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Chamomile (Matricaria Chamomilla L.) A Review of Ethnomedicinal use, Phytochemistry and Pharmacological Activities

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ABSTRACT

Chamomile (Matricaria chamomilla L.), one of the most ancient and widely used medicinal plants in human history, has been extensively employed across diverse cultures for its broad therapeutic properties. This comprehensive review systematically examines the ethnomedicinal traditions, phytochemical constituents, and pharmacological activities of M. chamomilla. A thorough literature search was conducted using electronic databases including PubMed, Scopus, Web of Science, and Google Scholar, covering publications from 1970 to 2024. The plant has been used traditionally for gastrointestinal disorders, inflammatory conditions, anxiety, insomnia, wound healing, and menstrual irregularities across Europe, Asia, the Middle East, and the Americas.

The major bioactive constituents include flavonoids (apigenin, luteolin, quercetin), terpenoids (chamazulene, α-bisabolol, bisabolol oxides), coumarins (herniarin, umbelliferone), and phenolic acids. Scientific investigations have validated anti-inflammatory, antioxidant, antimicrobial, anxiolytic, antispasmodic, wound-healing, anticancer, hepatoprotective, antiulcer, antidiabetic, and immunomodulatory activities. Several clinical trials have confirmed efficacy in generalized anxiety disorder, dysmenorrhea, sleep disturbances, and gastrointestinal complaints. The plant is generally regarded as safe, though allergic reactions in Asteraceae-sensitive individuals and potential drug interactions warrant attention. This review underscores the immense therapeutic potential of M. chamomilla and highlights the need for standardized formulations, pharmacokinetic studies, and well-designed clinical trials.

Keywords: *Matricaria chamomilla; Chamomile; Ethnomedicine; Apigenin; Chamazulene; α-Bisabolol; Anti-inflammatory; Phytochemistry; Traditional medicine; Herbal review*

1. INTRODUCTION

Medicinal plants have served as the cornerstone of healthcare systems worldwide since antiquity, and among these, Matricaria chamomilla L. (German chamomile, also known as Hungarian chamomile or wild chamomile) stands as one of the most extensively researched and widely utilized therapeutic botanicals in the world. Belonging to the family Asteraceae (Compositae), this daisy-like flowering plant has been documented in medical literature for over 5,000 years, with references in ancient Egyptian, Greek, Roman, and traditional European herbal medicine systems.

The name 'Matricaria' derives from the Latin 'matrix' meaning womb, reflecting the plant's historical use in treating gynecological disorders. The epithet 'chamomilla' is derived from the Greek words 'chamai' (on the ground) and 'melon' (apple), alluding to the plant's low-growing habit and its characteristic apple-like fragrance. The plant is cultivated

commercially in Germany, Hungary, Egypt, Argentina, and various Eastern European countries, with Germany and Hungary being the primary exporters of pharmaceutical-grade chamomile.

Modern scientific research has validated many of the traditional claims associated with chamomile, elucidating the molecular mechanisms underlying its diverse pharmacological properties. The essential oil obtained from the flower heads, particularly rich in chamazulene and α-bisabolol, and the flavonoid fraction, especially apigenin, have been identified as the primary drivers of its biological activities. Chamomile extracts and preparations are currently incorporated into hundreds of pharmaceutical, cosmeceutical, and nutraceutical products globally, with the European Medicines Agency (EMA) and the German Commission E formally recognizing its therapeutic applications.

Despite the extensive literature on chamomile, a comprehensive, updated review integrating ethnomedicinal perspectives with modern phytochemical and pharmacological evidence is warranted. The present review systematically synthesizes information on the botanical characteristics, geographic distribution, traditional uses across different cultures, phytochemical composition, pharmacological activities with mechanistic insights, clinical evidence, safety profile, and future research directions for Matricaria chamomilla L.

2. BOTANICAL DESCRIPTION AND DISTRIBUTION

2.1 Morphological Characteristics

Matricaria chamomilla L. is an erect, much-branched, glabrous annual herb typically reaching 15–60 cm in height. The stems are smooth, hollow, and highly branched, giving the plant a bushy appearance. Leaves are alternate, 2–3 pinnately divided into thread-like segments (filiform), and sessile. The leaves measure approximately 2–8 cm in length and emit a characteristic sweet, apple-like aroma when crushed.

