CHAMOMILE

Matricaria chamomilla L.

Family

Asteraceae or Compositae (commonly referred to as the aster, daisy, composite or sunflower family), a large and widespread family of flowering plants. *Matricaria chamomilla* is known as true, or German, chamomile while *Chamaemelum nobile* (formerly known as *Anthemis nobilis*) is known as English or Roman chamomile. True chamomile is often confused with plants of the genera *Anthemis*. Special attention has to be paid to avoid confusion with *Anthemis cotula* L., a poisonous plant with a revolting smell. In contrast to true chamomile, *A. cotula* similar to *A. arvensis* L. and *A. austriaca* Jacq., has prickly pointed paleae (scaly bracts) and a filled receptacle (the thickened part of a stem from which the flower organs grow). The latter species are nearly odourless.[1,2]

Parts Used

Flower.

Description

"It is so well known everywhere, that it is but lost time and labour to describe it." Nicholas Culpeper.[3]

Chamomile is one of the most important medicinal herbs native to southern and eastern Europe. It is grown in Germany, Hungary, France, Russia, Yugoslavia and Brazil. The plants can be found in North Africa, Asia, North and South America, Australia and New Zealand. Chamomile has a sweet, grassy and lightly fruity aroma. It is from the plant's fresh and dried flower heads that infusions, liquid extracts and essential oils are made. Chamomile is a herbaceous annual plant with ferny, fragrant leaves

and thin spindle-shaped roots penetrating flatly into the soil. The heavily branched smooth stem is erect and grows to a height of 10 to 80cm. The flower heads are placed separately. They have a diameter of 10 to 30mm. Its flowers are daisy-like, with yellow centres (approximately 1 to 1.5cm in diameter) and white petals (between 12 to 20). The flowers bloom in early to midsummer and have a strong, aromatic smell. The receptacle is 6 to 8mm wide, flat in the beginning and conical later, and hollow which is a very important distinctive characteristic of *Matricaria*, along with no paleae. The fruit is a yellowish brown achene (a small, one-seeded fruit containing a single seed) that does not split upon drying.[4]

Chamomile is known by an array of names such as baboonig, babuna, babuna camornile, babunj, German chamomile, Hungarian chamomile, Roman chamomile, English chamomile, camomilla, flos chamomile, single chamomile, sweet false chamomile, pinheads and scented mayweed suggesting its widespread use. Although the systematic status of chamomile is quite clear nowadays there are a number of inaccuracies concerning the names. Apart from misdeterminations and confusion, the synonymous use of the names *Anthemis, Chamomilla* and *Matricaria* leads to uncertainty with regard to the botanical identification. Moreover, the nomenclature is complicated by the fact that Linnaeus made mistakes in the first edition of his "Species Plantarum" that he corrected later on. The current accepted botanical name for true chamomile is *Matricaria chamomilla* (syn. *Matricaria recutita, Chamomilla recutita* and at least 20 others).[5,6]

Traditional Use

Chamomile is a widely recognised herb in Western culture and often referred to as the 'star among medicinal species'. Its medicinal usage dates back to antiquity where such notables as early Greek botanists/physicians Hippocrates (5th century BCE), Dioscorides (1st century CE) and the Roman physician Galen (2nd century CE) made written reference to it. Anglo-Saxons classed this herb as one of nine sacred herbs given to humans by the Lord. Ancient Egyptian, Greek and Roman medicine texts contain descriptions of using chamomile as a calming tisane (herbal tea infusion) and for treating erythema (superficial reddening of the skin) and xerosis (abnormally dry skin) caused by dry weather. In Slovakia a person was supposed to bow to chamomile plants when he or she encountered them. Several doctors from the 16th and 17th centuries suggest that chamomile was used in those times in intermittent fevers. The Unani system of medicine, which is practiced on the Indian subcontinent and in Sri Lanka, uses chamomile (called Gul-e-Babuna) by itself or in combination with other herbs for the following conditions: headache, gonorrhoea, conjunctivitis, chest pain, renal calculi (kidney stones), vesical calculi (bladder stones), general debility, hysteria, dyspepsia and fever. Nowadays it is a highly favoured and much used medicinal plant in folk and traditional medicine. Its multi-therapeutic, cosmetic and nutritional values have been established through years of traditional and scientific use and research. 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.[7,8]

The common name chamomile and specific name chamomilla come from the Greek *chamos*, meaning ground, and *melos*, meaning apple, which refers to the plant's low-growing habit and apple-like scent. The generic name, *Matricaria*, comes from the Latin *matrix*, meaning womb, because it was used historically to treat disorders of the female reproductive system. Chamomile is included in the pharmacopoeia of 26 countries. It is used mainly as an anti-inflammatory and antiseptic but also as an antispasmodic and mild sudorific (to induce sweating). It is used internally mainly as a tisane for disturbance of the stomach associated with pain, for sluggish digestion, for diarrhoea and nausea; more rarely and very effectively for inflammation of the urinary tract and for painful menstruation. Externally, the herb in powder form may be applied to wounds slow to heal, for skin eruptions and infections, such as shingles and boils, also for haemorrhoids and for inflammation of the mouth, throat and the eyes.[9,10]

The international demand for chamomile oil has been steadily growing. As a result the plant is widely cultivated in Europe and has been introduced in some Asian countries for the production of its essential oil. The oil is used as a mild sedative

and for digestion besides being antibacterial and fungicidal in action. In addition to pharmaceutical uses the oil is extensively used in perfumery, cosmetics and aromatherapy, and in the food industry. Because of its extensive pharmacological and pharmaceutical properties chamomile possesses great economic value and is in great demand in the European countries. Germany has always been a major producer and consumer of German/Hungarian chamomile. In addition to its German name Kamillenblüten, it is also known there as alles zutraut, which means 'capable of anything'. Between 1930 and 1945, Germany's average annual demand was about 1,000 metric tons, most of which was wild-collected with only six hectares being cultivated. As late as 1955 Germany was still its own main source of chamomile (mainly from the state of Saxony and the Franconia region of Bavaria) followed by imports from Hungary, the Balkan countries, the former Soviet Union, Czechoslovakia and Yugoslavia among others. In the 1950s an estimated 40 to 50% of world demand could be satisfied with wild-collected chamomile from Hungary. In the 1990s lower-cost production of cultivated chamomile, particularly in Egypt and Argentina, scaled up and eventually ruined the market for wild Hungarian chamomile.[11,12]

Constituents

Chamomile has a range of constituents including:

