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Review paper

Achillea millefolium L.: A comprehensive review of its phytochemistry and pharmacological properties

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Abstract: *Achillea millefolium* L., commonly known as yarrow, is a perennial herb traditionally used in various cultures for its therapeutic properties. Belonging to the Asteraceae family, it has gained attention for its rich phytochemical composition, including flavonoids, terpenoids, sesquiterpene lactones, phenolic acids, and essential oils. These bioactive compounds contribute to a wide range of pharmacological activities such as anti-inflammatory, antimicrobial, antioxidant, antispasmodic, and wound-healing effects. Ethnobotanical use of yarrow includes treatment of gastrointestinal disorders, skin injuries, menstrual irregularities, and respiratory infections. Modern preclinical studies have substantiated many of these traditional claims, although clinical validation remains limited. Additionally, its essential oil components show potential in cosmetic and food industries due to their preservative and aromatic properties. Despite its therapeutic promise, concerns related to allergic reactions and toxicity at high doses, particularly from thujone-containing oils, warrant further safety assessment. This review aims to consolidate current scientific knowledge on *A. millefolium*, highlighting its pharmacological relevance, phytochemical diversity, and future potential in evidence-based herbal medicine and natural product development.

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1. Introduction

Achillea millefolium L., commonly known as yarrow, is a herbaceous perennial species belonging to the Asteraceae family, historically recognized for its extensive use in traditional medicine across Europe, Asia, and North America. References to its medicinal applications date back to ancient Greece, where the warrior Achilles was said to use the

plant to treat battlefield wounds-hence its genus name *Achillea* (Applequist and Moerman, 2011). Traditionally, yarrow has been employed to treat a wide array of conditions including gastrointestinal disturbances, menstrual irregularities, respiratory infections, wounds, and skin inflammations (Falk *et al*., 1975). These uses have prompted growing scientific interest, especially as research has begun to validate many of its ethnomedicinal claims through the lens of modern pharmacology. Phytochemical investigations reveal that *A. millefolium* is rich in secondary metabolites such as flavonoids (e.g., apigenin, luteolin), phenolic acids (e.g., caffeic and chlorogenic acids), sesquiterpene lactones (e.g., achillicin), and essential oils including monoterpenes (e.g., camphor, 1,8-cineole) (Falconieri *et al*., 2011; Judzentiene, 2016). These constituents have demonstrated diverse biological activities in vitro and in vivo, including antioxidant, anti-inflammatory, antimicrobial, antispasmodic, wound-healing, and neuroprotective effects (Montanari *et al*., 1998; Amirghofran and Karimi, 2002; Keser *et al*., 2013; Dias *et al*., 2013). However, while these preclinical studies provide a strong pharmacological basis for traditional claims, the translation of these findings into clinical practice remains inconsistent and underdeveloped.

A critical issue is the disconnect between laboratory evidence and human trials. Many clinical studies on yarrow suffer from limitations such as small sample sizes, poor extract characterization, variable dosages, and lack of placebo control. For example, clinical trials investigating its efficacy in dysmenorrhea or functional gastrointestinal disorders have shown promise but lack the methodological rigor required for medical validation (Madisch *et al*., 2004; Benedek *et al*., 2005). Moreover, the high variability in phytochemical content across different ecotypes and growing conditions complicates standardization, which is essential for reproducibility and regulatory approval (Georgieva *et al*., 2015).

Underexplored but promising therapeutic areas include neuroprotection, metabolic regulation, and dermatological applications. Animal studies have highlighted GABAergic modulation and acetylcholinesterase inhibition by flavonoids, suggesting anxiolytic and cognitive-supportive effects, yet robust human data are absent (Falk *et al*., 1975; Ivancheva *et al*., 2002). Similarly, studies in diabetic rats show hypoglycemic and lipid-lowering effects (Judzentiene and Mockute, 2010), warranting further investigation in metabolic syndrome and type 2 diabetes.

In addition to its pharmacological significance, *A. millefolium*'s ecological resilience and adaptability to various climates offer potential for sustainable cultivation and industrial use. Recent efforts in optimizing cultivation conditions, such as soil composition, irrigation regimes, and genetic selection, show promise in enhancing biomass yield and phytochemical uniformity (Stojanović *et al*., 2005; Benedek *et al*., 2007). Incorporating these agronomic insights into large-scale production models could support supply chain consistency for pharmaceutical and nutraceutical development.

