International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

A Review on Therapeutic Applications of Chamomile

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ABSTRACT:
Chamomile (Matricaria chamomilla), a widely recognized medicinal herb from the Asteraceae family, is valued for its therapeutic applications. Known for its anti-inflammatory, antioxidant, antimicrobial, and anxiolytic properties, chamomile plays a significant role in traditional and modern medicine. Its chemical profile comprises essential oils, flavonoids, and terpenoids, which contribute to its pharmacological effects. This review highlights its potential benefits across various domains, including nervous system disorders, metabolic conditions, cardiovascular health, skin ailments, and its anticancer properties. Emphasis is laid on its bioactive components, including apigenin and bisabolol, which exhibit diverse mechanisms such as anti-proliferation, anti-inflammatory modulation, and antioxidant effects. . Chamomile remains a cornerstone in herbal medicine, offering promising therapeutic interventions for global health challenges.

Keywords:
Chamomile, Matricaria Chamomilla, Medicinal herb, Therapeutic applications, Apigenin, α-Bisabolol , Interleukin -10 (IL10) , T-helper Type 1 or 2 Cell (Th1 or Th2) Tumor Necrosis Factor (TNF), Diphenyl-1- picrylhydrazyl (DPPH), Ferric Reducing Antioxidant Power(FRAP)

INTRODUCTION:

The term Chamomile is derived from Greek, meaning “Ground apple”, which reflects its characteristics of an apple-like fragrance, Bansal, et al., 2010[2]. Matricaria Chamomilla, commonly known as chamomile, is a well recognized medicinal herb from the Asteraceae family. The flowers of the chamomile plant smell like apples. The chamomile is an annual plant adaptable to various soil types and is resilient in colder climates. Originating in Southern and Eastern Europe as well as part of Northern and Western Asia Lim, et al., 2014 [20]. Chamomile is now cultivated worldwide. Chamomile is highlighted as one of the most frequently utilized medicinal herbs, well documented for its healing properties. Singh, et al., 2011 [29]. Chamomile is among the oldest and most widely recognized medicinal plants on the globe. The chamomile herb was introduced by the Mughals in India. The plant is extensively utilized in various industries, including pharmaceuticals, cosmetics, perfumes, and food flavouring, due to its growing use of its essential oil. Bahmani, et al., 2015[1]. Traditionally, Chamomile [M. Chamomilla] has been used as

an anti-inflammatory, antioxidant and mild astringent and also used to produce chamomile tea by Chauhan, et al., 2017[5]. The Chamomile has played a significant role in human health for thousands of years with herbal remedies being integral to both traditional and contemporary medical practices for over 5000 years. This enduring legacy contributes to the continued use of herbal treatments, which is appreciated for their gradual effect and low toxicity its Srivastava, et al., 2010[32]. There are 120 chemical constituents that are extracted from the chamomile essential oil. These is helpful for the application of M. Chamomilla in a medicinal context EI Joumaa, et al.,2022[7]. Research on animal models and human subjects has highlighted the chamomile's therapeutic potential in managing nervous system problems, reproductive health issues, metabolic disease, cardiovascular problems, obesity, skin disorders, gastrointestinal disorders, Hassanpour, et al., 2023[12].

Fig.1 Matricaria Chamomilla

Common name and biological source

Botanical name: Matricaria Chamomilla**Family**: Asteraceae

Local name: Chamomile**Common name:**

Hindi: Babune ka phool / Babuna**Sanskrit Name**: Babunaka

Other name: German Chamomile, Roman Chamomile, English Chamomile, Hungarian Chamomile, Single Chamomile, Camomilla, Flos Chamomile, Scented Mayweed Sah.A et al;2022 [26].

Geographical sources of Matricaria Chamomilla

Chamomile is cultivated and sourced globally, but its quality and characteristics often depend on the geographical origin. Here are the primary geographical sources of chamomile:

1. Europe

- **Germany:** Known as the largest producer of Matricaria chamomilla (German chamomile), producing high-quality chamomile for medicinal and cosmetic purposes.
- **Hungary:** Renowned for chamomile with a high essential oil content.

- **Poland:** A significant source of medicinal-grade chamomile.
- **Bulgaria:** Produces chamomile with excellent essential oil properties.
- **Romania:** Cultivates chamomile for therapeutic and aromatic use.

