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PHARMACOLOGICAL POTENTIAL OF *MATRICARIA RECUTITA*: RECENT ADVANCES IN CANCER AND FUNGAL THERAPY

Biswajit Dash[1], Pankaj Kumar[2*], Shikha Kaushik[3], Richa Goel[4], Anil Chhetri[5], Kapil Sachan[6], Ajay Kumar

[1]Professor, Department of Pharmaceutical Technology, School of Medical Sciences, Adamas University, Barasat, Kolkata – 700126, West Bengal, India

[2]Professor, Department of Pharmacology, Adesh Institute of Pharmacy and Biomedical Sciences, Adesh University, Bathinda-151001

[3,4,6]KIET Group of Institutions (KIET School of Pharmacy), Delhi NCR, Muradnagar, Ghaziabad, UP, India

[5]Assistant Professor, Department of Pharmacognosy, NEF College of Pharmaceutical Education and Research, Nagaon, Assam, 782001

[7]University Institute of Pharmaceutical sciences, Panjab university, Chandigarh

ABSTRACT

German chamomile, commonly known as *Matricaria chamomilla*, is one of the many species that make up the Asteraceae family. In addition to being present in Australia and North America, chamomile is a native of Europe and western Asia. This study's goal was to assess the effectiveness of topical chamomile in cancer patients' oral mucositis (OM) prevention and/or treatment. German chamomile, commonly known as *Matricaria chamomilla*, is one of the many species that make up the Asteraceae family. In addition to being present in Australia and North America, chamomile is a native of Europe and western Asia. Chamomile, also known as *Matricaria recutita* or *Matricaria chamomilla*, is a fantastic choice for the treatment of yeast infections. This plant has many antifungal substances that provide a severe blow to *Candida* (*Candida* is the yeast that causes yeast infections). Search results revealed 90 publications. All investigations used the same OM measurement scale and the total sample size was 492 patients. The findings demonstrated that topical application of *Chamomile*, at doses ranging from 1% to 2.5% and for durations ranging from one to four times a day, was helpful in the prevention and/or treatment of OM in four of the six investigations.

KEYWORDS: *Matricaria recuitta*, *Chamomilla L*, pharmacognosy, therapeutic effects, Anticancer, Medical plants, Traditional medicine

INTRODUCTION

German Chamomile, also known as Matricaria chamomilla (Syn. Matricaria recutita), is an annual plant; the flower is the most used component. Additionally, chamomile is used cosmetically, primarily as a rinse for blonde hair and as a yellow fabric dye [1]. The idea of using chamomile as medicine is not new; for thousands of years, doctors have employed this herb. Chamomile was used by the ancient Egyptians, Romans, and Greeks to cure a wide range of medical conditions. This beneficial herb can also be used quickly and effectively to treat a yeast infection. The scientific