- essential oil: (0.3 to 1.9%) proazulenes like matricin and matricarin, which are at least partially converted during steam distillation into azulenes like chamazulene which gives the oil an intense blue colour (1 to 15%). In more detail sesquiterpenes: azulenes (2 to 18%), especially chamazulene (-)-alpha-bisabolol (up to 50%) bisabolol oxides A and B trans-β-farnesene (up to 45%), spiroethers (20 to 30%) (cis- and trans-en-in-dicycloethers)
- flavonoids (up to 6%) such as apigenin-7-glucoside (0.5%), apigenin and luteolin, apigetrin, apiin, quercetin, quercimeritrin and rutin
- sesquiterpene lactones such as matricin (0.03 to 0.2%)
- coumarins (0.01% to 0.08%) such as herniarin and umbelliferone
- spiroethers (cis- and trans en-in-dicycloethers)
- phenolic acid
- up to 10% mucilage polysaccharides
- the tannin level in chamomile is less than 1%
- amino acids, anthemic acid (bitter), choline, polysaccharide, plant and fatty acids, and triterpene hydrocarbons (e.g. triacontane)

Herbal teas prepared from chamomile flowers mainly contain flavonoids and their glycosides, mucilaginous constituents and only minor amounts of constituents of essential oil (about 10 to 15% depending on conditions of herbal tea preparations). The coumarins herniarin and umbelliferone are also soluble in hot water and matricin is extracted in concentrations which are pharmaceutically relevant.[13,14,15,16]

Actions

Anti-inflammatory, antioxidant, antibacterial, antiviral, antifungal, mild sedative, cholagogue, bitter tonic (digestive), antispasmodic, carminative, mild sudorific, diaphoretic, emmenagogue, anti-ulcer, relaxant, antiallergic, anticatarrhal.

Pharmacological Activity

Rigorous clinical research assessing the effects of chamomile is limited and randomised controlled clinical trials are required to establish the reported anti-inflammatory, wound healing and sedative effects.

Anti-inflammatory Activity

A prospective epidemiological study published in 2015 explored the connection between chamomile tea consumption and all-cause mortality over the course of seven years in a sample of older Mexican-Americans in south west United States. Of the sample, 13.95% consumed chamomile. Per the Kaplan-Meier estimator, chamomile consumers showed increased overall survival, with women consumers demonstrating even greater survival. In the Cox proportional hazards model for all-cause mortality, chamomile was linked to a 29% reduction in mortality risk for the entire sample, a 33% reduction in risk for women, and a nonsignificant reduction for men.[17]

A 2015 study claimed chamomile is effective on both the symptoms and pathogenesis of irritable bowel syndrome (IBS). A randomised, pre-post study investigated the efficacy of chamomile in treating IBS. Patients diagnosed with IBS took 20 drops per day of a chamomile extract (69.47mg/100mL bisabolol and chamazulene) for four weeks. Patients filled out a questionnaire on day one, at weeks two and four, and two and four weeks after the end of the intervention. Symptoms were significantly reduced at weeks two and four, and relief from symptoms continued up to two weeks after the intervention ended.[18]

In a 2015 age- and gender-matched case-control study, chamomile tea consumption was associated with a reduction in both benign and malignant thyroid diseases. The odds of developing any type of thyroid disease decreased significantly with increased frequency of chamomile consumption. Additionally, the risk of developing benign thyroid diseases or thyroid cancer was significantly reduced in those who had consumed chamomile tea for 30 or more years.[19]

A few studies, including one from 2015, have assessed the usefulness of chamomile in treating stomatitis, a painful inflammation of the oral mucosa that can include ulceration. In two experiments, chamomile was found to be as effective as the conventional pharmaceutical comparison drugs (allopurinol mouthwash vs. chamomile mouthwash, and triamcinolone in Orabase® vs. chamomile in Orabase®, respectively). In the first study, the allopurinol and chamomile mouthwashes were equally effective in reducing stomatitis in chemotherapy patients but the authors noted that the lower cost and greater availability of chamomile (i.e., it does not require a physician's prescription) may make it a better choice for some patients. In the second study, while chamomile did not resolve all symptoms as rapidly as the conventional pharmaceutical drug triamcinolone, pain intensity reduction and patient satisfaction scores were similar between groups.[20,21]

In a third study conducted in 2014, chamomile mouthwash was more effective in treating recurrent aphthous stomatitis (RAS) than placebo. Chamomile was effective in the treatment of RAS, controlling the pain and burning sensation without producing any adverse side effects and could be advised as an alternative RAS treatment. RAS is a common clinical condition producing painful ulcerations in the oral cavity. However, there has been no optimal therapeutic approach. Topical and systemic steroids commonly prescribed for the condition have local and systemic side-effects. Recently, there is growing tendency toward herbal medication in the modern society. In this triple-blind study, 50 patients with aphthous lesions were randomised to receive either chamomile tincture or placebo. Patients were instructed to apply 10 drops three times per day, rinse for three minutes, expectorate, and refrain from eating for 30 minutes. Patients were examined after two, four and six days, then weekly. The changes in the chamomile group included fewer number of lesions, smaller lesion size and less pain and burning sensation and were statistically significant at each examination compared to the placebo group.[22]

Chamomile oil decreased the analgesic demand of patients with knee osteoarthritis a 2015 study has shown. In addition, it may show some beneficial effects on physical function, and stiffness of the patients. In the Iranian study that investigated the efficacy of chamomile in treating knee osteoarthritis (OA), 84 patients with OA were randomised to three groups and instructed to apply their assigned medication to the knee and surrounding area three times per day for three weeks. One group applied 1.5mL chamomile oil; the second group applied diclofenac gel; and the control group applied paraffin. Patients were allowed to take 500mg acetaminophen as needed, and use of the analgesic was examined as one of the outcome measures, along with a self-administered Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire at the beginning of the study and every week during the study. The number of acetaminophen tablets taken by the chamomile group was significantly lower than those taken by the other two groups, and, while the chamomile oil showed some beneficial effects on pain, stiffness, and physical activity, these effects did not differ significantly from the other two groups. The authors recommended further research with larger study populations.[23]

In a randomised, double-blind, placebo-controlled pilot study published in 2015, chamomile oil

obtained through traditional direct-heat method was investigated for its efficacy in treating severe carpal tunnel syndrome (sCTS) when applied topically as a complementary therapy. Twenty-six patients with documented sCTS were randomised to apply chamomile oil or placebo (paraffin, sesame oil, and 1% chamomile essential oil to mimic the aroma of the chamomile oil) twice daily for four weeks, in addition to wearing an immobilizing wrist splint at night. Primary and secondary outcomes were measured at enrolment and after four weeks. The patients in the chamomile oil group showed significant improvements in severity of symptoms and functional ability compared to placebo.[24]