2. Asia

- **India:** Chamomile is grown primarily in the Himalayan region (Himachal Pradesh, Uttarakhand) for herbal tea and essential oils.
- **Iran:** Produces high-quality chamomile used in traditional medicine and aromatherapy.
- **Turkey:** A significant producer, with chamomile used in traditional Turkish medicine.

3. Africa

- **Egypt:** A leading producer of chamomile, particularly valued for its export quality, essential oils, and floral tea blends.
- **Morocco:** Grows chamomile used in cosmetics and pharmaceuticals.

4. Americas

- **United States:** Cultivates chamomile, primarily in the Pacific Northwest, for commercial herbal teas and oils.
- **Mexico:** Produces chamomile used in traditional medicine and herbal teas.

5. Other Regions

- **Argentina:** A prominent producer in South America, exporting chamomile for medicinal purposes.
- **Australia:** Cultivates chamomile for essential oils and herbal products.

Morphological Characteristics of Matricaria Chamomilla:

The morphological characteristics of Matricaria Chamomilla [German Chamomile], commonly known as chamomile, are essential for its identification and understanding its growing habits. Here are the key features:

- Plant type: Chamomile can be either an annual or perennial plant, which means it can complete its life cycle in one year or live for multiple years, respectively. This adaptability allows it to thrive in various climates, particularly temperate regions of Asia and Europe.
- Height and Structure: The stems of chamomile can grow between 10 and 80 cm tall. They are typically straight and slender, contributing to the plant's overall upright appearance [Fig 2 a].
- Leaves: The leaves of chamomile are long, narrow, and pinnate, which means they are divided into smaller leaflets arranged on either side of a central stem. This leaf structure is characteristic of many plants in the Asteraceae family, to which the chamomile belongs.
- Roots: Chamomile has thin, spindle-shaped roots that grow straight down into the soil. This root structure helps the plant absorb nutrients and water effectively [Fig 2 c].
- Flowers: The flowers of the chamomile are typically daisy-like, with white petals surrounding a yellow central disc. These flowers are not only visually appealing but also play a crucial role in attracting pollinators [Fig 2 b].

  In summary, Matricaria chamomilla exhibits distinct morphological characteristics, including its height, leaf structure, root type, and flower appearance, which are important for its identification and cultivation. Understanding these features can aid in the effective use and study of chamomile in both traditional and modern medicinal contexts, Dai et al.; 2022[9].