name for this herb, Matricaria recutita, is also given by the alias Matricaria chamomilla; as a result, both names refer to the same herb, German chamomile [2]. According to Murti, Krishna, and others, chamomile has many different medical applications. It appears that certain of this herb's chemical components are quite effective at preventing various bacteria, fungi, and viruses [3]. The herb chamomile can be taken as a pill, ointment, gel, wash, or oil infusion. It is reported to have analgesic, antioxidant, antibacterial, anti-inflammatory, and antiallergenic properties. The German Commission E has approved chamomile for the treatment of wounds and burns, as well as inflammatory mucocutaneous disorders. Levomenol, matricin, chamazulene, and bisabolol are the main anti-inflammatory ingredients. German chamomile's main volatile oil component, chamazulene, prevents the formation of leukotriene B4 by blocking lipoxygenase and cyclooxygenase, lipid peroxidation, leukocyte infiltration, and histamine release. Levomenol, on the other hand, has moisturising properties that eliminate photodamage symptoms and reduce pruritis [4]. Clinical studies showed that topical chamomile cream was superior to 0.5% hydrocortisone for treating dermatitis and sunburn and that it statistically significantly reduced the wound area and healing time [5]. Since at least the time of Hippocrates, chamomile has been used in herbal treatments for thousands of years. Additionally, it is mentioned in the monographs of the German Commission E, the European Scientific Cooperative on Phytotherapy (ESCOP), and the World Health Organization. It is listed as an official drug in the pharmacopoeias of 26 countries, including Germany, Belgium, France, and the United Kingdom [6]. Through the use and research in both traditional and modern medicine, chamomile has been proven to provide a variety of therapeutic benefits. In traditional medicine, chamomile has been used to treat a variety of illnesses and conditions, including digestive problems, conjunctivitis, dysmenorrhea, colds, coughs, kidney stones, eye infections, headaches, and insomnia colic and nervousness, sinusitis, burns, wounds, ulcers, and stomach aches [7]. Based on its long-standing use, the European Medicines Agency's Committee on Herbal Medicinal Products determined that chamomile flower-based medications can be used to treat the following conditions: minor gastrointestinal (stomach and gut) complaints such as bloating and minor spasms; relieving common cold symptoms; treating minor ulcers (open sores); and inflammation of the mouth and throat, as an add-on treatment for irritation of the skin and area [8]. The most popular way to consume chamomile is as an herbal tea, but it can also be applied topically, taken internally as drops, capsules, or pills, or inhaled. The flower head, which can be prepared and utilised in a variety of ways, is the main component of the chamomile plant that is used for therapeutic and nutraceutical purposes, as was previously indicated. Aqueous, ethanolic, and/or methanolic extracts are produced when dried flower heads are extracted with water, ethanol, or methanol, respectively. The ideal ethanol-to-water ratio for extracts is 1:1. The extracts are dried and used as tablets, capsules, or coated pills; or they are concentrated and added to gels, ointments, and lotions [9]. The most popular way to consume chamomile is as a hot-water infusion (tea), which is made from the dried flower heads. A million cups of chamomile tea are drunk daily, making it one of the most popular single-ingredient herbal beverages in the world. According to the German Commission E monograph, to make chamomile tea, add 150 ml of boiling water to a large spoonful (or roughly 3 g) of flower

heads, soak for 5–10 minutes in a covered cup, and then drain [10]. The process of making tinctures involves homogenising the dried flower heads at room temperature in a 1:5 mixture of ethanol and water. The essential oil of chamomile is also used. Although essential oils can be found in all parts of the plant, the flower head is where they are most commonly used in medicine. In the procedure known as steam distillation or hydro distillation, flower heads are subjected to high pressure, temperature, and steam to obtain the oil. Many pharmacopoeias stipulate that chamomile flower heads used for medical purposes must have at least 0.4% essential oil [11].

PHYTOCHEMICALS IN CHAMOMILE

The main characteristic constituents of chamomile flowers are the essential oil and flavonoid derivatives such as apigenin-7-glucoside. The essential oil contains about 50% of the sesquiterpenes alpha-bisabolol and its oxides A, B, and C, bisaboloneoxide A, up to 25% of cis- and transenin-dicycloethers, and matricine, which is converted into chamazulene during distillation. Other constituents of chamomile flowers include coumarins (herniarin and umbelliferone), phenolic acids, and polysaccharides [12]. A technical consideration by herbal technicians: the **phytocomplex** of common chamomile contains both a series of components of a lipophilic nature, which are soluble in oils and organic solvents (sesquiterpenes contained in the essential oil), and a series of components of a hydrophilic nature, soluble in water and organic solvents (which are flavonoids). The combination of these two groups of substances confers the known **spasmolytic-antiphlogistic activity,** but they must be extracted with an effective **extraction method.** For example, extraction with a 70% hydroalcoholic solvent would be the best method to obtain the phytocomplex in its entirety, both for extracts and tinctures. Chamomile flowers contain a wide range of phytochemicals, the majority of which are used in cosmetics or medicinal preparations [13]. Chamomile contains 0.24–1.9% volatile oil, which turns dark yellow after storage. Approximately 120 secondary metabolites are reported, including 28 terpenoids and 36 flavonoids [14]. The terpenoids -bisabolol and its oxide azulenes, including chamazulene and acetylene derivatives, are the main components of the essential oil extracted from German chamomile flowers. Chamazulene and bisabolol are very unstable and are best preserved in an alcoholic tincture. Roman chamomile contains less chamazulene than German chamomile and is mainly composed of esters of angelic acid and tiglic acid [15]. It also contains farnesene, -pinene, and germacranolide sesquiterpene lactones, primarily nobilin and 3-epinobilin. -Bisabolol, bisabolol oxides A and B, chamazulene or azulenesse, farnesene, and spiro ether quiterpene lactones, glycosides, hydroxycoumarins, flavonoids (apigenin, luteolin, patuletin, and quercetin), coumarins (herniarin and umbelliferone), terpenoids, and mucilage are the major bioactive ingredients [16]. Apigenin and its glycosides are the most promising compounds, having important biological activities. Free apigenin is present in 4–6% of the body, with the rest being present in its glycoside form [17]. Some of the flavonoids identified in *Matricaria chamomilla*, such as apigenin, luteolin, and apiin, are also present in Roman chamomile, as are phenolic carboxylic acids (caffeic and ferulic acids), coumarins, and thiophene derivatives. Chamomile is administered as an oil for infusion, tea, ointment, gel, wash, gargle, or capsule. It is reputed for its antiallergic,