A 2014 prospective, randomised, double-blind study compared chamomile extract to mefenamic acid (MA; a non-steroidal anti-inflammatory drug [NSAID] used to treat pain) for reducing the intensity of mastalgia (breast pain) associated with premenstrual syndrome. Ninety female university students were randomised to receive either 100mg chamomile or 250mg MA three times per day from the 21st day of their menstrual cycle until onset for six months. Both chamomile and MA relieved mastalgia intensity with no significant difference between the groups. The authors recommended further studies that do not rely on data collection through subject self-reporting.[25]

Chamomile performed well in a 2011 controlled study comparing its efficacy in managing peristomal skin lesions in colostomy patients versus treatment with hydrocortisone ointment. Participants were assigned to the chamomile group or control group based on matching demographics, history and skin-condition variables. Patients in the experimental group applied a chamomile compress (6g air-dried and powdered flower heads steeped in 150mL boiled water for 10 minutes, strained, and applied to gauze) to the wound for one hour once per day. The control group applied 1% hydrocortisone ointment to their wound once per day. Lesions were evaluated every three days for 28 days and healing occurred significantly faster in the chamomile group than in the hydrocortisone group. Additionally, pain and itching around the stoma was relieved more quickly in the chamomile group.[26]

A 2005 controlled, double-blind, crossover study investigated a chamomile mouthwash for its ability to reduce dental plaque and gingival inflammation. For two four-week periods separated by a washout period of two weeks, 25 randomly assigned patients with gingivitis rinsed with either a chamomile mouthwash (air-dried and powdered chamomile flowers percolated at room temperature with 55% ethanol, extracts filtered, evaporated under vacuum at low temperature, dried residue suspended in water) or control (solvent with no other ingredients). Both groups were instructed to dilute 20 drops of mouthwash with 20mL water and rinse twice a day for two minutes, once before bedtime. Plaque, gingival inflammation, and stain indices were recorded at baseline and measured at the end of each experimental period and the end of the washout period. Mean reduction for plaque and gingival indices were significantly greater for the chamomile mouthwash than for the control. Also, there was no significant staining or reduction in baseline staining in the chamomile group.[27]

Mucositis, characterised 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 100mL 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% developed intermediate grade mucositis, and 30% 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.[28]

In an open, bilateral comparative trial 161 patients with eczema on their hands, forearms and lower

legs initially treated with 0.1% diflucortolone valerate received one of four treatments: chamomile cream (Kamillosan), 0.25% hydrocortisone, 0.75% fluocortin butyl ester (a glucocorticoid), or 5.0% bufexamac (a nonsteroidal anti-inflammatory). After 3 to 4 weeks, the chamomile cream was found to be as effective as hydrocortisone and demonstrated superior activity to bufexamac and fluocortin butyl ester.[29]

Chamomile extract can optimise the healing of traumatic oral ulcers in diabetic rats through the reduction of apoptosis in the epithelium and Tumor Necrosis Factor alpha (TNF-α) expression a 2016 study has found. The study evaluated the influence of TNF-α and apoptosis in rats with diabetes mellitus (DM) treated with chamomile extract or triamcinolone.[30]

DM is a chronic metabolic disease characterised by deficiency in insulin production or resistance to its action, resulting in hyperglycaemia and metabolic alterations. The incidence of DM is increasing in the world and it is considered the biggest health problem in the 21st century. It is estimated that in 2025 there will be twice as many diabetic patients compared with the year 2000, totalling approximately 300 million affected individuals worldwide. Chronic hyperglycaemia causes numerous events that promote structural changes in tissue. High levels of blood glucose affect oral wound healing negatively. Wound healing in an uncontrolled diabetic patient occurs more slowly compared with normoglycaemic or controlled diabetic patients. This delay in oral wound healing can cause chronicity of oral lesions in patients with DM. It is associated with delayed wound healing, increased susceptibility to infection, alterations in neutrophil activity and reduction of chemotaxis, adhesion, phagocytosis and angiogenesis. Clinically, the wound healing disorder manifests itself as hypertrophic scars or chronic unhealed wounds (ulcers), being ulcers the most prevalent problem in healing. In the oral cavity, traumatic ulcers are caused by mechanical trauma due to maladjusted dentures, orthodontic brackets, accidental bites or iatrogenic factors. Typically, when the causal agent is removed, healing occurs spontaneously from one to two weeks; however, in a few cases, the ulcer can persist for longer periods of time. It can be extremely painful and interfere with eating and speaking. Corticosteroids are commonly prescribed for the treatment of painful symptoms of traumatic oral ulcers; however, conflicting results have been reported in literature regarding the effects of this therapeutic modality on the healing process. Glucocorticoids have potent anti-inflammatory and immunosuppressive effects. Triamcinolone is commonly used in clinical dentistry because of its analgesic effects on oral ulcers. It has a potent anti-inflammatory effect and is effective in reducing oral scores of mucositis and pain in patients undertaking radiotherapy. But corticoids used in treatment of inflammatory conditions not only inhibit the symptoms of acute inflammation but also retard wound healing. In contrast, the use of natural products in the treatment of ulcerated oral lesions has increased over the past several decades. Chamomile has compounds such as flavonoids (quercetin and apigenin), terpenes and acetylated derivatives that confer anti-inflammatory effects, antibacterial, antifungal, antioxidant, hypocholesterolaemic, and sedative properties. These drugs have been indiscriminately used in dental clinics for the treatment of persistent ulcerative lesions but mechanisms of the diseases can be different in diabetic patients. Hyperglycaemia leads keratinocytes and fibroblasts to high apoptosis levels that can modify the biological profile of wound closure and healing and interfere in collagen deposition. Drugs used in the treatment of oral ulcer in diabetics should show a good efficacy in modifying these parameters. The anti-inflammatory effects of chamomile have been linked to compounds present in its extract such as flavonoids, alpha-bisabolol, and acetylated derivatives. The mechanism of action of chamomile in the inflammatory process involves direct inhibition of ciclooxigenase-2 and synthesis of inflammatory mediators such as prostaglandin E228.[31]

In this study, the chamomile group (DCG) was the single treatment that showed reduction in TNF-α expression in diabetic rats that are likely to augment in proinflammatory cytokines corroborating the anti-inflammatory effects of this extract. These actions lead to a reduction in vascular and cellular events, including acute inflammation. Furthermore, alpha-bisabolol has been associated with promoter activity in the formation of granulation tissue during the process of wound repair.[32]

