitivity to chamomile experienced acute rhinitis from merely using chamomile-scented toilet paper.[35]

Dosage

In adults, oral administration for traditional uses are generally as follows: (1) dried flower heads: 2-8 g as an infusion three times daily; (2) liquid extract/tincture: 1-6 mL up to three times daily of 1:1 potency; 7-15 mL up to three times daily of 1:5 potency.

Warnings and Contraindications

Individuals with known hypersensitivity to members of Asteraceae/Compositae family (ragweed, chrysanthemum, marigold, daisy, etc.), should avoid use of chamomile-containing products to reduce the likelihood of an allergic reaction.

References

1. *European Pharmacopoeia*. 5th ed. Strasbourg, France: European Directorate for the Quality of Medicines of the Council of Europe; 1996:1976-1977.
2. Berry M. The chamomiles. *Pharm J* 1995;254:191-193.
3. Cinco M, Banfi E, Tubaro A, et al. A microbiological survey on the activity of a hydroalcoholic extract of camomile. *Int J Drug Res* 1983;21:145-151.
4. Aggag ME, Yousef RT. Study of antimicrobial activity of chamomile oil. *Planta Med* 1972;22:140-144.
5. Annuk H, Hirmo S, Turi E, et al. Effect on cell surface hydrophobicity and susceptibility of *Helicobacter pylori* to medicinal plant extracts. *FEMS Microbiol Lett* 1999;172:41-45.
6. Turi M, Turi E, Koljalg S, Mikelsaar M. Influence of aqueous extracts of medicinal plants on surface hydrophobicity of *Escherichia coli* strains of different origin. *APMIS* 1997;105:956-962.
7. Szelenyi I, Isaac O, Thiemer K. Pharmacological experiments with compounds of chamomile. III. Experimental studies of the ulcerprotective effect of chamomile (author's transl). *Planta Med* 1979;35:218-227. [Article in German]
8. Isaac O. Pharmacological investigations with compounds of chamomile i. on the pharmacology of (-)-alpha-bisabolol and bisabolol oxides (review) (author's transl). *Planta Med* 1979;35:118-124. [Article in German]
9. Isaac O, Thiemer K. Biochemical studies on camomile components/III. *In vitro* studies about the antipeptic activity of (--)-alpha-bisabolol (author's transl). *Arzneimittelforschung* 1975;25:1352-1354. [Article in German]
10. Hormann H, Korting H. Evidence for the efficacy and safety of topical herbal drugs in dermatology: part 1: anti-inflammatory agents. *Phytomedicine* 1994;1:161-171.
11. Achterrath-Tuckermann U, Kunde R, Flaskamp E, et al. Pharmacological investigations with compounds of chamomile. V. Investigations on the spasmolytic effect of compounds of chamomile and Kamillosan on the isolated guinea pig ileum. *Planta Med* 1980;39:38-50. [Article in German]
12. Breinlich VJ, Scharnagel K. Pharmacologic characteristics of the en-yn-dicycloethers from *Matricaria chamomilla*. *Arzneimittelforschung* 1968;18:429-431. [Article in German]
13. Mann C, Staba EJ. 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. 1*. Binghamton, NY: Haworth Press; 1986:235-280.
14. Holzl J, Ghassemi N, Hahn B. Preparation of 14C-spiro ethers by chamomile and their use by an investigation of absorption. *Planta Med* 1986;52:553.
15. Torrado S, Torrado S, Agis A, et al. Effect of dissolution profile and (-)-alpha-bisabolol on the gastrotoxicity of acetylsalicylic acid. *Pharmazie* 1995;50:141-143.