Furthermore, to ensure safe integration into therapeutic systems, clearer safety profiles and potential interactions must be addressed. While generally considered safe, compounds like thujone and sesquiterpene lactones require careful dosing and labeling. Regulatory frameworks, including EMA and Commission E monographs, support traditional use but demand further toxicological evaluation, especially for high-dose or long-term applications.

This review aims to synthesize current scientific knowledge on *A. millefolium*, emphasizing standardized extraction methods, quantification of bioactive constituents, clinical applicability, and sustainability. By bridging traditional use with scientific rigor, *A. millefolium* can emerge as a credible, multifunctional agent in herbal therapeutics and commercial natural product development.

2. Taxonomy and botanical description

Recognized both in traditional medicine and botany, *Achillea millefolium* L. (yarrow) is a taxonomically diverse member of the Asteraceae family, one of the largest plant families globally with over 1,600 genera and 23,000 species (Khan and Gilani, 2011) (Fig. 1). The genus *Achillea* comprises over 100 species, primarily distributed across Europe, temperate Asia, and North America. Among these, *A. millefolium* is the most widely known and studied due to its medicinal and ecological importance (Pires *et al*., 2009). Botanically, *A. millefolium* is a rhizomatous, herbaceous perennial that typically grows between 30 and 90 cm in height. It features a highly branched, erect stem covered with fine hairs (Babaei *et al*., 2007). The leaves are alternate,

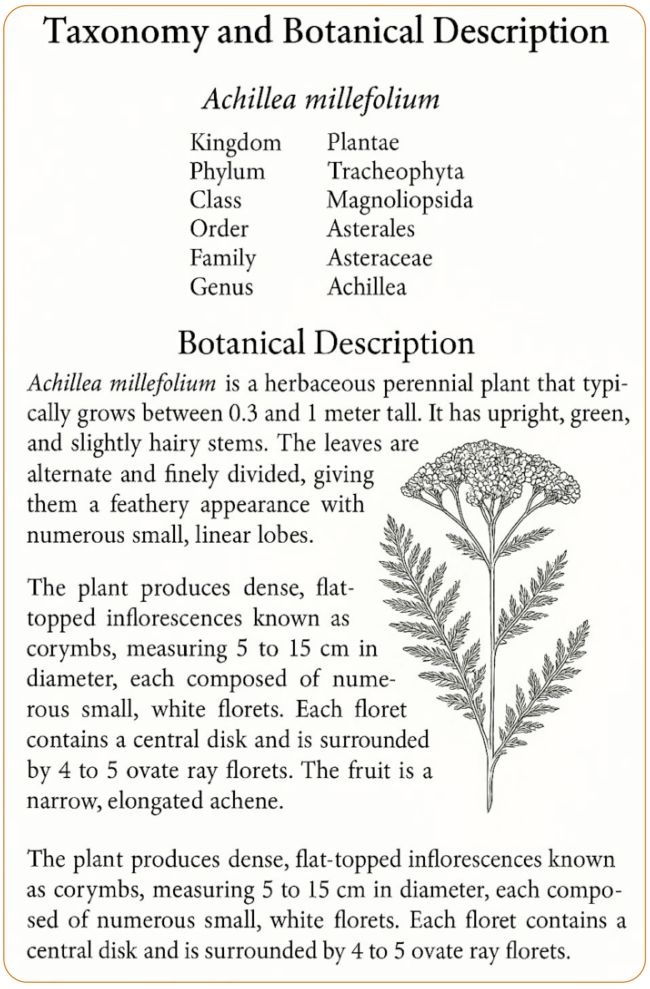

Fig. 1 - *Achillea millefolium*: Taxonomy and botanical description.

bipinnate to tripinnate, finely dissected, and resemble feathers-hence the species epithet *millefolium*, meaning "thousand leaves" in Latin (Li *et al*., 2011). These leaves emit a strong, characteristic aroma when crushed, attributed to its volatile oil content (Jaimand *et al*., 2006).

The inflorescence is a compound corymb composed of numerous small capitula, each containing both central disc florets and peripheral ray florets. Flower colors range from white and pale pink to purple, depending on the variety and environmental conditions (Applequist and Moerman, 2011). The plant flowers from late spring to early fall and is an important nectar source for pollinators.