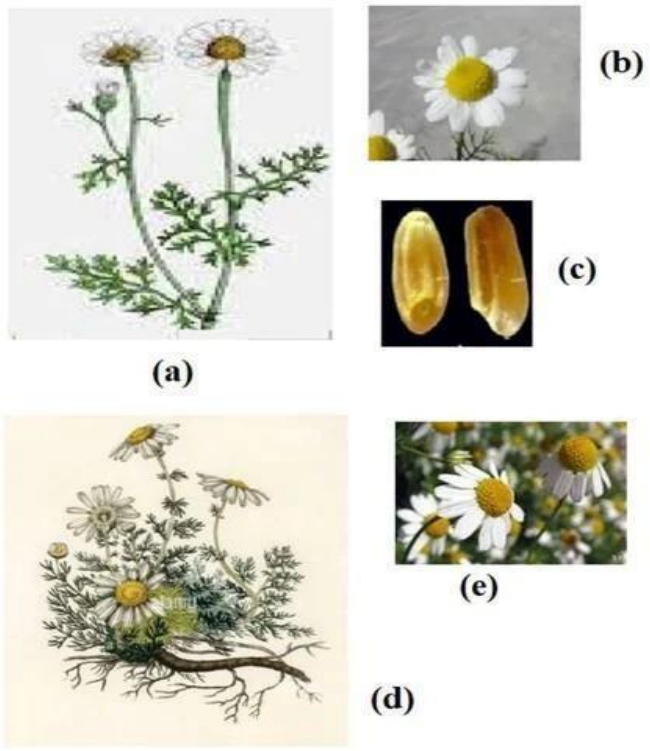
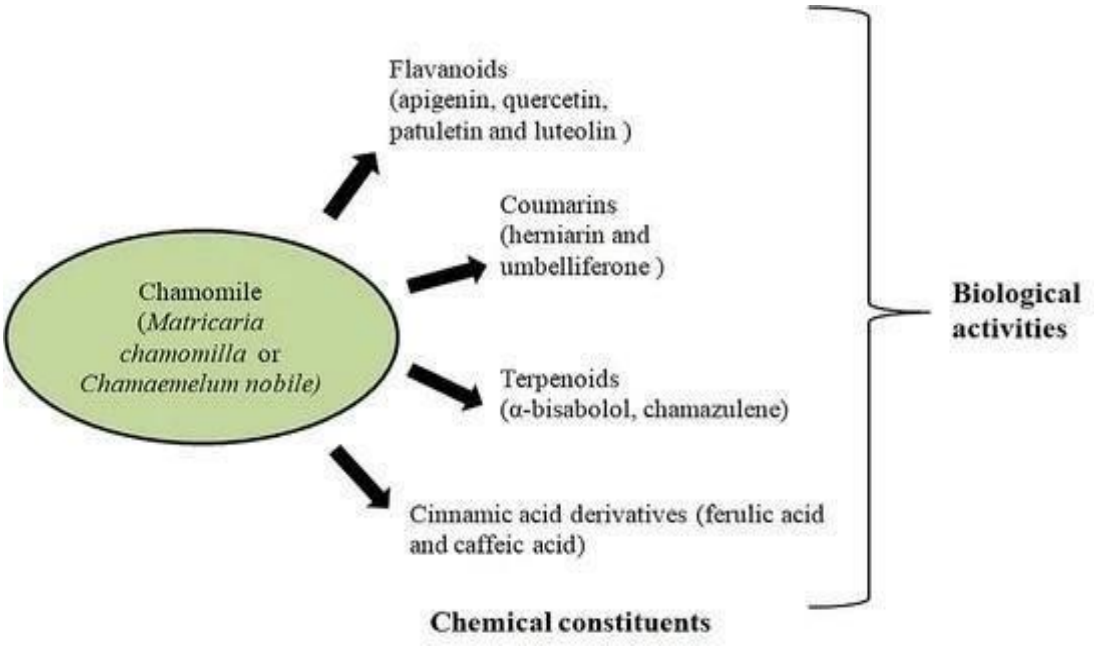


Figure 2: Morphology of German and Roman chamomile. The figure showsGerman chamomile plant (a), its flower head (b), seeds (c), Roman chamomile plant (d), and its flower head (e).

CHEMICAL CONSTITUENTS:

Biological applications of chamomile are related to its chemical components. The active constituents are mainly present in fresh or dried flowers; therefore, infusions or essential oils are used in medicinal preparations. The flower yields a maximum of 2% of volatile oil, which houses more than 120 constituents. The main constituents of the oil include terpenoids, mainly sesquiterpenes and bisabolol Pino et al., 2002[25]. The components present in essential oil, chamazulene, bisabolol, and cis-farnesene, are hydrophobic in nature. Chamazulene is not naturally present, but proazulene and matricin present in chamomile flower heads are known to degrade into chamazulene during steam distillation processes. Other components such as flavonoids, coumarins, and phenolic acids are water-soluble and, hence, exert therapeutic effects when chamomile is consumed as tea by Catani et al.; 2021[4]. The major flavonoids present is apigenin, quercetin, patuletin, and luteolin in concentrations of 16.8%, 9.9%, 6.5%, and 1.9%, respectively, of course, again depending on the species and cultivation. Approximately, 28 terpenoids and 36 flavonoids have been isolated from different varieties of chamomile. The coumarins present are herniarin and umbelliferone at 0.1% concentration. Mulinacci et al; 2000[22]. Investigated the presence of 39% cinnamic acid derivatives such as ferulic acid and caffeic acid. An author claimed that leaves also house chemical components such as terpenoids, phenolic compounds, flavonoids, tannins, and phytosterols by Chauhan et al.; 2018[6]. Organic acids contain carboxylic acid, and sulfonic acid functional groups. A total of 26 organic acids have been isolated from chamomile, among which four acids are primary metabolites and are essential compounds for the growth and development of living organisms. Wang et al. ;2016[36]

Fig 3. Chemical Constituents



THERAPEUTIC APPLICATION OF CHAMOMILE:

Anti-Inflammatory Activity:

The anti-inflammatory properties of M. chamomilla extracts have been documented in the literature. The findings from this investigation indicate that the anti-inflammatory efficacy of the ethanolic extract of M. chamomilla on macrophages was linked to a reduction in nitric oxide synthesis and cell viability, whereas its impact on lymphocytes was associated with the stimulation of anti-inflammatory cytokine production (IL-10) alongside a decline in cell viability. Conversely, the aqueous extract of M. chamomilla resulted in a decrease in nitric oxide synthesis and an enhancement in cell viability among macrophages, while simultaneously serving as an effective suppressor of T helper Th2 cells by perturbing the Th1/Th2 equilibrium. The disparity observed between these two extracts may be ascribed to the variation in their respective active compounds. In a separate investigation, Singh et al. explored the anti-inflammatory characteristics of M. chamomilla tea extract. The outcomes indicated that the extract effectively inhibited protein denaturation and stabilized human erythrocyte membranes, thereby underscoring its anti-inflammatory capabilities. Singh et al.; 2018[30]. The anti-inflammatory properties of Matricaria chamomilla were also examined through the use of animal models. Both the volatile and non-volatile constituents of Matricaria chamomilla, encompassing essential oil, flower water, and aqueous extract, exhibit a substantial capacity to mitigate edema in mouse auricles induced by xylene, as well as pedal edema in rats instigated by carrageenan, and the elevation of celiac capillary vessel permeability in mice. Furthermore, these components demonstrated a noteworthy inhibitory influence on the escalation of prostaglandin E2 and nitric oxide concentrations in rat pedal edema induced by carrageenan Ortizet al;2017[23] Moreover, the implications of Chamomile hydro alcoholic extract on the levels of inflammatory biomarkers in the bloodstream were examined in a rat model by Nargesi et al. Administration of 110 mg/kg of the hydroalcoholic extract effectively mitigated a notable elevation in serum concentrations of Tumor Necrosis Factor (TNF-α), C- Reactive Protein (CRP), Interleukin 6 (IL-6), and fibrinogen. Conversely, the synergistic effects of the ethanolic extract in conjunction with diclofenac or indomethacin, both of which are classified as non-steroidal anti-inflammatory agents,

demonstrated compelling synergistic anti-inflammatory properties in the context of carrageenan-induced paw inflammation and gastric injury in rats by Ionita et al.; 2018[14].

Antioxidant Activity:

The activities of antioxidants and anti-inflammatory agents are interrelated phenomena. Free radicals are generated within cellular and tissue environments during standard physiological processes and fulfill critical roles essential for proper biological function. Nonetheless, an overabundance of free radicals can be detrimental, as it may lead to oxidative stress, resulting in cellular, lipidic, and protein damage. Concurrently, oxidative stress stimulates the upregulation of cyclooxygenase (COX) and lipooxygenase (LOX) enzymes, which subsequently activate the release of inflammatory mediators. Numerous investigations have been undertaken that substantiate the antioxidant properties of chamomile. For example, Wang et al.; 2020[37]. Numerous investigations have examined the antioxidant properties of M. chamomilla essential oil, extracts, and cell suspension culture. These studies employed a variety of assays, including DPPH, ABTS, FRAP, beta-carotene bleaching, ferrous ion chelation capacity, and inhibition of lipid peroxidation. Additionally, the activities of several enzymes were evaluated, specifically catalase, acetylcholinesterase, glutathione peroxidase, ascorbate peroxidase, and superoxide dismutase. The DPPH assay is recognized as the most prevalent method for evaluating antioxidant activity. Utilizing this assay, M. chamomilla essential oil demonstrated the highest DPPH scavenging efficacy following a 90-minute reaction period by Stanojevic et al.; 2016[34].

The herbal extract demonstrated a pronounced attenuation of reactive oxygen species (ROS) concentrations, with the most significant impact observed at a dosage of 1000 mg/ml. The most widely recognized biomarker for oxidative stress is 8-iso-prostaglandin F2 (8-iso-PGF2), which is generated from the peroxidation of ROS. A notable decrease in 8-iso-PGF2 unequivocally indicated the radical scavenging capabilities of chamomile. Moreover, a 50% decrease in prostaglandin E2 (PGE2) levels was recorded, which is associated with the suppression of cyclooxygenase (COX) activity. In addition, the investigator also assessed the anti-inflammatory properties utilizing a lipopolysaccharide (LPS) induced model. A substantial decrease in tumor necrosis factor (TNF) and interleukin-6 (IL-6) was noted, suggesting the presence of anti-inflammatory effects. This research indicates that the chamomile possesses the potential for application in the context of colorectal cancer. Although these investigations have not pinpointed the specific chemical constituents responsible for the antioxidant activity, Parham et al.; 2020[24].