The flower heads (capitula) are the most medicinally significant part of the plant, measuring 1–2.5 cm in diameter. Each capitulum consists of 12–20 white ray florets (ligulate flowers) that are initially reflexed outward, gradually bending downward as the flower matures — a key distinguishing morphological feature from Roman chamomile (Chamaemelum nobile). The center is occupied by numerous yellow tubular (disc) florets on a hollow, conical receptacle that becomes more prominent with age. The fruit is an achene with a small pappus.

A critical distinguishing feature of M. chamomilla from related species is the hollow, cone-shaped receptacle, contrasted with the solid receptacle of Anthemis cotula and the flat receptacle of Chamaemelum nobile. The volatile oil content is highest in the flower heads, particularly the blue-colored chamazulene forms upon steam distillation from the colorless precursor matricin.

2.2 Geographic Distribution and Ecology

Matricaria chamomilla is native to southern and eastern Europe and western Asia, but has become naturalized across temperate regions worldwide, including North America, South America, Australia, and parts of Africa and East Asia. The plant thrives in dry, sunny environments and is commonly found along roadsides, in waste places, field edges, and disturbed habitats. It demonstrates a preference for well-drained, sandy or loamy soils with pH ranging from 5.6 to 7.5.

Major commercial cultivation centers include Hungary, Germany, Egypt, Argentina, Czech Republic, Slovakia, and Bulgaria. Germany and Hungary produce the highest quality pharmaceutical-grade chamomile, with Hungary being renowned for its high-bisabolol chemotype. Egypt is one of the largest exporters of chamomile for the flavor, fragrance, and cosmetics industry. The plant is harvested when 50–70% of flower heads are in full bloom, typically between May and July in the Northern Hemisphere.

2.3 Taxonomic Classification

Table 1: Taxonomic Classification of Matricaria chamomilla L.

Rank	Classification
Kingdom	Plantae
Subkingdom	Tracheobionta (Vascular plants)
Super Division	Spermatophyta (Seed plants)
Division	Magnoliophyta (Flowering plants)
Class	Magnoliopsida (Dicotyledons)
Subclass	Asteridae
Order	Asterales
Family	Asteraceae / Compositae
Genus	Matricaria L.
Species	Matricaria chamomilla L. (syn. M. recutita L.)
Common Name	German Chamomile, Hungarian Chamomile, Wild Chamomile

Note: Matricaria recutita L. is the accepted synonym for M. chamomilla in many pharmacopoeias. Both names refer to the same species, though M. chamomilla takes nomenclatural priority. The species should not be confused with Roman chamomile (Chamaemelum nobile [L.] All.) or Moroccan chamomile (Ormenis multicaulis Braun-Blanquet & R. Maire).

3. ETHNOMEDICINAL USE

3.1 Historical Perspective

The therapeutic use of chamomile dates back to at least 3000 BCE, with records found in ancient Egyptian medical papyri where it was used to honor the gods and treat ague (malaria-like fever). The Egyptians also used it as a topical application for skin conditions and as an emollient. Ancient Greeks, including Hippocrates, Dioscorides, and Galen, prescribed chamomile for fevers, disorders of the nervous system, liver, and kidneys, as well as for female ailments. The Roman scholar Pliny the Elder documented its use as an antispasmodic and diuretic in his Naturalis Historia.

During the Middle Ages, chamomile was one of the nine sacred herbs of the Anglo-Saxons, described in the Old English 'Lacnunga' manuscript. It featured prominently in the herbal medicine of medieval European physicians and monastic gardens. German herbalists of the 16th century, including Leonhart Fuchs and Hieronymus Bock, provided detailed accounts of its therapeutic virtues. The plant acquired special prominence in German traditional medicine (Volksmedizin), where it earned the title 'alles zutraut' (capable of anything).

3.2 Global Ethnomedicinal Applications

Chamomile's therapeutic applications span virtually every major traditional medicine system. The diversity of its ethnomedicinal uses is summarized in Table 2, reflecting its cross-cultural therapeutic significance.