Data from a 2016 study suggests that a diclofenac (a non-steroidal anti-inflammatory drugs – NSAID) and chamomile combination can interact at a systemic level in a synergic manner and may have therapeutic advantages for the clinical treatment of inflammatory pain. Chamomile is widely used as a remedy for pain and gastric disorders. The association of NSAIDs with medicinal plant extracts may increase its antinociceptive activity, permit the use of lower doses and limit side effects. The aim of the study was to isolate and identify the main chemical constituents of chamomile (MCE) as well as to explore their activity as cyclooxygenase (COX) inhibitors in silico (performed on computer). The researchers also examined the interaction between MCE and diclofenac on nociception in the formalin test by isobolographic analysis, and to determine the level of gastric injury in rats. Three terpenoids, α-bisabolol, bisabolol oxide A and guaiazulene, were isolated and identified. Docking simulation predicted COX inhibitory activity for those terpenoids. Diclofenac, MCE or their combinations produced an antinociceptive effect. The sole administration of diclofenac and the highest combined dose diclofenac-MCE produced significant gastric damage but that effect was not seen with MCE alone. An isobologram was constructed and the derived theoretical ED35 for the antinociceptive effect was significantly different from the experimental ED35; hence, the interaction between diclofenac and MCE that mediates the antinociceptive effect is synergist. The MCE contains three major terpenoids with plausible COX inhibitory activity in silico, but α-bisabolol showed the highest affinity.[33]

The findings of a 2016 *in vivo* study suggest that chamomile inhibits neutrophil reactive oxygen species (ROS) production and protects against ethanol (EtOH)-induced haematologiacal parameter changes and erythrocytes oxidative stress. The haematoprotection offered by chamomile might involve in part its antioxidant properties as well as its opposite effect on some intracellular mediators such as plasma hydrogen peroxide (H2O2), free iron and calcium. ROS are involved in a wide range of processes such as aging and diseases. ROS are not only an aspect of normal metabolism but are also implicated in several physiological phenomena such as substantial protection against severe infections and the redox regulation of protein phosphorylation, ion channels and transcription factors. However enhanced ROS production may lead to oxidative stress and oxidation of vital cellular components which induce cellular damage and cell death. Therefore, the cytotoxicity of ethanol was attributed to increased ROS generation which in turn consequently lead to injuries and oxidative stress in many organ systems. To protect cells against these harmful species synthetic or natural antioxidants molecules can be used. The latter are able to scavenge ROS and to up-regulate endogenous antioxidant defence systems.[34]

In a 2016 *in vivo* study chamomile prevented inflammation and alveolar bone resorption by reducing TNF-α and IL-1β.[35]

In vitro chamomile extract inhibits both cyclooxygenase and lipoxygenase, and consequently prostaglandins and leukotrienes.[36]

Co-medication with the ethyl acetate extract, or essential oil of German chamomile and antihistamines might be effective for pruritus which could not be perfectly resolved alone by conventional antihistamines. In mice fed a diet containing 1.2% (w/w) of an ethyl acetate extract of dried chamomile flower for 11 days, induced scratching behaviour was suppressed in a dose-dependent manner.[37]

Chamomile clearly has a protective effect against ethanol-induced gastric mucosal lesions, and this effect, at least in part, depends upon the reduction in lipid peroxidation and augmentation in antioxidant activity a recent *in vivo* study concluded. Pre-treatment with chamomile at some doses significantly reduced gastric lesions in rats.[38]

A freeze dried extract of chamomile given to rats suppressed both the inflammatory effect and leucocyte infiltration induced by simultaneously given carrageenan and prostaglandin E1.[39]

The topical application of a hydroalcoholic extract of chamomile to the inner surface of the ear reduced induced oedema in mice. One mL of extract corresponded to 50mg dry extract.[40]

Topical treatment with an extract of fresh chamomile was as effective as the reference drug in preventing inflammation in mice subjected to induced oedema.[41]

Antibacterial, Antiviral and Antifungal Activity

An ethanolic extract of chamomile inhibited the growth of herpes and polio virus.[42,43]

In general aqueous extracts of chamomile were more effective against moulds and yeast, while alcoholic extracts showed higher activities against bacteria.[44]

Antimicrobial activity of the aqueous extract of chamomile against various microorganisms *(Pseudomonas aeruginosa, beta haemolytic streptococci, Enterobacter agglomerans, Escherischia coli, Staphylococcus aureus)* was assessed. These germs were resistant to the extract.[45]

Whole plant chamomile extract at 10 mg/mL demonstrates antibacterial and fungicidal activity completely inhibiting growth of group B *Streptococcus in vitro*. In addition, chamomile extract blocks aggregation of *Helicobacter pylori* and various strains of *Escherichia coli*.[46,47]

Toxicity of acetone-extract of chamomile against larvae of *Gulex pipens* L. has been reported.[48]

Sedative and Anxiolytic Activity

Chamomile tea may be recommended to postpartum women as a supplementary approach to alleviating depression and sleep quality problems suggest the preliminary results of a 2016 study. The purpose of this study was to evaluate the effects of chamomile tea on sleep quality, fatigue and depression in postpartum women. Sleep quality is a significant issue for postnatal women and chamomile is widely used as a folk remedy for its presumed sedative-hypnotic effects. Six weeks after childbirth sleep-disturbed Taiwanese women were randomised into a control group (no treatment) or drinking German chamomile tea (1 cup/day) for two weeks. Tea was prepared using 2g of dried flowers steeped in 300mL hot water and infused for 10 to 15 minutes. Characteristics of the participants included normal childbirth, no postnatal complications, Postpartum Sleep Quality Scale (PSQS) greater than or equal to 16 and not having a history of allergy to herb teas, food or medicine. Compared to the control group, those drinking chamomile tea demonstrated significantly lower scores in physical symptom-related sleep inefficiency and in symptoms of depression. There was no effect on self-perceived fatigue.[49]

Chamomile may provide clinically meaningful antidepressant activity that occurs in addition to its previously observed anxiolytic activity a 2012 study reported. Anxiety and depression are the most commonly reported psychiatric conditions and frequently occur as comorbid disorders. While the advent of conventional drug therapies has simplified treatment, a large segment of the population goes untreated or declines conventional therapy for financial, cultural or personal reasons. Therefore, the identification of inexpensive and effective alternative therapies for anxiety and depression is of relevance to public health. Based upon prior observations from *in vivo* and *in vitro* animal studies suggesting that chamomile may possess antidepressant activity the researchers conducted this secondary, exploratory analysis of their prior clinical chamomile trial in humans to examine whether chamomile demonstrated antidepressant activity along with its antianxiety effects. The study explores data from a 2009 clinical chamomile trial in humans to determine if chamomile provides clinically meaningful antidepressant activity versus a placebo. In the 2009 randomised, double-blind, placebo-controlled study, the research team examined the antianxiety and antidepressant action of oral chamomile extract in participants with symptoms of comorbid anxiety and depression. Of the 57 participants in the 2009 trial, 19 had anxiety with comorbid depression; 16 had anxiety with a past history of depression; and 22 had anxiety with no current or past depression. The intervention and placebo groups in the 2009 trial received identically appearing 220mg capsules containing either pharmaceutical-grade chamomile extract standardized to a content of 1.2% apigenin or a placebo (ie, lactose monohydrate NF), respectively. In the 2012 study, the research team used generalised estimating equations analysis to identify clinically meaningful changes over time in scores from the Hamilton Depression Rating (HAM-D) questionnaire among treatment groups. The research team observed a significantly greater reduction over time in total HAM-D scores for chamomile vs placebo in all participants. The team also observed a clinically meaningful but nonsignificant trend for a greater reduction in total HAM-D scores for chamomile vs placebo in