antimicrobial, antiinflammatory, and antioxidant analgesic actions. Chamomile has been approved by the German Commission E for inflammatory mucocutaneous diseases and wound and burn therapy. Bisabolol, chamazulene, levomenol, and matricin are the main anti-inflammatory components [18]. Chamazulene, the major volatile oil constituent of German chamomile, inhibits leukotriene B4 synthesis through inhibiting lipoxygenase and cyclooxygenase, lipid peroxidation, leukocyte infiltration, and histamine release. On the other hand, levomenol possesses hydrating properties to abolish photodamage signs and decrease pruritis [18]. Clinical trials demonstrated that topical chamomile cream was superior to 0.5% hydrocortisone in treating dermatitis and sunburn and statistically significantly decreased the wound area and healing time [19]. Very little is known about the pharmacokinetics of chamomile. Doses in adults vary widely and range from 25 mg to 2000 mg per day. The half-life may be short because it is often recommended to take chamomile three times per day. Usually, chamomile is ingested when brewed as a tea, and tablets are more difficult to locate but may offer better dosage control. Liquid extract is generally dosed at 1–4 ml three times per day (TID), and tincture is dosed at 15 ml three to four times per day (TID or QUID). Children and adolescents should begin with low TID doses and gradually increase while response and adverse effects are closely monitored [20].

Habitat and distribution

Matricaria recutita it is a plant present in many countries. It is a species native to Eurasia, and grows in temperate regions on the rest of the continents. It is distributed from 2250 to 2800 meters above sea level. Especially in Mexico it has been found in Chiapas, Coahuila, Chihuahua, Federal District, Jalisco, Michoacán, Morelos, Oaxaca, Puebla, Potosí, Sinaloa, Tlaxcala, San Luis de Potosí, Veracruz and Zacatecas. It grows on the edge of roads, next to hedges, is cultivated in gardens, and can occasionally behave as a weed [21].

Mechanism of Action

The anti-inflammatory activity of chamomile involves the release of LPS-induced prostaglandin E via inhibition of COX-2 enzyme activity. Methanolic extracts of chamomile exert anti-allergic effects by inhibiting histamine release from mast cells. Neuroprotective activity has occurred via decreased lipid peroxidation and increased superoxide dismutase, catalase, glutathione, and total thiol levels [22]. In hamsters with oral mucositis, topical chamomile reduced tissue IL-1 and TNF-. In another study, a chamomile extract provided gastroprotection against ethanol-induced ulceration by increasing glutathione levels. Apoptosis was induced in an animal model of radiation-induced intestinal mucositis by increased cytosolic cytochrome c and caspase3, as well as depletion of the mitochondrial Bcell lymphoma2/Bax ratio [23]. Apigenin, a flavone component of chamomile, inhibits locomotor behaviour in rats and interacts with GABA(A)-benzodiazepine receptors in vitro [24]. It also affected alternative splicing of key mRNAs by inhibiting dimerization of hnRNPA2, a factor associated with many cellular malignancies and in mRNA metabolism and splicing. Oral chamomile appears to have modest benefits in chronic insomnia, mild cyclic mastalgia and moderate cyclic migraine. Chamomile tea had positive effects on

glycemic control in patients with diabetes [25]. Several studies have reported that chamomile extracts are effective against mild-to-moderate and moderate-to-severe generalised anxiety disorder (GAD). Chamomile may also reduce depressive symptoms in subjects with comorbid GAD and depression and improve biological markers of stress in people with chronic anxiety [26]. In other controlled trials, application of a chamomile compress was effective and superior to hydrocortisone ointment in facilitating healing of peristomal skin lesions following colostomy, and a chamomile oleogel affected pain relief in patients who had migraine without aura. Chamomile has also been evaluated in oral rinses and topical formulations for inflammatory conditions related to cancer treatment. There is conflicting evidence on whether these products can reduce or prevent mucositis [27]. Other preliminary findings suggest some benefit with a chamomile gel in preventing acute radiation dermatitis [28]. Additional studies are needed.