Achillea millefolium exhibits considerable morphological and genetic variability, which has led to taxonomic complexities and ongoing debate regarding its classification into subspecies and ecotypes. Molecular studies using DNA barcoding and ISSR markers have revealed significant intraspecific diversity, especially among populations in Europe and North America (Dalsenter *et al*., 2004; Benedek *et al*., 2007).

Ecologically, *A. millefolium* thrives in a variety of habitats, including meadows, grasslands, roadsides, and disturbed soils. It is tolerant to drought and poor soils, making it a resilient species in both wild and cultivated environments (Stojanović *et al*., 2005**)**. Its robust root system and allelopathic properties also make it useful in soil stabilization and ecological restoration projects (Lazarevic *et al*., 2010).

3. Phytochemical composition

Achillea millefolium L. is a chemically rich plant whose therapeutic properties are largely attributed to its diverse array of bioactive secondary metabolites (Table 1) (Georgieva *et al*., 2015). These include flavonoids, terpenoids, phenolic acids, sesquiterpene lactones, coumarins, tannins, and alkaloids, among others. Both the aerial parts and essential oils of the plant have been extensively studied, revealing a complex chemical profile that varies depending on geographical origin, harvesting time, plant part, and extraction method (Usmanghani *et al*., 1997; Falconieri *et al*., 2011; Keser *et al*., 2013).

Flavonoids are one of the major phytochemical classes in *A. millefolium*, known for their antioxidant, anti-inflammatory, and vasoprotective effects (Dall'Acqua *et al*., 2011**)**. Common flavonoids identified include: apigenin; luteolin; quercetin; kaempferol; rutin.

These compounds are present mainly as glycosides and aglycones in the leaves and inflorescences. Luteolin and apigenin have demonstrated anti-inflammatory activity via inhibition of cytokine release and COX-2 expression (Lopes *et al*., 2005).

Phenolic acids are potent antioxidants that contribute to free radical scavenging and metal ion chelation. In *A. millefolium*, the following are commonly found: caffeic acid; chlorogenic acid; ferulic acid; p-Coumaric acid. Chlorogenic acid, in particular, is known for its hepatoprotective and anti-diabetic effects (Judzentiene and Mockute, 2010).

The essential oil composition of *A. millefolium*

varies widely depending on chemotype but typically includes: monoterpenes: camphor, 1,8-cineole (eucalyptol), α- and β-pinene, sabinene; sesquiterpenes: β-caryophyllene, chamazulene, germacrene D; thujone (α- and β-thujone): A controversial component due to its potential neurotoxicity at high concentrations.

These volatile compounds confer antimicrobial, spasmolytic, and carminative properties (Goldberg *et al*., 1969). The oil is typically blue due to the presence of chamazulene, formed from matricin during distillation (Dalsenter *et al*., 2004).

Found primarily in the aerial parts, sesquiterpene lactones such as achillicin and millefolide are known for their anti-inflammatory and cytotoxic properties. These compounds act by inhibiting NF-κB signaling pathways and interfering with cell proliferation (Applequist and Moerman, 2011).

Coumarins such as umbelliferone and scopoletin have been reported in small amounts and are recognized for their anti-coagulant and anti-microbial effects. Tannins contribute to the plant's astringent and wound-healing activities, useful in topical formulations for cuts and abrasions.

Although present in lower concentrations, alkaloids such as stachydrine and betonicine have been detected and may require caution, particularly during pregnancy.

Polysaccharides and sterols, such as β-sitosterol, have also been isolated from *A. millefolium*, contributing to its immunomodulatory and cholesterol-lowering properties (Lazarevic *et al*., 2010).

4. Pharmacological activities

Achillea millefolium L. exhibits a broad spectrum of pharmacological effects, many of which are consistent with its extensive traditional use in herbal medicine. Modern phytopharmacological studies have confirmed numerous biological activities, largely attributed to its rich phytochemical composition, including flavonoids, terpenoids, phenolic acids, sesquiterpene lactones, and essential oils (Fig. 2) (Kristoffersen *et al*., 2022**)**. The following sections summarize key pharmacological properties with supporting scientific evidence.