participants with current comorbid depression. When the team examined the HAM-D core mood item scores, it observed a significantly greater reduction over time for chamomile vs placebo in all participants and a clinically meaningful but nonsignificant trend for a greater reduction over time for chamomile vs placebo in participants without current or past depression. Chamomile's mode of antidepressant action is unknown, although it may be independent of its anxiolytic activity. Several lines of evidence suggest that one or more of chamomile's flavonoid constituents may exert an antidepressant effect via modulation of central noradrenalin (NA), dopamine (DA), serotonin (5-HT), and γ-amino butyric acid (GABA) neurotransmission. In addition, chamomile also appears to modulate hypothalamic-pituitary-adrenocortical (HPA) axis activity.[50]

The same researchers from the previous study above conducted another 2009 randomised, double-blind, placebo-controlled study investigated the efficacy of chamomile extract on generalised anxiety disorder (GAD). The results suggest that chamomile may have modest anxiolytic activity in patients with mild to moderate GAD. Over an eight-week period, 57 patients with mild-to-moderate GAD took either chamomile extract standardised to 1.2% apigenin or placebo at the rate of one 22mg capsule per day for the first week, increasing one capsule per day over a four week period. Patients with up to a 50% reduction in symptoms were increased to five capsules daily for weeks five through eight of therapy. Symptoms were measured at baseline and after two, four, six, and eight weeks of treatment. A statistically significant superiority in anxiety test scores was seen in the chamomile group compared to placebo.[51]

The haemodynamic effects of chamomile tea in patients with cardiac disease were evaluated in the 1970s. It was found in general that the patients fell into deep sleep after taking the beverage. In the 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 the 12 patients in the study achieved deep sleep within 10 minutes of drinking the tea. The patients had a small but significant increase in mean brachial artery pressure. No other significant haemodynamic changes were observed.[52]

Choleretic Activity

An infusion prepared from chamomile exercised a marked stimulatory action on the secretory function of the liver.[53]

Wound Healing Activity

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.[54]

A recent *in vivo* study discovered that the increased rate of wound contraction, together with the increased wound-breaking strength, hydroxyproline content and histological observations, support the use of chamomile in wound management. Wound contraction and epithelisation were significantly better in their test group resulting in healing three days earlier using an acqueous extract of chamomile. Wound-breaking strength in incision wounds was significantly higher in the test group.[55]

Another recent *in vivo* and *in vitro* study concluded that chamomile, in comparison to corticosteroids, promotes a faster wound healing process. In the clinical analysis all rats in the chamomile group had healed ulcers at five days whereas healing did not occur in the other groups until after 14 days. Wound healing in the corticosteroid groups was significantly lower than in the control group.[56]

Previous studies conducted on the anti-inflammatory, antimicrobial and antioxidant effects of chamomile led researchers to study the effect of topical chamomile extract on burn-wound healing in rats. This study concluded that chamomile extract in the form of rubbing oil had good potential for accelerating burn-wound healing in rats. The results showed that there was a significant difference between the vehicle and treatment groups.[57]

Antispasmodic and Gastrointestinal Activity

A double-blind study observed the efficacy of an herbal decoction consisting of chamomile, vervain, liquorice, fennel and balm mint on 68 healthy infants with colic. For seven days the infants (ages two to eight weeks) received 150mL of the herbal preparation or placebo with each colic episode, but

no more than three times daily. After seven days, 57% of the infants receiving the herbal preparation experienced colic relief compared to 26% in the placebo group ($p < .01$).[58]

In a prospective, randomised, multicentre, double-blind, parallel group trial, 79 children (ages six months to five years) with acute, non-complicated diarrhoea 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 diarrhoea alleviation compared to the placebo group (58%) ($p < .05$). The children on the pectin/chamomile combination experienced a significant 5.2 hour shorter duration of symptoms compared to the placebo group.[59]

Clinical evidence suggests that the herbal formulation ColiMil (which contains chamomile flowers extract, *Foeniculum vulgare* fruit extract and *Melissa officinalis* aerial parts extract) is effective in the treatment of breastfed colic in infants. Therefore the effect of this phytotherapeutic formulation and its herbal constituents on upper gastrointestinal transit was investigated *in vivo*. Oral administration of the herbal formulation dose-dependently delayed upper gastrointestinal transit. Among the herbal components, chamomile and *Melissa officinalis* extract , but not *Foeniculum vulgare*, reduced motility significantly. These results suggest that ColiMil reduces upper gastrointestinal motility in mice, with a major contribution by chamomile and *Melissa officinalis*.[60]

An *in vitro* study demonstrated the effectiveness of an ethanol extract of chamomile on spasms induced by acetylcholine and histamine. At doses of 2.5 and 10mL/l the chamomile extract increased the median effective dose of acetylcholine and histamine in a dose-related manner, also when the effect of ethanol was subtracted.[61]

Mechanisms underlying the spasmolytic activity of chamomile still remain unclear. Inhibition of cAMP- and cGMP-phosphodiesterases (PDE) is one of the mechanisms operated by spasmolytic drugs. The cyclic nucleotides cAMP and cGMP regulate the smooth muscle tone of the intestinum causing relaxation. Inhibition PDEs, which catalyse the hydrolysis of cAMP and cGMP to 5'-AMP and 5'-GMP, is one of the mechanisms operated by spasmolytic drugs. In this study, the effect of chamomile on PDE was investigated. Human platelet cAMP-PDE and recombinant PDE5A1 were assayed in the presence of infusions prepared from sifted flowers and capitula. LC-ESI-MS/MS analysis showed different compositions in infusions made with sifted flowers and capitula. Chamomile inhibited cAMP-PDE activity while cGMP-PDE5 was less affected. Among the individual compounds tested, only flavonoids showed an inhibitory effect, contributing to around 39% of the infusion inhibition; other compounds responsible for cAMP-PDE inhibition still remain unknown. Although experimental evidence supporting the use of chamomile for gastrointestinal minor spasms dates back to the fifties, cAMP-PDE inhibition as a likely mechanism underlying the spasmolytic activity was reported for the first time.[62]