GENERAL PHARMACOLOGICAL ACTIVITIES

Anti-inflammatory

The freeze-dried extracts of camomile (*Matricaria chamomilla* L.) were found to suppress both the inflammatory effect and the leukocyte infiltration. *Matricaria chamomilla* was assessed for its anti-inflammatory activity on intact rats by measuring the suppression of carrageenan-induced paw edoema produced by 1/10 of the intraperitoneal LD50 dose for the 80 percent ethanol extract. Results showed that the plant possessed good anti-inflammatory activity [29]. Immunomodulatory activity Intragastric and parenteral administration of *Matricaria chamomilla* L. heteropolysaccharides was found to normalise the development of the immune response during air cooling and to enhance (but not normalize) this process during immersion cooling. The immunomodulating effect of the heteropolysaccharides upon cooling is attributed to the initiation of immunostimulant properties of heavy erythrocytes (macrocytes), activation of immunoregulation cells in peripheral blood, and increased sensitivity of effector cells to helper signals [29]. This mite species is responsible for otoacariasis in domestic animals. Mites were exposed to the extracts for 24 hours, 48 hours, or 72 hours. All the extracts tested showed highly significant acaricidal activity when compared with controls. Among them, a decoction of 10% was the only formulation that gave 100% activity at all three observation times [30]. Anti hyperglycemic *Matricaria chamomilla* L. ethanolic extract treatment protected the majority of the pancreatic islet cells with respect to the control group. As a result, *Matricaria chamomilla* L. ethanolic extract exhibited a significant antihyperglycemic effect and protected beta-cells in STZ-diabetic rats in a dose-dependent manner and diminished the hyperglycemia-related oxidative stress [31]. Cancer-fighting properties. The aqueous and methanolic extracts of chamomile showed differential apoptosis in cancer cells but not in normal cells at similar doses.

Antipruritic effect

The single oral administration of the ethyl acetate extractor essential oil of German chamomile (*Matricaria recutita* L.) showed remarkable antipruritic effects in the compound 48/80-induced scratching test in ddY mice [32].

Wound healing property

The aqueous extract of *M. recutita* (120 mg/kg/day) showed an increased rate of wound contraction, together with increased wound-breaking strength and hydroxyproline content. The chamomile extract in the form of rubbing oil had a good potential for accelerating burn wound healing in rats [33]. The extract of *M. chamomilla* administered topically has wound-healing potential in a linear incisional wound model in rats. Animals treated with chamomile presented significantly faster wound healing in comparison to those treated with corticosteroids. Treatment of oral mucositis Methotrexate-induced oral mucositis in a patient with rheumatoid arthritis was successfully treated with wild chamomile mouthwashes [34].

Intracanal irritant

Chamomile or tea tree oil was effective in removing the smear layer. Treatment of infant botulism Chamomile (principally, unwrapped chamomile) is an apotencial vehicle of *C. botulinum* spores, and ingestion of chamomile tea could represent a risk for infant *botulism. Locicidal*, ovicidal, and repellent properties *Matricaria chamomilla* essential oil has lousicidal, ovicidal, and repellent efficacy against lice and flies infesting water buffalo. Virucidal agent Camomile oil exhibited a high selectivity index and seems to be a promising candidate for topical therapeutic applications as virucidal agents for the treatment of herpes genitalis [35]. Treatment of gastrointestinal disorders Methanol extracts of *Matricaria recutita* (flowers) and Ginkgo biloba (leaves) had a MIC > 100 microg/mL against the gram-negative bacterium Helicobacter pylori (HP).