Anti-Allergic Activity:

The presence of allergic diseases has been increasing worldwide. Mast cells are present in most organs and tissues, and their activation triggers the release of histamine; inflammatory mediators such as leukotrienes, prostaglandins, and proteases; and pro-inflammatory cytokines. In a study by Chandrashekhar et al.; 2011[7]. The induction of allergy was accomplished through the administration of compound 48/80, a known mast cell activator, and subsequently treated with the standard pharmacological agent, disodium chromoglycate (control), alongside a methanolic extract of chamomile. The chamomile extracts, administered at concentrations of 300 mg/kg, demonstrated a significant inhibition of mast cell degranulation, achieving an efficacy rate of 73.3% in comparison to 67.75% noted for disodium chromoglycate. Furthermore, histamine levels exhibited a marked reduction in the treated groups relative to the control cohort. Additionally, the levels of nitric oxide (NO) in serum, peritoneal, and bronchoalveolar fluids were evaluated, revealing a reduction of nearly three-fold with standard treatment modalities, while chamomile extracts at a dosage of 300 mg/kg yield a maximal reduction of five-fold by

Lee et al.; 2010 [19]. Another researcher evaluated the therapeutic effectiveness of topical chamomile oil in the context of 2, 4-dinitrochlorobenzene-induced allergic dermatitis. Notably, serum levels of IgE and IgG1, as well as histamine concentrations, exhibited a significant decrease after four weeks and two weeks of chamomile oil application, respectively, by Lee et al.; 2010[19]. As a traditional remedy, chamomile is commonly employed to alleviate diverse allergic manifestations. For instance, antiallergic herbal tea demonstrates beneficial anti-allergic properties and cosmetic effects when consumed over an extended period by Chandrashekhar et al.; 2011[7].

Anti-Microbial Activity:

Research has indicated that chamomile possesses bisabolol, which imparts it with anti-microbial characteristics. It has demonstrated efficacy against both Gram-positive and Gram-negative bacterial strains. The antibacterial capabilities were investigated by Kazemian et al.; 2018[15]. Wounds were induced through incision with a blade and subsequently exposed to Pseudomonas aeruginosa strains. Chamomile and tetracycline ointments were then administered, and the outcomes were systematically compared. It was observed that the cohort receiving chamomile treatment exhibited diminished wound healing durations (5.3 days) in contrast to the antibiotic cohort (6.3 days).

The management of any microbial infection frequently becomes exceedingly challenging due to the formation of biofilms. Biofilms consist of intricately organized microbial cells that encapsulate themselves within a self-generated extracellular matrix. They contribute to bacterial or fungal resistance, rendering eradication nearly unattainable. Research has additionally indicated that the chamomile possesses the capacity to disrupt biofilms. An in vitro investigation was conducted wherein tissue specimens exhibiting multi-drug resistance to P. aeruginosa were gathered and cultivated in a soya broth medium. A diluted methanolic chamomile extract was employed, and the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) were ascertained through broth microdilution methodologies. A chamomile extract volume of 50 µL and 150 µL of bacterial inoculums were introduced into 96- well microtiter plates and incubated at 37 °C for 24 hours. The MIC and MBC were determined to be 12.5-50 mg/mL and 25 mg/L, respectively. The biofilm inhibition assay was also performed, revealing that chamomile extracts in the concentration spectrum of 1.6 to 100 mg/mL demonstrated inhibition of the biofilm. Koch et al.; 2008 [18].