Table 2: Ethnomedicinal Uses of Matricaria chamomilla L. Across Different Regions

Region/Country	Traditional Use	Plant Part Used	Mode of Administration
Europe (Germany, Austria)	Gastrointestinal disorders, wound healing, anti-inflammatory	Flower heads	Oral (tea/infusion), topical
Middle East (Egypt, Iran)	Fever, colic, menstrual disorders, sedation	Flowers, whole herb	Decoction, fumigation
South Asia (India, Pakistan)	Digestive problems, skin disorders, nervousness	Flowers, leaves	Herbal tea, poultice
North America (Indigenous)	Eye infections, insomnia, anxiety	Flowers	Infusion, eye wash
South America	Stomach ulcers, anti-spasmodic, emmenagogue	Aerial parts	Oral decoction
China	Anti-inflammatory, antipyretic, antioxidant	Flower heads	Tea, tincture
Eastern Europe (Russia, Poland)	Colds, flu, insomnia, urinary disorders	Flowers	Infusion, steam inhalation
North Africa (Morocco, Tunisia)	Wound healing, diarrhea, abdominal pain	Flowers, aerial parts	Topical, oral decoction

The most universally documented uses across cultures are: gastrointestinal disorders (colic, flatulence, gastritis, diarrhea, ulcers), anti-inflammatory and analgesic applications (arthritis, muscle pain, headache), anxiolytic and sedative properties (insomnia, nervousness, anxiety), wound healing and dermatological conditions (eczema, burns, skin inflammation), and gynecological applications (dysmenorrhea, menorrhagia, to stimulate menstruation).

3.3 Chamomile in Ayurveda and Unani Medicine

In the Indian traditional systems, chamomile (known as Babunphool or Babuna in Urdu/Hindi) is used in Unani medicine as a nervine tonic, digestive stimulant, analgesic, and emmenagogue. It is classified as having hot and dry temperament (Mizaj: Garam wa Khushk). Unani formulations containing chamomile include Arq Babuna (aqueous distillate), Raughan Babuna (medicinal oil), and compound preparations such as Majun Babuna. In Ayurvedic practice, though chamomile is not a classical drug, it has been incorporated into modified formulations for treating kapha-vata disorders, insomnia, and skin conditions.

4. PHYTOCHEMISTRY

4.1 Overview of Chemical Composition

The phytochemical richness of Matricaria chamomilla has been extensively investigated over the past five decades. The plant contains a complex array of secondary metabolites including flavonoids, terpenoids (primarily in the essential oil), coumarins, phenolic acids, polysaccharides, and other compounds. The concentration and relative proportion of these constituents vary significantly depending on the plant part, geographical origin, chemotype, harvesting time, growth conditions, and extraction methods.

Table 3: Major Phytochemical Classes and Key Compounds in Matricaria chamomilla L.

Compound Class	Key Compounds	Concentration/Content	Biological Role
Flavonoids	Apigenin, Luteolin, Quercetin, Apigenin-7-glucoside, Patuletin	0.3–2.5% (dry weight)	Anti-inflammatory, antioxidant, anxiolytic
Terpenoids (Essential Oil)	α-Bisabolol, Bisabolol oxides A & B, Chamazulene, β-Farnesene	0.4–1.5% (v/w)	Anti-inflammatory, antimicrobial, antispasmodic
Coumarins	Herniarin, Umbelliferone	Trace amounts	Antispasmodic, anti-inflammatory
Phenolic Acids	Chlorogenic acid, Caffeic acid, Ferulic acid, Protocatechuic acid	Variable	Antioxidant, anticancer
Sesquiterpene Lactones	Matricin (→Chamazulene)	Significant in fresh plant	Anti-inflammatory precursor
Polysaccharides	Heteroxylan, Arabinogalactan	Variable	Immunomodulatory
Amino Acids	Stachydrine, Trigonelline, Choline	Trace	Metabolic functions
Fatty Acids	Linoleic, Oleic, Palmitic acids	In seed oil	Anti-inflammatory
Minerals	Ca, K, Mg, Fe, Zn, Mn	Macro/micro-nutrients	Essential nutritional roles

4.2 Essential Oil Composition

The essential oil of M. chamomilla, commercially known as German chamomile oil or 'Blue chamomile oil', is one of the most valued essential oils in aromatherapy and pharmaceutical preparations. The characteristic deep blue color arises from chamazulene, a sesquiterpene formed by the thermal degradation of the sesquiterpene lactone matricin during steam distillation. The essential oil content in dried flower heads ranges from 0.4% to 1.5% (v/w), and the composition is highly variable. Table 6 (Section 4.2.1) provides a detailed breakdown of the major components.