Indications

- Symptomatic treatment of gastrointestinal complaints such as bloating, minor spasms, dyspepsia, impaired digestion, colitis, colic, diverticulitis, constipation (children), Crohn's disease, infantile colic and flatulence
- Gastric and duodenal ulcers
- Adjuvant in the treatment of inflammatory conditions of the gastrointestinal tract including irritable bowel syndrome and gastrointestinal spasms
- Anxiety, restlessness, sleep disorders and mild cases of insomnia due to nervous disorders
- Menopausal tension
- Teething problems in children
- Migraine
- Vertigo
- Travel sickness
- Morning sickness, dysmenorrhea, amenorrhea
- Asthma
- Relief of symptoms of the common cold, hayfever, sinusitis, bronchitis, nasal congestion
- To relieve eye strain
- Urinary infections

- Diarrhoea
- External use: Minor inflammation and irritations of the skin and mucosa (superficial wounds, skin cracks, eczema, bruises, small boils, sunburn, frostbite and insect bites) including irritations, infections and minor ulcers of the mouth, gums and throat, and haemorrhoids
- Inhalation: Symptomatic relief of irritations of the respiratory tract due to the common cold

Energetics

Bitter, pungent, cooling.

Use in Pregnancy

Pregnant women may use chamomile herbal tea however for all other preparations there is a lack of data, therefore the use during pregnancy and lactation for all other herbal preparations is not recommended.[63]

Contraindications

Contraindicated in patients with a known sensitivity or allergy to plants of the Asteraceae (Compositae) family such as ragweed, asters, marigold, daisy and chrysanthemums. For patients after renal transplantation taking high dosages for longer periods (about two months) interactions based on effects on CYP450 have been reported.[64]

Drug Interactions

Monitor with hormonal replacement therapy, oral contraceptives, anticoagulant/antiplatelet (such as warfarin) and antidiabetic drugs. Caution with central nervous system depressant drugs, including benzodiazepoines (commonly prescribed to treat stress, anxiety or insomnia), and tamoxifen (used for certain types of breast cancer).