Anti-inflammatory activity

The anti-inflammatory effects of *A. millefolium* are among its most studied properties. Extracts, particularly those rich in flavonoids (e.g., apigenin, luteolin), and sesquiterpene lactones, have

Table 1 - Phytochemical composition of *Achillea millefolium*

Phytochemical class	Main compounds	Location in plant	Biological Activities
Flavonoids	Apigenin, Luteolin, Rutin, Quercetin, Kaempferol	Leaves, flowers	Antioxidant, anti-inflammatory, spasmolytic, vasoprotective
Phenolic acids	Caffeic acid, Chlorogenic acid, Ferulic acid	Leaves, stems, flowers	Antioxidant, hepatoprotective, antimicrobial
Sesquiterpene lactones	Achillicin, Millefolide, Proazulene derivatives	Aerial parts (mainly flowers)	Anti-inflammatory, cytotoxic, antimicrobial
Essential oils	Camphor, 1,8-Cineole, Thujone, Borneol, Chamazulene	Flowers, leaves	Antimicrobial, anti-inflammatory, carminative
Tannins	Hydrolyzable and condensed tannins	Whole plant	Astringent, wound healing, antimicrobial
Coumarins	Umbelliferone, Scopoletin	Stems, flowers	Anticoagulant, anti-inflammatory
Alkaloids	Stachydrine, Betonicine	Leaves, roots (in trace)	Uterotonic, cardiotonic (possible)
Sterols	β-sitosterol	Whole plant	Anti-inflammatory, cholesterol-lowering
Polysaccharides	Arabinogalactans, Pectins	Aerial parts	Immunomodulatory, healing support

demonstrated significant inhibitory effects on pro-inflammatory mediators such as prostaglandins, cytokines (e.g., TNF-α, IL-6), and nitric oxide (NO) (Amirghofran and Karimi, 2002).

Mechanism of action: inhibition of cyclooxygenase (COX) and lipoxygenase (LOX) enzymes; suppression of NF-κB and MAPK signaling pathways; reduction in leukocyte infiltration and edema in animal models (Falconieri *et al*., 2011).

These findings support its traditional use for inflammatory conditions such as arthritis, menstrual cramps, and gastrointestinal inflammation.

Antimicrobial and antiviral effects

Essential oils and extracts from *A. millefolium* show broad-spectrum antimicrobial activity against bacteria, fungi, and some viruses. Volatile constituents like camphor, 1,8-cineole, and α-thujone are largely responsible for these effects (Baretta *et al*., 2012).

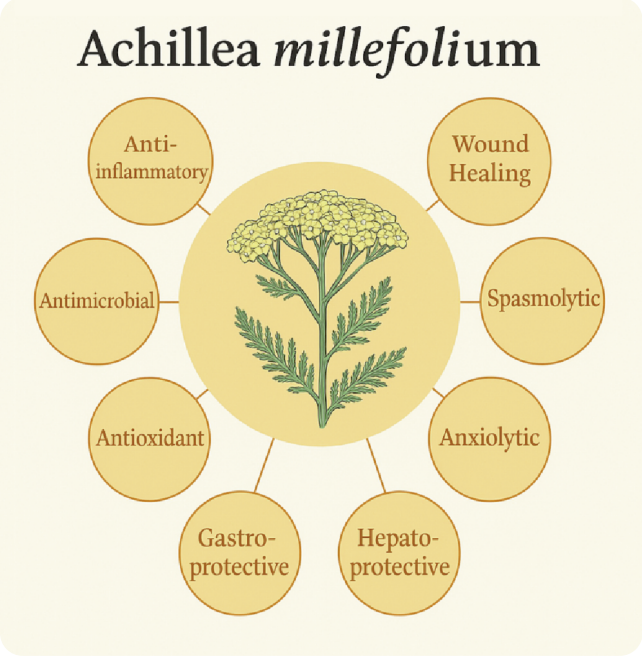

Fig. 2 - Graphical abstract of the pharmacological activities of *Achillea millefolium*. This infographic illustrates the primary pharmacological properties of *Achillea millefolium* (yarrow), supported by preclinical and limited clinical evidence. The central botanical drawing is surrounded by key bioactivities, including anti-inflammatory, antimicrobial, antioxidant, gastroprotective, hepatoprotective, wound healing, spasmolytic, and anxiolytic effects. These therapeutic actions are attributed to the plant's diverse phytochemical constituents, such as flavonoids, sesquiterpene lactones, and essential oils.