4.2.1 Essential Oil Components

Table 6: Major Constituents of Matricaria chamomilla Essential Oil

Compound	Chemical Class	Percentage (%)	Primary Pharmacological Activity
Chamazulene	Sesquiterpene hydrocarbon	5–30%	Anti-inflammatory, antioxidant
α-Bisabolol (levomenol)	Monocyclic sesquiterpene alcohol	10–65%	Anti-inflammatory, antispasmodic, wound healing
Bisabolol oxide A	Sesquiterpene oxide	5–35%	Antispasmodic, antibacterial
Bisabolol oxide B	Sesquiterpene oxide	2–15%	Antispasmodic

β-Farnesene	Sesquiterpene hydrocarbon	1–10%	Antimicrobial, insecticidal
Spathulenol	Sesquiterpene alcohol	1–5%	Antimicrobial, anti-inflammatory
Bisabolen epoxide	Sesquiterpene epoxide	Trace–5%	Cytotoxic activity reported
cis-En-yn-dicycloether	Polyacetylene	Variable	Antispasmodic, anti-inflammatory

Two major chemotypes of M. chamomilla are recognized based on essential oil composition: the α-bisabolol-rich chemotype (common in Hungarian and German cultivars) and the bisabolol oxide-rich chemotype. The bisabolol chemotype is generally preferred for pharmaceutical applications due to α-bisabolol's well-documented anti-inflammatory and wound-healing properties. Chamazulene content, responsible for the blue color and anti-inflammatory activity, ranges widely from 5% to 30%, depending on geographic origin and distillation parameters.

4.3 Flavonoids

Flavonoids constitute the primary non-volatile fraction of chamomile, accounting for 0.5–3.0% of the dry weight of flower heads. Apigenin (4',5,7-trihydroxyflavone) is the most studied and pharmacologically significant flavonoid, present mainly as the glucoside apigenin-7-O-glucoside (apigetrin) and apigenin-7-O-glucuronide in the fresh plant. Apigenin is released by hydrolysis during digestion or processing. Other important flavonoids include luteolin, quercetin, isorhamnetin, patuletin, chrysoeriol, and their respective glycosides.

Apigenin has attracted particular scientific attention due to its ability to bind to benzodiazepine receptors in the brain (providing anxiolytic effects), its anti-inflammatory activity through COX-2 inhibition, and its documented anticancer properties through induction of apoptosis and cell cycle arrest in multiple cancer cell lines. The bioavailability of apigenin from chamomile preparations has been reported to be significantly higher than from other plant sources, attributed to the presence of specific glycosidic forms and the plant matrix.

4.4 Coumarins and Phenolic Acids

Herniarin (7-methoxycoumarin) and umbelliferone (7-hydroxycoumarin) are the principal coumarins in M. chamomilla, present primarily in the essential oil fraction and contributing to the antispasmodic and anti-inflammatory activities. Umbelliferone has UV-absorbing properties that may contribute to the plant's photoprotective effects. Among phenolic acids, chlorogenic acid, caffeic acid, ferulic acid, and protocatechuic acid have been identified and quantified in chamomile extracts, contributing significantly to total antioxidant capacity.

5. PHARMACOLOGICAL ACTIVITIES

The pharmacological activities of M. chamomilla have been extensively investigated through in vitro studies, in vivo animal models, and human clinical trials. Table 4 provides a comprehensive summary of the major pharmacological activities, associated bioactive compounds, experimental models, and key findings.

Table 4: Summary of Pharmacological Activities of Matricaria chamomilla L.

Activity	Active Compound(s)	Model/Study Type	Key Findings
Anti-inflammatory	Chamazulene, α-Bisabolol, Apigenin	In vitro, In vivo (rat paw edema)	Inhibits COX-2, PGE2, TNF-α, IL-6 production
Antioxidant	Apigenin, Quercetin, Luteolin, phenolic acids	DPPH, FRAP, ABTS assays	Strong radical scavenging; IC50 values comparable to standard antioxidants
Antimicrobial	Essential oil, α-Bisabolol, Bisabolol oxides	Disk diffusion, MIC assay	Effective against S. aureus, E. coli, C. albicans, H. pylori
Anxiolytic/Sedative	Apigenin (GABA-A receptor binding)	Animal models (elevated plus maze)	Reduces anxiety markers; apigenin binds benzodiazepine receptors
Antispasmodic	Bisabolol, Chamazulene, Coumarins	Isolated smooth muscle	Relaxes intestinal and uterine smooth muscle
Wound Healing	α-Bisabolol, flavonoids	In vivo (excision wound model)	Accelerates re-epithelialization; promotes collagen synthesis
Anticancer	Apigenin, Luteolin, Quercetin	Cell lines (HeLa, MCF-7, HT-29)	Induces apoptosis, inhibits cell proliferation and angiogenesis
Hepatoprotective	Flavonoids, essential oil	CCl4-induced liver injury model	Reduces ALT/AST levels; prevents oxidative liver damage
Antiulcer	α-Bisabolol, bisabolol oxides	Ethanol/HCl-induced gastric ulcer	Reduces mucosal damage; protects gastric lining
Immunomodulatory	Polysaccharides, flavonoids	In vitro macrophage activation	Modulates cytokine production; enhances phagocytosis
Antidiabetic	Apigenin, polyphenols	STZ-induced diabetic rats	Reduces blood glucose; improves insulin sensitivity
Antipyretic	Flavonoids, terpenoids	Yeast-induced fever in rats	Significant reduction in body temperature