Antimicrobial activity: Essential oil of and *M. chamomila* was found to be effective against three strains of S. aureus and two strains of Candida, and it can be used to treat acute otitis externa [36]. Antiulcer activity Extracts from the plants Iberis amara, Melissa officinalis, *Matricaria recutita*, *Carum carvi, Mentha x piperita, Glycyrrhiza glabra, Angelica archangelica, Silybummarianum*, and *Chelidonium majus*, singly and combined in the form of a commercial preparation, STW-5 (Iberogast), All extracts produced a dose-dependent anti-ulcerogenic activity associated with a reduced acid output, increased mucin secretion, an increase in prostaglandin E2 release, and a decrease in leukotrienes [37].

A significant reduction in mean total Hamilton Anxiety Rating (HAM-A) scores was observed during chamomile versus placebo therapy (P = 0.047). Prevent osteoporosis The aqueous extracts derived from *Marticaria chamomilla* may form the basis for the design of "functional foods" for the prevention of osteoporosis. *M. chamomila* is a popular medicinal plant useful for various ailments. A number of old Ayurvedic texts have mentioned the tremendous benefits and variety of uses of *Matricaria recutita*. Today, evidence-based studies are needed to establish these facts so that these wonder drugs with their multifarious therapeutic activities can be put to human use [38].

Anticarcinogenic activity

Chamomile, peppermint, and rooibos teabags were tested for their anticancer activity. High levels of dehydro PAs were shown its carcinogenic activity. In an animal study, the artery intimal proliferation after balloon injuries were studied. Anticancer activity of this plant showed through the dynamic expressions of proteins after a balloon injury during intimal proliferation [39].

Antimicrobial activity

The antimicrobial activity of chamomile was assessed, and it showed that chamomile MrBBS incorporate enantiopure (-)--bisabolol as a terpene and are triggered to produce (-)--bisabolol. The antioxidant properties of chamomile ethanolic extracts were examined. Its antioxidant property was confirmed by the presence of a high concentration of rosmarinic acid. The antibacterial effect of the fractions of chamomile was evaluated against two gram-negative bacteria. Results confirmed its antibacterial effect through its main essential oil components, including coumarin, flavonoids, phenolic acids, and fatty acids. Hypersensitivity reactions, including asthma, contact dermatitis, and anaphylaxis, can occur following exposure to chamomile [40].

Case reports

Premature constriction of foetal ductus arteriosus: following consumption of chamomile tea by the mother during pregnancy [31]; Severe anaphylaxis: generalised urticaria, angioedema, and severe dyspnea in a 38-year-old Caucasian man, 1 hour after consuming chamomile tea. Symptoms improved following treatment with IV antihistamines [18].

Pollen-food allergy syndrome: A 65-year-old Japanese woman with mugwort allergies experienced hives, vomiting, and shortness of breath 30 minutes after drinking chamomile tea. About a dozen other cases of allergic reactions to chamomile have also been associated with mugwort pollen allergies [32]. The patient was advised to avoid all chamomile-containing products. Multiple internal haemorrhages in a 70-year-old woman following concurrent use of chamomile products and warfarin Her symptoms resolved after treatment with intravenous heparin. Occupational allergic rhino conjunctivitis caused by inhaling dried chamomile flowers. Increased lactogenesis and breast tension: in a lactating woman, a few hours after consuming chamomile [39].

Conclusions

Chamomile has the potential to be used in cancer treatment. Chamomile has been used as an herbal medication since ancient times, is still popular today, and probably will continue to be used in the future. Establishing whether CAM therapies are beneficial to patients will require research and the generation of scientific evidence. Without such evidence, it will remain unclear whether these untested and unproven medical treatments are truly beneficial to patients. Clearly, some patients report improvements, but it is unclear whether the improvements are due to medication, spontaneous disease remission, or a placebo. Scientists play an important role in conducting studies and helping the public understand the benefits of CAM therapies. Very few CAM therapies have undergone rigorous scientific testing. Clinicians should await reports of well-conducted scientific research, including clinical studies of various herbs that clearly demonstrate the efficacy of CAM, before recommending such treatments to their patients. Chamomile, an herb that has been familiar

to practitioners and in common use for centuries in traditional herbal medicine, has recently been receiving attention from the scientific community about more clearly defining its potential usefulness as a therapeutic entity for a variety of maladies.

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