Administration and Dosage

Liquid Extract:	1:1
Alcohol:	60%
Weekly Dosage:[65]	20 to 80mL

References

1. Singh O, Khanam Z, Misra N, Srivastava MK. Chamomile (Matricaria chamomilla L.): An overview.Pharmacogn Rev. 2011 Jan;5(9):82-95. doi: 10.4103/0973-7847.79103.
2. The Plant List. [Internet]. Kew and Missouri: Royal Botanic Gardens, Kew and Missouri Botanical Garden; c2013 Version 1.1 [accessed 2016 Jul 8] Available from http://www.theplantlist.org/tpl1.1/record/gcc-113893
3. Culpeper N. Culpeper's Complete Herbal. Hertfordshire: Wordsworth Reference, 1995 p. 218.
4. Singh O, Khanam Z, Misra N, Srivastava MK. Chamomile (Matricaria chamomilla L.): An overview.Pharmacogn Rev. 2011 Jan;5(9):82-95. doi: 10.4103/0973-7847.79103.
5. The Plant List. [Internet]. Kew and Missouri: Royal Botanic Gardens, Kew and Missouri Botanical Garden; c2013 Version 1.1 [accessed 2016 Jul 8] Available from http://www.theplantlist.org/tpl1.1/record/gcc-103038
6. Singh O, Khanam Z, Misra N, Srivastava MK. Chamomile (Matricaria chamomilla L.): An overview.Pharmacogn Rev. 2011 Jan;5(9):82-95. doi: 10.4103/0973-7847.79103.
7. Singh O, Khanam Z, Misra N, Srivastava MK. Chamomile (Matricaria chamomilla L.): An overview.Pharmacogn Rev. 2011 Jan;5(9):82-95. doi: 10.4103/0973-7847.79103.
8. Natural Medicines (US). German Chamomile [Internet]. Somerville (MA): Therapeutic Research Center; 2016 [updated 2016 July 12; cited 2016 July 15]. Available from https://naturalmedicines.therapeuticresearch.com/databases/food,-herbs-supplements/professional.aspx?productid=792
9. Singh O, Khanam Z, Misra N, Srivastava MK. Chamomile (Matricaria chamomilla L.): An overview.Pharmacogn Rev. 2011 Jan;5(9):82-95. doi: 10.4103/0973-7847.79103.
10. Natural Medicines (US). German Chamomile [Internet]. Somerville (MA): Therapeutic Research Center; 2016 [updated 2016 July 12; cited 2016 July 15]. Available from https://naturalmedicines.therapeuticresearch.com/databases/food,-herbs-supplements/professional.aspx?productid=792
11. Singh O, Khanam Z, Misra N, Srivastava MK. Chamomile (Matricaria chamomilla L.): An overview.Pharmacogn Rev. 2011 Jan;5(9):82-95. doi: 10.4103/0973-7847.79103.
12. Natural Medicines (US). German Chamomile [Internet]. Somerville (MA): Therapeutic Research Center; 2016 [updated 2016 July 12; cited 2016 July 15]. Available from https://naturalmedicines.therapeuticresearch.com/databases/food,-herbs-supplements/professional.aspx?productid=792
13. Essential Medicines and Health Products Information Portal. A World Health Organization resource. [Internet] WHO Monographs on Selected Medicinal Plants - Volume 1. Flos Chamomillae c1999 [accessed 2016 Jul 17] Available from http://apps.who.int/medicinedocs/en/d/Js2200e/11.html#Js2200e.11
14. [No authors listed] Matricaria chamomilla (German chamomile). Monograph. Altern Med Rev. 2008 Mar;13(1):58-62.
15. European Medicines Agency, Committee on Herbal Medicinal Products (HMPC). Assessment report on Matricaria recutita L., flos and Matricaria recutita L., aetheroleum [Internet]. London: European Medicines Agency; c1995-2016 [updated 2015 Jul 7;cited 2016 Jul 21]. Available from http://www.ema.europa.eu/docs/en_GB/document_library/Herbal_-_HMPC_assessment_report/2016/04/WC500204296.pdf
16. Pharmaceutical Press Editorial. Herbal Medicines. 4th ed. London:Pharmaceutical Press; 2013. p. Chamomile
17. Howrey BT, Peek MK, McKee JM, Raji MA, Ottenbacher KJ, Markides KS. Chamomile consumption and mortality: a prospective study of Mexican origin older adults [published online April 29, 2015]. The Gerontologist.doi:10.1093/geront/gnv051.
18. Agah S, Taleb A, Moeini R, Gorji N, Nikbakht H, Soltani-Kermanshahi M. Chamomile efficacy in patients of the irritable bowel syndrome. Der Pharma Chemica. 2015;7(4):41-45.
19. Riza E, Linos A, Petralias A, de Martinis L, Duntas L, Linos D. The effect of Greek herbal tea consumption on thyroid cancer: a case-control study [published online April 4, 2015]. European Journal of Public Health.doi:http://dx.doi.org/10.1093/eurpub/ckv063.
20. Shabanloei R, Ahmadi F, Vaez J, Ansarin K, Hajizadeh E, Dolatkhah R, et al. Alloporinal, chamomile and normal saline mouthwashes for the prevention of chemotherapy-induced stomatitis. Journal of Clinical and Diagnostic Research. 2009;3:1537-1542.
21. Tadbir AA, Pourshahidi S, Ebrahimi H, Hajipour Z, Memarzade MR, Shirazian S. The effect of Matricaria chamomilla(chamomile) extract in Orabase on minor aphthous stomatitis, a randomized clinical trial. Journal of Herbal Medicine. 2015;5:71-76.
22. Seyyedi SA, Sanatkhani M, Pakfetrat A, Olyaee P. The therapeutic effects of chamomilla tincture mouthwash on oral aphthae: A Randomized Clinical Trial. J Clin Exp Dent. 2014 Dec 1;6(5):e535-8. doi: 10.4317/jced.51472. eCollection 2014.
23. Shoara R, Hashempur MH, Ashraf A, Salehi A, Dehshahri S, Habibagahi Z. Efficacy and safety of topical Matricaria chamomilla L. (chamomile) oil for knee osteoarthritis: A randomized controlled clinical trial. Complement Ther Clin Pract. 2015 Aug;21(3):181-7. doi: 10.1016/j.ctcp.2015.06.003. Epub 2015 Jun 9.
24. Hashempur MH, Lari ZN, Ghoreishi PS, Daneshfard B, Ghasemi MS, Homayouni K, et al. A pilot randomized double-blind placebo-controlled trial on topical chamomile (Matricaria chamomilla L.) oil for severe carpal tunnel syndrome. Complement Ther Clin Pract. 2015 Nov;21(4):223-8. doi: 10.1016/j.ctcp.2015.08.001. Epub 2015 Aug 12.
25. Sharifi F, Simbar M, Mojab F, Majd HA. Comparison of the effects of Matricaria chamomila (Chamomile) extract and mefenamic acid on the intensity of premenstrual syndrome. Complement Ther Clin Pract. 2014 Feb;20(1):81-8. doi: 10.1016/j.ctcp.2013.09.002. Epub 2013 Oct 9.
26. Charousaei F, Dabirian A, Mojab F. Using chamomile solution or a 1% topical hydrocortisone ointment in the management of peristomal skin lesions in colostomy patients: results of a controlled clinical study. Ostomy Wound Manage. 2011 May;57(5):28-36.
27. Pourabbas R, Delazar A, Chitsaz MT. The effect of German chamomile mouthwash on dental plaque and gingival inflammation. Iranian Journal of Pharmaceutical Research. 2005;2:105-109.
28. Carl W, Emrich LS. Management of oral mucositis during local radiation and systemic chemotherapy: a study of 98 patients. J Prosthet Dent. 1991 Sep;66(3):361-9.
29. Aertgeerts P, Albring M, Klaschka F, Nasemann T, Patzelt-Wenczler R, Rauhut K, 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].[Article in German] Z Hautkr. 1985 Feb 1;60(3):270-7.
30. Oliveira BV, Barros Silva PG, Nojosa Jde S, Brizeno LA, Ferreira JM, Sousa FB, et al. TNF-alpha expression, evaluation of collagen, and TUNEL of Matricaria recutita L. extract and triamcinolone on oral ulcer in diabetic rats. J Appl Oral Sci. 2016 May-Jun;24(3):278-90. doi: 10.1590/1678-775720150481.
31. Oliveira BV, Barros Silva PG, Nojosa Jde S, Brizeno LA, Ferreira JM, Sousa FB, et al. TNF-alpha expression, evaluation of collagen, and TUNEL of Matricaria recutita L. extract and triamcinolone on oral ulcer in diabetic rats. J Appl Oral Sci. 2016 May-Jun;24(3):278-90. doi: 10.1590/1678-775720150481.
32. Oliveira BV, Barros Silva PG, Nojosa Jde S, Brizeno LA, Ferreira JM, Sousa FB, et al. TNF-alpha expression, evaluation of collagen, and TUNEL of Matricaria recutita L. extract and triamcinolone on oral ulcer in diabetic rats. J Appl Oral Sci. 2016 May-Jun;24(3):278-90. doi: 10.1590/1678-775720150481.