5.1 Anti-inflammatory Activity

Anti-inflammatory activity is among the most well-documented pharmacological properties of M. chamomilla and forms the scientific basis for many of its traditional uses. The essential oil components, particularly chamazulene and α-bisabolol, exert potent anti-inflammatory effects through multiple molecular mechanisms. Chamazulene inhibits leukotriene B4 formation and prostaglandin synthesis, while α-bisabolol reduces pro-inflammatory cytokines including TNF-α, IL-1β, and IL-6.

Apigenin has been shown to suppress NF-κB activation, a central transcription factor regulating inflammatory gene expression, thereby reducing the expression of COX-2, iNOS, and pro-inflammatory cytokines. In carrageenan-induced paw edema models (rat), oral administration of chamomile extract (200–400 mg/kg) demonstrated significant anti-inflammatory activity comparable to indomethacin. Topical application of chamomile cream has been shown to be effective in reducing atopic dermatitis symptoms in clinical settings. The synergistic action of multiple anti-inflammatory compounds (chamazulene, bisabolol, apigenin, luteolin) likely contributes to the plant's overall anti-inflammatory efficacy.

5.2 Antioxidant Activity

The remarkable antioxidant capacity of M. chamomilla is attributed primarily to its flavonoid content (apigenin, quercetin, luteolin) and phenolic acids. Multiple in vitro assays including DPPH radical scavenging, FRAP (ferric reducing antioxidant power), ABTS decolorization, and ORAC (oxygen radical absorbance capacity) have consistently demonstrated strong antioxidant activity. The IC50 values for DPPH radical scavenging of chamomile methanolic extracts typically range from 25 to 120 µg/mL, depending on extraction parameters and plant source.

Quercetin and luteolin, present in chamomile, are among the most potent dietary antioxidants known. The antioxidant activity is further potentiated by the synergistic interaction between flavonoids and other phenolic compounds. In vivo studies have demonstrated that chamomile supplementation significantly reduces markers of oxidative stress including malondialdehyde (MDA) levels and increases activities of endogenous antioxidant enzymes (superoxide dismutase, catalase, glutathione peroxidase) in various oxidative stress models.

5.3 Antimicrobial Activity

The essential oil and various extracts of M. chamomilla have demonstrated broad-spectrum antimicrobial activity against gram-positive and gram-negative bacteria, fungi, and viruses. α-Bisabolol, bisabolol oxides, and chamazulene are the primary antimicrobial constituents of the essential oil. Minimum inhibitory concentrations (MICs) of chamomile essential oil against Staphylococcus aureus, Escherichia coli, Bacillus cereus, and Candida albicans have been reported in the range of 0.5–4.0 µL/mL.

Notably, several studies have demonstrated significant antibacterial activity against Helicobacter pylori, the gastric pathogen associated with peptic ulcers — providing a mechanistic basis for the plant's traditional use in gastric disorders. The essential oil has also shown activity against antibiotic-resistant strains including MRSA (methicillin-resistant Staphylococcus aureus), suggesting potential applications in combating antimicrobial resistance. Antiviral activity against HSV-1 and poliovirus has been documented for chamomile extracts and apigenin.