Various concentrations of chamomile oil, specifically 16 g/mL, 32g/mL, 125 g/mL, and 250 g/mL, were subjected to experimental analysis. It was determined that the oil exhibited toxicological effects exclusively at the maximum concentration. Moreover, the investigator conducted evaluations of antibacterial efficacy against Gram-negative bacterial strains, including Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, and Enterobacter aerogenes, as well as Gram-positive strains such as Staphylococcus aureus, taking into account both methicillin-resistant and methicillin-susceptible characteristics, in addition to Enterococcus faecalis. The minimum inhibitory concentration (MIC) for all evaluated strains was ascertained to be greater than 1000 µg/mL. In the assessment of synergistic interactions, an additive effect was identified when combined with amoxicillin and doxycycline against Staphylococcus aureus, while a synergistic effect was noted with penicillin V in relation to Pseudomonas aeruginosa. Similarly, an alternative investigation documented that chamomile acetone extracts exhibited enhanced antimicrobial activity against Staphylococcus aureus and Candida albicans in comparison to conventional antibiotics by Chaves et al.; 2020[18].

Analgesic activity:

In a research endeavor conducted by Chaves et al., the analgesic efficacy of a crude extract of chamomile

was evaluated through formal assays. Chamomile was delineated based on its composition, which included polysaccharides, arabinose, galactose, xylose, and uronic acid. A significant reduction in nociception (by 96%) was noted when administering a dosage of 30 mg/kg in contrast to the control group receiving 10 mL/kg of saline solution, thus indicating its analgesic properties Srivastava et al.; 2007[33].

Anti-Cancer Activity:

Chamomile extracts are characterized by their anticancer properties. The authors conducted an investigation into the effects of these extracts on human prostate cancer cell lines. Both aqueous and methanolic extracts demonstrated a dose-dependent decrease in cell viability, with reductions ranging from 6% to 37%; notably, the responses were more significant in the case of methanolic extracts. Moreover, the underlying mechanism of action was explored, revealing a three-fold increase in apoptosis induced by methanolic extracts. The anti-proliferative effects were further examined, yielding IC50 values of 1650–4000 µg/mL for aqueous extracts and 165-300 µg/mL for methanolic extracts, respectively Srivastava et al.; 2007[33].

The ethanolic extract's impact was evaluated by a separate researcher for its anti-proliferative efficacy against the human hepatoma cancer cell line. An IC50 value of 300 g/mL was determined, alongside DPPH scavenging activities of 94% at a concentration of 1.5 mg/mL. The analysis of the chemical constituents indicated substantial levels of polyphenols and flavonoids. A diverse array of clinical cancer models has been employed to explore the anticancer properties of chamomile, demonstrating effectiveness against various forms of cancer including breast cancer, lung cancer, skin cancer induced by ultraviolet B (UV-B), oral carcinogenesis, and colon cancer, among others. A comprehensive investigation highlighted that apigenin serves as the principal component accountable for anticancer effects through mechanisms involving apoptosis, anti-proliferation, and autophagy by Sung et al.; 2016 [35].

Glioma represents a prevalent category of malignant intracranial neoplasms characterized by a significant incidence rate, rapid proliferation, elevated recurrence frequency, high mortality rates, and a generally unfavorable prognosis. A-Bisabolol, a lipophilic sesquiterpene compound abundantly present in Chamomile essential oil, has been empirically demonstrated to possess the capacity to influence glioma. Yan et al. conducted an investigation into the effects of a-bisabolol on human glioblastoma cell lines (U251 and U87) utilizing scratch assay methodology. The study sought to elucidate its impact on cellular migration and invasion. Protein expression analysis was performed employing Western blot techniques. The findings indicated that a-bisabolol effectively inhibited the migratory and invasive capabilities of glioblastoma cells through the downregulation of central mucoepidermoid tumor (c-Met) expression. Furthermore, a-bisabolol oxide A and apigenin-7-B-D-glucoside, extracted from the flowers and stems of chamomile, have been reported to impede the migration of Caco-2 colon cancer cells and to inactivate the vascular endothelial growth factor receptor-2 (VEGFR2) angiogenic enzymes Shaaban et al.; 2022[27]. Chamomile, when subjected to fermentation with Lactobacillus plantarum for a duration of 72 hours, demonstrated a preferential cytotoxic effect on cancerous cells in contrast to normal cells, specifically the medical research council cell strain 5 (MRC-5) Sung et al.; 2016 [35].