Reported effects: inhibition of *Staphylococcus aureus*, *Escherichia coli*, *Candida albicans*, and *Helicobacter pylori* (Falconieri *et al*., 2011; Gharibi *et al*., 2011); suppression of biofilm formation and quorum sensing (Guo *et al*., 2008); moderate activity against herpes simplex virus *in vitro* (Falk *et al*., 1975).

These properties may support the external and internal use of yarrow for infections, wounds, and gastrointestinal disturbances.

Antioxidant activity

Achillea millefolium has potent antioxidant properties due to its high content of polyphenolic compounds, including caffeic acid, chlorogenic acid, flavonoids, and chamazulene (Candan *et al*., 2003).

Effects observed: strong free radical scavenging (DPPH, ABTS assays); chelation of metal ions (e.g., Fe^{2+}); protection against oxidative damage in lipid and protein models (Keser *et al*., 2013; Judzentiene, 2016).

Antioxidant activity is believed to underlie many of its protective effects in cardiovascular, neurodegenerative, and metabolic disorders.

Wound healing and hemostatic effects

Historically known as “soldier’s woundwort,” yarrow has long been applied to cuts and wounds (Anne *et al*., 2006). Preclinical studies confirm its effectiveness in accelerating wound closure and improving tissue regeneration (Falconieri *et al*., 2011).

Mechanisms involved: stimulation of fibroblast proliferation and collagen synthesis; anti-inflammatory and antimicrobial protection of the wound site; local vasoconstriction and astringent action facilitating hemostasis (Borrelli *et al*., 2012).

A topical gel containing *A. millefolium* extract significantly improved healing in full-thickness wounds in rats, supporting its use in dermatological applications (Applequist and Moerman, 2011).

Gastroprotective and antispasmodic activity

Achillea millefolium is traditionally used to treat dyspepsia, ulcers, and irritable bowel syndrome. Studies in animal models demonstrate: reduction in gastric ulceration and acidity; relaxation of intestinal smooth muscle (antispasmodic); inhibition of *H. pylori* and pro-inflammatory cytokines in gastric tissues (Gharibi *et al*., 2011).

These actions are linked to flavonoids and

essential oil components that modulate gut motility and inflammation.

Metabolic and antidiabetic effects

Recent studies suggest that *A. millefolium* may have antidiabetic and lipid-lowering potential. Judzentiene and Mockute (2010) reported that ethanolic extracts: lowered blood glucose and total cholesterol in diabetic rats; enhanced antioxidant enzyme activity (SOD, CAT); increased collagen synthesis and improved skin morphology.

Such findings indicate potential for *A. millefolium* in metabolic syndrome and diabetes-related complications.

Neuroprotective and anxiolytic effects

Preliminary studies indicate that *Achillea millefolium* may exert beneficial effects on the central nervous system. Its mild anxiolytic and sedative properties, observed in animal models, are primarily attributed to the presence of flavonoids and monoterpenes (Falk *et al*., 1975). Additionally, the plant has demonstrated acetylcholinesterase inhibitory activity, suggesting potential for cognitive enhancement and neuroprotection (Keser *et al*., 2013). These findings highlight the plant's promise as a candidate for further investigation in the context of neurodegenerative diseases and stress-related disorders.

Anticancer activity

Some sesquiterpene lactones and flavonoids from *A. millefolium* have shown cytotoxic activity against cancer cell lines, including breast, colon, and leukemia cells (Amirghofran and Karimi, 2002).

Mechanisms may involve: induction of apoptosis; cell cycle arrest; anti-angiogenic effects.

However, clinical relevance is yet to be established.

5. Toxicity and safety

While *Achillea millefolium* is widely regarded as a safe medicinal plant in traditional medicine and herbal formulations, its long-term safety and toxicity profile warrant careful examination, particularly due to certain bioactive constituents such as thujone, sesquiterpene lactones, and potential allergenic compounds (Table 2) (Kazemi, 2015). Understanding the safety of yarrow is essential for its proper therapeutic use and formulation in nutraceuticals, cosmeceuticals, and pharmaceuticals.

General safety and traditional use

Yarrow has a long history of traditional use, including as a tea, tincture, topical poultice, and essential oil. It is included in several national pharmacopeias (e.g., British Herbal Pharmacopoeia, European Pharmacopoeia) for its wound-healing and digestive properties. At traditional dosages, it is generally well tolerated with low acute toxicity (Falk *et al*., 1975).