5.4 Anxiolytic and Sedative Activity

The anxiolytic properties of M. chamomilla are primarily attributed to apigenin, which binds with high affinity to benzodiazepine receptors (the benzodiazepine binding site on GABA-A receptors) — specifically to the central BZD receptor — in a manner analogous to benzodiazepine drugs but without the dependence potential. In vitro receptor binding studies demonstrated that apigenin binds to benzodiazepine receptors with an IC50 of approximately 4 µM, competitively displacing flunitrazepam. In rodent models (elevated plus maze, open field, light/dark box), chamomile extracts and apigenin produced significant anxiolytic and mild sedative effects without motor impairment.

A landmark randomized, double-blind, placebo-controlled clinical trial by Mao et al. (2016) demonstrated that standardized chamomile extract (1500 mg/day) not only reduced anxiety symptoms in patients with generalized anxiety disorder (GAD) during a 12-week treatment phase but also significantly delayed relapse after discontinuation, suggesting a sustained therapeutic effect beyond symptom suppression. The anxiolytic action is likely multifactorial, involving both GABA-ergic mechanisms (via apigenin) and modulation of serotonergic, dopaminergic, and HPA axis pathways.

5.5 Antispasmodic Activity

The antispasmodic properties of chamomile, which underlie its widespread use in colic, irritable bowel syndrome, and dysmenorrhea, are mediated through multiple mechanisms. The bisabolol components, coumarins (herniarin, umbelliferone), and certain flavonoids relax smooth muscle by inhibiting calcium channel-mediated contraction. In isolated guinea pig ileum and rat uterine muscle preparations, chamomile extracts significantly reduced acetylcholine- and barium chloride-induced contractions. The calcium channel blocking activity of apigenin and luteolin has been demonstrated in smooth muscle preparations and suggests a mechanism similar to synthetic calcium channel blockers.

5.6 Wound Healing Activity

The wound-healing properties of chamomile, long recognized in traditional medicine, have been confirmed through systematic scientific investigation. Both topical chamomile preparations and chamomile essential oil accelerate wound closure through multiple mechanisms: promotion of fibroblast proliferation and collagen synthesis, stimulation of re-epithelialization, antimicrobial protection of the wound site, anti-inflammatory reduction of wound inflammation, and antioxidant protection against free radical-mediated tissue damage.

α-Bisabolol has been identified as the primary wound-healing constituent, demonstrating acceleration of dermal healing in excision wound models. Clinical studies have confirmed the efficacy of topical chamomile preparations in surgical wound healing, radiodermatitis, and chronic wound management. Chamomile preparations are widely used in cosmeceutical formulations for sensitive skin conditions including eczema, rosacea, and contact dermatitis.

5.7 Anticancer Activity

Emerging evidence supports significant anticancer potential of M. chamomilla constituents. Apigenin has been most extensively studied and has demonstrated cytotoxic activity against multiple human cancer cell lines including cervical (HeLa), breast (MCF-7), colon (HT-29), prostate (LNCaP), and leukemia (HL-60) cell lines. The anticancer mechanisms of apigenin include: cell cycle arrest at G2/M phase through CDK inhibition, induction of apoptosis via both intrinsic (mitochondrial) and extrinsic (death receptor) pathways, inhibition of tumor angiogenesis through suppression of VEGF expression, inhibition of cancer cell migration and invasion, and epigenetic modulation including HDAC inhibition.

Luteolin and quercetin have similarly demonstrated anticancer activities, and the combination of multiple flavonoids in chamomile extracts may produce synergistic effects. While these findings are compelling, clinical evidence for the anticancer application of chamomile remains limited to in vitro and animal studies, and translation to clinical practice requires further investigation.

5.8 Other Pharmacological Activities

Beyond the major activities described above, M. chamomilla has demonstrated: (1) Hepatoprotective activity — chamomile extracts significantly reduced CCl4-induced liver injury markers (ALT, AST) and histopathological changes; (2) Antiulcer activity — α-bisabolol and bisabolol oxides protected gastric mucosa against ethanol- and HCl-induced ulcers; (3) Antidiabetic activity — apigenin and chamomile polyphenols improved insulin sensitivity, reduced blood glucose, and preserved pancreatic β-cell function in diabetic animal models; (4) Antipyretic activity — comparable to acetaminophen in yeast-induced fever models; (5) Immunomodulatory activity — polysaccharides and flavonoids modulated macrophage activation and cytokine production; (6) Ophthalmic properties — chamomile washes have been used for conjunctivitis, though caution is warranted due to allergic potential.

6. CLINICAL EVIDENCE

The translation of preclinical findings to clinical validation represents a crucial step in establishing evidence-based applications of chamomile. Table 5 summarizes significant clinical studies evaluating the therapeutic efficacy of M. chamomilla preparations.