16. Viola H, Wasowski C, Levi de Stein M, et al. Apigenin, a component of *Matricaria recutita* flowers, is a central benzodiazepine receptors-ligand with anxiolytic effects. *Planta Med* 1995;61:213-216.
17. Loggia RD, Traversa U, Scarcia V, Tubaro A. Depressive effects of *Chamomilla recutita* (L.) rausch, tubular flowers, on central nervous system in mice. *Pharmacol Res Commun* 1982;14:153-162.
18. Srivastava JK, Gupta S. Antiproliferative and apoptotic effects of chamomile extract in various human cancer cells. *J Agric Food Chem* 2007;55:9470-9478.
19. Gould L, Reddy CV, Gomprecht RF. Cardiac effects of chamomile tea. *J Clin Pharmacol* 1973;13:475-479.
20. de la Motte S, Bose-O'Reilly S, Heinisch M, Harrison F. Double-blind comparison of an apple pectin-chamomile extract preparation with placebo in children with diarrhea. *Arzneimittelforschung* 1997;47:1247-1249. [Article in German]
21. Weizman Z, Alkrinawi S, Goldfarb D, Bitran C. Efficacy of herbal tea preparation in infantile colic. *J Pediatr* 1993;122:650-652.
22. Glowania HJ, Raulin C, Swoboda M. Effect of chamomile on wound healing – a clinical double-blind study. *Z Hautkr* 1987;62:1262,1267-1271. [Article in German]
23. Maiche AG, Grohn P, Maki-Hokkonen H. Effect of chamomile cream and almond ointment on acute radiation skin reaction. *Acta Oncol* 1991;30:395-396.
24. Carl W, Emrich LS. Management of oral mucositis during local radiation and systemic chemotherapy: a study of 98 patients. *J Prosthet Dent* 1991;66:361-369.
25. Fidler P, Loprinzi CL, O'Fallon JR, et al. Prospective evaluation of a chamomile mouthwash for prevention of 5-FU-induced oral mucositis. *Cancer* 1996;77:522-525.
26. Aertgeerts P, Albring M, Klaschka F, et al. Comparative testing of Kamillosan cream and steroidal (0.25% hydrocortisone, 0.75% fluocortin butyl ester) and non-steroidal (5% bufexamac) dermatologic agents in maintenance therapy of eczematous diseases. *Z Hautkr* 1985;60:270-277. [Article in German]
27. Segal R, Pilote L. Warfarin interaction with *Matricaria chamomilla*. *CMAJ* 2006;174:1281-1282.
28. Majerus PW, Tollefsen DM. Anticoagulant, thrombolytic, and antiplatelet drugs. In: Hardman JG, Limbird LE, Molinoff PB, Gilman AG, eds. *Goodman & Gilman's The Pharmacological Basis of Therapeutics*. 10th ed. New York, NY: McGraw-Hill; 2001:1519-1538.
29. Habersang S, Leuschner F, Isaac O, Thiemer K. Pharmacological studies with compounds of chamomile. IV. Studies on toxicity of (-)-alpha-bisabolol (author's transl). *Planta Med* 1979;37:115-123. [Article in German]
30. Shoukry IF. Toxicological deteriorations of two volatile oils of *Matricaria chamomilla* and *Clerodendron inerme* on the adult house fly *Musca domestica* L. *J Egypt Soc Parasitol* 1997;27:893-904.
31. Jakovlev V, Isaac O, Flaskamp E. Pharmacologic studies on chamomile compounds. VI. Studies on the antiphlogistic effect of chamazulene and matricine. *Planta Med* 1983;49:67-73. [Article in German]
32. Opdyke DL. Chamomile oil German. *Food Cosmet Toxicol* 1974;12:851-852.
33. U.S. Food and Drug Administration www.accessdata.fda.gov/scripts/crrh/cfdocs/cfcfr/CFRSearch.cfm?fr=182.20 [Accessed December 5, 2007]
34. Subiza J, Subiza JL, Hinojosa M, et al. Anaphylactic reaction after the ingestion of chamomile tea: a study of cross-reactivity with other composite pollens. *J Allergy Clin Immunol* 1989;84:353-358.
35. Scala G. Acute, short-lasting rhinitis due to camomile-scented toilet paper in patients allergic to Compositae. *Int Arch Allergy Immunol* 2006;139:330-331.