33. Ortiz MI, Fernández-Martínez E, Soria-Jasso LE, Lucas-Gómez I, Villagómez-Ibarra R, González-García MP, et al. Isolation, identification and molecular docking as cyclooxygenase (COX) inhibitors of the main constituents of Matricaria chamomilla L. extract and its synergistic interaction with diclofenac on nociception and gastric damage in rats. Biomed Pharmacother. 2016 Mar;78:248-56. doi: 10.1016/j.biopha.2016.01.029. Epub 2016 Feb 2.
34. Jabri MA, Sani M, Rtibi K, Marzouki L, El-Benna J, Sakly M, et al. Chamomile decoction extract inhibits human neutrophils ROS production and attenuates alcohol-induced haematological parameters changes and erythrocytes oxidative stress in rat. Lipids Health Dis. 2016 Mar 31;15:65. doi: 10.1186/s12944-016-0233-4.
35. Guimarães MV, Melo IM, Adriano Araújo VM, Tenazoa Wong DV, Roriz Fonteles CS, Moreira Leal LK, et al. Dry Extract of Matricaria recutita L. (Chamomile) Prevents Ligature-Induced Alveolar Bone Resorption in Rats via Inhibition of Tumor Necrosis Factor-α and Interleukin-1β. J Periodontol. 2016 Jun;87(6):706-15. doi: 10.1902/jop.2016.150411. Epub 2016 Jan 16.
36. Hörmann HP1, Korting HC. Evidence for the efficacy and safety of topical herbal drugs in dermatology: Part I: Anti-inflammatory agents. Phytomedicine. 1994 Sep;1(2):161-71. doi: 10.1016/S0944-7113(11)80036-X.
37. Kobayashi Y, Takahashi R, Ogino F. Antipruritic effect of the single oral administration of German chamomile flower extract and its combined effect with antiallergic agents in ddY mice. J Ethnopharmacol. 2005 Oct 3;101(1-3):308-12.
38. Cemek M, Yilmaz E, Büyükokuroğlu ME. Protective effect of Matricaria chamomilla on ethanol-induced acute gastric mucosal injury in rats. Pharm Biol. 2010 Jul;48(7):757-63. doi: 10.3109/13880200903296147.
39. Shipochliev T, Dimitrov A, Aleksandrova E. [Anti-inflammatory action of a group of plant extracts]. [Article in Bulgarian] Vet Med Nauki. 1981;18(6):87-94.
40. Tubaro A, Zilli C, Redaelli C, Loggia RD. Evaluation of antiinflammatory activity of a chamomile extract after topical application. Planta Med. 1984 Aug;50(4):359.
41. 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 Feb;14(2):153-62.
42. Aggag ME, Yousef RT. Study of antimicrobial activity of chamomile oil. Planta Med 1972, 22(2):140144
43. Vilagines P, Delaveau P, Vilagines R. Inhibition of poliovirus growth by Matricaria chamomilla (L.) extract. C R Acad Sci III-Vie 1985, 301:289
44. Al-Ismail KM, Talal A. A Study of the effect of water and alcohol extracts of some plants as antioxidants and antimicrobial on long-term storage of anhydrous butter fat. Dirasat Agric Sci 2003, 30:330-337
45. Nayak BS, Raju SS, Rao AV. Wound healing activity of Matricaria recutita L. extract. J Wound Care. 2007 Jul;16(7):298-302.
46. Cinco M, Banfi E, Tubaro A, Della Loggia R. A microbiological survey on the activity of a hydroalcoholic extract of camomile. Int J Drug Res 1983;21:145-151.
47. Annuk H, Hirmo S, Türi E, Mikelsaar M, Arak E, Wadström T. Effect on cell surface hydrophobicity and susceptibility of Helicobacter pylori to medicinal plant extracts. FEMS Microbiol Lett. 1999 Mar 1;172(1):41-5
48. Gayar F, Shazli A. Toxicity of certain plants to Culex pipens L.larvae (Diptera: Culicidae) Bull Soc Entomol (Egypt) 1968;52:467–75.
49. Chang SM, Chen CH. Effects of an intervention with drinking chamomile tea on sleep quality and depression in sleep disturbed postnatal women: a randomized controlled trial. J Adv Nurs. 2016 Feb;72(2):306-15. doi: 10.1111/jan.12836. Epub 2015 Oct 20.
50. Amsterdam JD, Shults J, Soeller I, Mao JJ, Rockwell K, Newberg AB. Chamomile (Matricaria recutita) may provide antidepressant activity in anxious, depressed humans: an exploratory study. Altern Ther Health Med. 2012 Sep-Oct;18(5):44-9.
51. Amsterdam JD, Li Y, Soeller I, Rockwell K, Mao JJ, Shults J. A randomized, double-blind, placebo-controlled trial of oral Matricaria recutita (chamomile) extract therapy for generalized anxiety disorder. J Clin Psychopharmacol. 2009 Aug;29(4):378-82. doi: 10.1097/JCP.0b013e3181ac935c.
52. Gould L, Reddy CV, Gomprecht RF. Cardiac effects of chamomile tea. J Clin Pharmacol. 1973 Nov-Dec;13(11):475-9.
53. Pasechnik IK. [Choleretic action of Matricaria officinalis].[Article in Russian] Farmakol Toksikol. 1966 Jul-Aug;29(4):468-9.
54. Glowania HJ, Raulin C, Swoboda M. [Effect of chamomile on wound healing--a clinical double-blind study]. [Article in German] Z Hautkr. 1987 Sep 1;62(17):1262, 1267-71.
55. Nayak BS, Raju SS, Rao AV. Wound healing activity of Matricaria recutita L. extract. J Wound Care. 2007 Jul;16(7):298-302.
56. Martins MD, Marques MM, Bussadori SK, Martins MA, Pavesi VC, Mesquita-Ferrari RA, et al. Comparative analysis between Chamomilla recutita and corticosteroids on wound healing. An *in vitro* and *in vivo* study. Phytother Res. 2009 Feb;23(2):274-8. doi: 10.1002/ptr.2612.
57. Jarrahi M. An experimental study of the effects of Matricaria chamomilla extract on cutaneous burn wound healing in albino rats. Nat Prod Res. 2008 Mar 20;22(5):422-7. doi: 10.1080/14786410701591713.
58. Weizman ZVI, Alkrinawi S, Goldfarb DAN, Bitran G. Efficacy of herbal tea preparation in infantile colic. J Pediatr. 1993;122:650–2.
59. de la Motte S, Böse-O'Reilly S, Heinisch M, Harrison F. [Double-blind comparison of an apple pectin-chamomile extract preparation with placebo in children with diarrhea]. [Article in German] Arzneimittelforschung. 1997 Nov;47(11):1247-9.
60. Capasso R, Savino F, Capasso F. Effects of the herbal formulation ColiMil on upper gastrointestinal transit in mice *in vivo*. Phytother Res. 2007 Oct;21(10):999-1101.
61. Forster HB, Niklas H, Lutz S. Antispasmodic effects of some medicinal plants. Planta Med. 1980 Dec;40(4):309-19.
62. Maschi O, Cero ED, Galli GV, Caruso D, Bosisio E, Dell'Agli M. Inhibition of human cAMP-phosphodiesterase as a mechanism of the spasmolytic effect of Matricaria recutita L. J Agric Food Chem. 2008 Jul 9;56(13):5015-20. doi: 10.1021/jf800051n. Epub 2008 Jun 13.
63. European Medicines Agency, Committee on Herbal Medicinal Products (HMPC). Assessment report on Matricaria recutita L., flos and Matricaria recutita L., aetheroleum [Internet]. London: European Medicines Agency; c1995-2016 [updated 2015 Jul 7;cited 2016 Jul 21]. Available from http://www.ema.europa.eu/docs/en_GB/document_library/Herbal_-_HMPC_assessment_report/2016/04/WC500204296.pdf
64. European Medicines Agency, Committee on Herbal Medicinal Products (HMPC). Assessment report on Matricaria recutita L., flos and Matricaria recutita L., aetheroleum [Internet]. London: European Medicines Agency; c1995-2016 [updated 2015 Jul 7;cited 2016 Jul 21]. Available from http://www.ema.europa.eu/docs/en_GB/document_library/Herbal_-_HMPC_assessment_report/2016/04/WC500204296.pdf
65. British Herbal Medicine Association Scientific Committee. British Herbal Pharmacopoeia. Cowling:BHMA; 1983. p.139.