Central-Nervous-System-Related Disorders:

Chamomile tea has historically been utilized for promoting tranquility and addressing sleep-related disorders. Certain researchers have indicated that the sedative properties can be attributed to a flavonoid known as apigenin, which is present in chamomile. Apigenin functions by engaging with the benzodiazepine receptors located within the brain. The sedative effects were evaluated through the examination of locomotor activity in murine models, utilizing diazePAM as a control. A dose-dependent

reduction in locomotor activity was documented, with optimal effects observed at a dosage of 30 mg/kg of the chamomile crude extract. Typically, mice exhibit anxiolytic behavior by burying aversive stimuli. The quantity of marbles buried was assessed, revealing a significant reduction following the administration of chamomile, thereby indicating potential antianxiety effects Shaaban et al; 2022[27]. A recent investigation has indicated that the chamomile possesses the capacity to markedly reduce anxiety in a zebrafish light-dark test paradigm. Through gas chromatography-mass spectrometry (GC-MS) analyzes, it was determined that the principal constituents identified were pentadecyl-3-methyl-2-butenoate, hexadecyl-3- methyl-2-butenoate, 1-piperidinol, and trans-1-ethyl-3-methyl-cyclopentane Silveira et al.; 2022[31]. Chamomile has been identified to contain compounds that are significant in the context of central nervous system disorders, including epilepsy and Alzheimer's disease. In a research investigation conducted by Hashemi and colleagues, convulsions were provoked through the administration of kainic acid, followed by the oral administration of apigenin at a dosage of 50 mg/kg over a period of 6 days. The intervention resulted in a notable reduction in both the initiation and intensity of seizures. Immunohistochemical evaluations indicated that apigenin mitigated neurodegeneration by enhancing the population of viable neurons within the hippocampus. Furthermore, the study demonstrated that apigenin effectively ameliorates memory impairments associated with epilepsy. The chronic presence of oxidative stress is implicated as a catalyst for neurodegenerative processes. Given its properties as a natural antioxidant, chamomile exhibits the capacity to neutralize free radicals, thereby presenting potential efficacy in the management of neurological pathologies such as Alzheimer's disease, Parkinson's disease, and cerebral ischemia, Kim et al.; 2019[17].

Anti-Hypertensive Activity:

Chamomile extracts are recognized for their antihypertensive properties. The chamomile extract was administered orally at a dosage of 200 mg/kg to normotensive rats. It was observed that this treatment resulted in a significant decrease in both systolic and diastolic blood pressure, as well as heart rate. Subsequently, the identical dosage was provided for hypertensive rats induced by a high salt-sucrose diet, which again exhibited a significant reduction in blood pressure (BP) and heart rate. Mechanistic studies indicated that this effect was attributed to a 38% decrease in the activity of angiotensin-converting enzyme (ACE). Moreover, comparative analyzes with the standard antihypertensive medication, captopril, demonstrated that chamomile exhibited superior efficacy. A comprehensive investigation was undertaken by another researcher who examined the potential of apigenin as a possible antihypertensive agent Gao et al.; 2021 [11]. Chronic inflammation and oxidative stress are intricately associated with the pathogenesis of hypertension, which subsequently contributes to cardiac hypertrophy induced by hypertension. The administration of apigenin at a dosage of 20 g/h over a period of four weeks resulted in a significant decrease in both hypertension and heart rate. Furthermore, there was a marked reduction in the levels of oxidative stress indicators, including reactive oxygen species (ROS) and superoxide dismutase (SOD). Additionally, levels of inflammatory cytokines, specifically IL-1, TNF, and IL-6, were also diminished. The findings of the study substantiate that apigenin functions as an antihypertensive agent via the modulation of nicotinamide adenine dinucleotide phosphate hydrogen (NADPH) oxidase-dependent ROS production and inflammatory pathways Shebbo et al.; 2020[28].

Hepatoprotective Properties:

To establish the hepatoprotective effects of chamomile, 1,2-dimethylhydrazine was administered to rats to induce hepatic toxicity, following the assessment of liver enzyme levels, including aspartate transaminase (AST) and alanine transaminase (ALT). The results indicated that treatment with aqueous

extracts of chamomile led to a reduction in the levels of AST and ALT by 33% to 37%. Moreover, pre-treatment with chamomile prior to the induction of toxicity exhibited a protective effect. A comprehensive investigation suggested that chamomile exerts its protective effects by modulating cyclooxygenase-2 (COX-2) and nitric oxide synthase (NOS), both of which are pro-inflammatory enzymes. Additionally, the hepatoprotective effects may also be attributed to the antioxidant properties displayed by chamomile through the modulation of SOD and glutathione peroxidase Shebbo et al.; 2020 [28].