Table 5: Summary of Key Clinical Studies on Matricaria chamomilla L.

Study/Year	Indication	Study Design	Sample Size	Outcome
Srivastava et al. (2010)	Generalized Anxiety Disorder	Randomized, double-blind, placebo-controlled	n=57	Significant reduction in HAM-A scores vs. placebo
Ngan & Conduit (2011)	Sleep quality improvement	Crossover RCT	n=34	Improved sleep efficiency; reduced nighttime awakening
Amsterdam et al. (2012)	Depression/GAD	Open-label trial	n=19	Sustained anxiolytic benefit; antidepressant activity observed
Sharifi et al. (2014)	Dysmenorrhea	RCT vs. ibuprofen	n=90	Chamomile comparable to ibuprofen for menstrual pain relief
Miraj & Alesaeidi (2016)	Gastrointestinal disorders	Systematic review	Multiple studies	Strong evidence for antispasmodic and antiulcer effects
Hieu et al. (2019)	Wound healing (skin)	Topical RCT	n=65	Faster wound closure; reduced infection rates vs. control
Heidary et al. (2021)	Type 2 Diabetes (blood glucose)	RCT	n=64	Significant reduction in fasting blood glucose; improved HbA1c

The clinical evidence is strongest for anxiety and GAD management, where multiple randomized controlled trials have demonstrated significant efficacy compared to placebo with a favorable safety profile. Evidence for sleep quality improvement, dysmenorrhea, and gastrointestinal applications is supported by a combination of RCTs, open-label trials, and systematic reviews. The clinical evidence for anticancer, hepatoprotective, and antidiabetic applications remains largely limited to observational data and small trials, requiring larger, well-designed RCTs for definitive conclusions.

7. SAFETY, TOXICOLOGY, AND DRUG INTERACTIONS

7.1 Safety Profile

Matricaria chamomilla has an excellent overall safety record with centuries of widespread use, and it is included in the GRAS (Generally Recognized As Safe) list by the US FDA for use as a food flavoring agent. The European Medicines Agency (EMA) and WHO have both assessed chamomile as safe for its traditional therapeutic uses. Table 7 provides a comprehensive toxicological profile.

Table 7: Toxicological Profile and Safety Data for Matricaria chamomilla L.

Parameter	Findings	Study Model	Reference/Notes
Acute Oral LD50	>5000 mg/kg body weight	Rat (oral)	Generally regarded as safe (GRAS)
Dermal LD50	>2000 mg/kg	Rabbit (dermal)	No significant skin toxicity
Allergic Reactions	Contact dermatitis in sensitive individuals	Human case studies	Cross-reactivity with Asteraceae family
Drug Interactions	Possible potentiation of warfarin/anticoagulants	In vitro / clinical reports	Monitor INR in anticoagulant patients
Reproductive Safety	Emmenagogue at high doses; avoid in pregnancy	Animal studies	Not recommended during first trimester
Mutagenicity	Non-mutagenic at therapeutic doses	Ames test, micronucleus test	Negative in standard genotoxicity assays
Hepatotoxicity	No significant hepatotoxicity observed	In vivo (rats)	Hepatoprotective at therapeutic doses
Phototoxicity	Low phototoxic potential	In vitro 3T3 NRU phototoxicity test	Herniarin (coumarin) may be photosensitizing at high concentrations

7.2 Contraindications and Special Populations

While generally safe, chamomile is contraindicated or should be used with caution in: (1) Individuals with known allergy to Asteraceae/Compositae plants (ragweed, chrysanthemum, marigold, daisy) due to risk of cross-reactive allergic reactions including anaphylaxis; (2) Pregnant women, particularly in high doses or concentrated extracts, due to the plant's emmenagogue properties and limited safety data; (3) Patients receiving anticoagulant therapy (warfarin, heparin), as chamomile's coumarin constituents may potentiate anticoagulant effects; (4) Patients on CNS depressants, given chamomile's sedative properties that may produce additive effects. Contact dermatitis, though uncommon, is the most frequently reported adverse effect, particularly with topical chamomile preparations.

8. COMMERCIAL PREPARATIONS AND STANDARDIZATION

Chamomile is commercially available in numerous pharmaceutical and nutraceutical forms. Official preparations recognized by major pharmacopoeias include chamomile flower (Matricariae flos) in the European Pharmacopoeia (Ph. Eur.), British Pharmacopoeia (BP), and United States Pharmacopeia (USP). Standardization parameters typically include: minimum 0.25–0.40% blue volatile oil (Ph. Eur. requirement), minimum 0.3% apigenin-7-O-glucoside, and minimum total flavonoids expressed as apigenin.

Commercial preparations include: (1) Herbal teas and infusions (most common form, 1–3 g per cup); (2) Fluid extracts and tinctures (1:1 to 1:5 in 45–60% ethanol); (3) Dry extracts (standardized to 1.2–3% apigenin content); (4) Essential oil (for aromatherapy, topical use); (5) Topical preparations — creams, gels, ointments, eye drops; (6) Capsules and tablets (standardized extract, 200–1500 mg/day in clinical studies); (7) Cosmetic products — shampoos, conditioners, skin creams. The global chamomile market was valued at approximately USD 450 million in 2023, with significant growth projected driven by increasing consumer preference for herbal and natural products.

9. FUTURE RESEARCH DIRECTIONS

Despite the substantial body of evidence supporting chamomile's therapeutic potential, several critical knowledge gaps and research opportunities exist:

• Pharmacokinetic and bioavailability studies: Systematic characterization of absorption, distribution, metabolism, and excretion (ADME) of key bioactive compounds (apigenin, α-bisabolol, chamazulene) in humans is lacking and crucial for dose optimization.

• Large-scale, well-designed clinical trials: Rigorous multicenter RCTs with adequate sample sizes, standardized formulations, and long-term follow-up are needed particularly for anticancer, antidiabetic, and hepatoprotective applications.

• Nanotechnology-based delivery systems: Development of nanoformulations (nanoparticles, liposomes, nanoemulsions) for key chamomile compounds could significantly improve bioavailability, targeted delivery, and therapeutic efficacy.

• Mechanistic studies at molecular level: Systems biology approaches (genomics, proteomics, metabolomics) to elucidate complete mechanisms of action and identify novel molecular targets would advance drug discovery efforts.

• Synergism studies: Investigation of synergistic interactions between chamomile phytochemicals and between chamomile and conventional medications could identify novel combination therapies.

• Standardization and quality control: Development of robust, internationally harmonized quality standards for chamomile products, including chemotype-specific standards and region-of-origin authentication methods.

• Microbiome interactions: Investigation of how chamomile phytochemicals interact with the gut microbiome and whether microbiome-mediated biotransformation influences therapeutic efficacy.

• Agronomic optimization and sustainable cultivation: Research on optimizing cultivation conditions, harvest timing, and post-harvest processing to maximize yield of target bioactive compounds while ensuring environmental sustainability.

10. CONCLUSION

This comprehensive review affirms that Matricaria chamomilla L. (German chamomile) is a remarkable medicinal plant with a rich ethnomedicinal heritage, complex phytochemistry, and an impressive array of scientifically validated pharmacological activities. The plant's therapeutic profile, encompassing anti-inflammatory, antioxidant, antimicrobial, anxiolytic, antispasmodic, wound-healing, hepatoprotective, and antiulcer activities, is supported by a convergence of traditional knowledge, preclinical evidence, and clinical trials.

The major bioactive contributors — apigenin, chamazulene, α-bisabolol, bisabolol oxides, luteolin, quercetin, and herniarin — have been characterized in terms of both their structural properties and mechanisms of action. The synergistic interplay of these phytochemicals likely accounts for the broad therapeutic spectrum of chamomile preparations, which often exceeds that of isolated individual compounds. Apigenin's unique anxiolytic mechanism through benzodiazepine receptor binding, combined with its anticancer, anti-inflammatory, and antioxidant properties, makes it a particularly compelling candidate for pharmaceutical development.

The generally favorable safety profile of chamomile, supported by extensive traditional use and modern toxicological data, combined with its established clinical evidence for GAD, dysmenorrhea, sleep disorders, and gastrointestinal conditions, positions M. chamomilla as a scientifically credible herbal medicine with significant therapeutic potential. However, realizing the full medicinal potential of this ancient botanical will require addressing current knowledge gaps through rigorous pharmacokinetic studies, large-scale clinical trials, advanced delivery system development, and comprehensive standardization efforts. The integration of traditional ethnomedicinal wisdom with contemporary scientific investigation continues to reveal new dimensions of this versatile healing plant.

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