Protective Effects on Metabolic Syndrome:

It has been posited that elevated levels of reactive oxygen species (ROS) are correlated with the differentiation of adipocytes. A comprehensive examination of blood and adipose tissue demonstrated increased levels of lipid peroxidation, along with protein and DNA oxidation byproducts. The constituents of chamomile function as natural antioxidants; consequently, they assume an crucial role in the treatment of metabolic disorders, including obesity. Furthermore, ethanolic extracts of chamomile provide protective benefits to pancreatic cells in diabetic rat models exposed to ROS. Aqueous extracts have also been observed to diminish fasting glucose concentrations and exhibit moderate antihyperglycemic effects. Additionally, anti-lipidemic properties have been identified in aqueous extracts, as they were shown to lower serum cholesterol levels in hyperlipidemic rat populations; in a study involving Roman chamomile, six novel octulosonic acid derivatives were isolated and subsequently evaluated for their anti-inflammatory properties. Bayliak etal; 2021 [3]. The resultant compounds facilitated the inhibition of inducible nitric oxide synthase (iNOS) and consequently curtailed the production of reactive oxygen species (ROS). Inflammation serves as a significant risk factor in the pathogenesis of metabolic disorders, including obesity and cardiovascular complications. Accordingly, additional investigations were undertaken to ascertain their role in the activation of peroxisome proliferator-activated receptors (PPAR), peroxisome proliferator-activated receptors (PPAR), and liver X receptor (LXR). These receptors are regarded as pivotal factors in the orchestration of lipid and carbohydrate metabolism. The constituents exhibited a 1-2 fold enhancement in the activity of PPAR, PPAR, and LXR. Furthermore, it resulted in a 50% reduction in the activity of nuclear factor kappa B (NF-κB), strongly suggesting anti-inflammatory mechanisms. Although German chamomile has not been examined with respect to these compounds, it warrants investigation to elucidate its potential effects on metabolic disorders by Hajaji et al; 2018 [13].

Other Therapeutic Applications:

Chamomile has demonstrated therapeutic efficacy in various other medical conditions. For example, the essential oil derived from chamomile was evaluated for its amebicidal properties against Acanthamoeba castellanii Neff. The IC50 values for the essential oil ranged between 20.83 and 92.01, which are relatively elevated in comparison to the standard antiamoebic agent chlorhexidine (2.643 ± 0.55), indicating that the essential oil exhibits cytotoxicity toward amoebic cells while exhibiting minimal toxicity to the murine macrophage cell line. The elucidation of the mechanism of action revealed that bisabolol present in chamomile essential oils caused the leakage of intracellular contents by enhancing the permeability of the plasma membrane, thereby inducing apoptosis. In a similar vein, its efficacy as an antileshmanial agent has also been substantiated, as another study investigated the anti-pruritic effects of chamomile essential oil, which resulted in reduced scratching behavior in animal models compared to controls receiving fexofenadine (10 mg/kg) chamomile Hajaji et al.; 2018 [13]. The administration of essential oils via oral routes demonstrated a dose-dependent response, with the most plausible explanation being the antihistaminic properties manifested by bisabolol oxide A, as evidenced by chemical analyzes. Furthermore, chamomile has been recognized for its therapeutic applications in alleviating premenstrual

syndrome, given that its effectiveness as an analgesic has already been thoroughly examined by Khalesi et al.; 2019[16].

Conclusion:

Chamomile has established itself as a potent medicinal herb with diverse therapeutic applications. Its efficacy in treating inflammatory conditions, metabolic syndromes, neurodegenerative diseases, and certain cancers underscores its potential in integrative medicine. The herb's versatility lies in its chemical richness, especially its flavonoids and terpenoids, which mediate its bioactivity. Chamomile also presents fewer side effects compared to synthetic drugs, making it a viable option for long-term use in managing chronic ailments. However, further clinical trials and research are essential to standardize its use and confirm its efficacy in broader medical applications. Chamomile stands as a testament to the enduring relevance of traditional medicine in addressing modern health issues.

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