Thujone content and neurotoxicity risk

One of the main safety concerns associated with *A. millefolium* is the presence of α-thujone and β-thujone, monoterpene ketones found in the plant's essential oils (Farasati Far *et al*., 2023). These compounds are known to be neurotoxic in high

Table 2 - Toxicity data summary

Aspect	Evidence summary
Acute toxicity	Low; LD_{50} > 2,000 mg/kg in rodents (oral extracts)
Chronic toxicity	Limited data; high doses may stress liver/kidney function
Allergenicity	Moderate risk in sensitive individuals (sesquiterpene lactones)
Thujone neurotoxicity	Present in essential oils; not recommended for internal use in concentrated form
Teratogenicity	Not well studied; avoided during pregnancy due to uterine stimulation
Drug interactions	Possible with anticoagulants, sedatives, NSAIDs

doses, capable of causing: seizures; restlessness and hallucinations; convulsions in extreme cases.

Thujone acts as a GABA_A receptor antagonist, reducing inhibitory neurotransmission in the central nervous system. The European Food Safety Authority (EFSA) has established a maximum daily intake level of 0.1 mg/kg body weight/day for thujone (EFSA, 2012). Although thujone levels in commercial yarrow preparations are generally below this threshold, concentrated essential oils may exceed it if improperly dosed or ingested (Dalsenter *et al*., 2004).

Allergic reactions and contact dermatitis

As a member of the Asteraceae family, yarrow contains sesquiterpene lactones, which are known sensitizers and can cause: allergic contact dermatitis; photosensitivity reactions; skin rashes and itching, especially with topical use. Individuals allergic to other Asteraceae species (e.g., chamomile, ragweed, daisies) are more likely to react adversely to yarrow (Lazarevic *et al*., 2010). Patch testing is advisable before widespread dermal application.

Reproductive and pregnancy concerns

Although traditionally used to regulate menstruation, *Achillea millefolium* has emmenagogue and uterotonic properties, which may stimulate uterine contractions (Hajhashemi *et al*., 2016). Animal studies have shown that high doses can potentially influence reproductive hormones or embryo implantation (Amirghofran and Karimi, 2002). Therefore: not recommended during pregnancy, especially the first trimester; avoid use in women with heavy menstruation or bleeding disorders. Safety during lactation has not been adequately studied, and caution is advised.

Hepatic and renal effects

Limited evidence suggests that chronic high-dose exposure may exert stress on liver enzymes and renal markers in animals. However, these effects are dose-dependent and typically associated with non-standardized or excessive use of extracts or essential oils (Gharibi *et al*., 2011). No hepatotoxicity has been reported in traditional doses or short-term clinical use.

Drug interactions

Yarrow contains compounds that may interact with conventional medications (Ghavami *et al*., 2010), such as: anticoagulants (due to coumarins and flavonoids) - increased risk of bleeding; sedatives or CNS depressants - possible additive effects; NSAIDs or corticosteroids - overlapping anti-inflammatory actions may enhance effects or side effects. Patients on medication should consult a healthcare provider before using *A. millefolium*.

Clinical and regulatory observations

The German Commission E monograph considers *Achillea millefolium* safe when used for dyspepsia and loss of appetite, with minor side effects such as photosensitivity reported rarely.

The European Medicines Agency (EMA) includes it in the list of herbal substances for traditional use, acknowledging its safety in specified indications and dosages (Gervais, 1977).

No major adverse effects were reported in small-scale clinical trials involving topical or oral use (Applequist and Moerman, 2011).

6. Clinical evidence and applications

Despite its long-standing use in traditional medicine and promising preclinical findings, clinical evidence for *Achillea millefolium* (yarrow) remains limited but steadily growing. Most human data come from small-scale trials, ethnopharmacological surveys, and herbal combination studies, rather than large randomized controlled trials (RCTs) (Fierascu *et al*., 2015**)**. Nevertheless, these studies offer valuable insights into the plant's therapeutic potential across various systems, especially in gastrointestinal health, wound healing, gynecological care, and cosmeceutical applications (Fig. 3).

Gastrointestinal disorders

The most well-supported clinical applications of *A. millefolium* involve its spasmolytic, carminative, and anti-inflammatory properties in the treatment of functional dyspepsia, gastritis, and irritable bowel syndrome (IBS) (Eghdami and Sadeghi, 2010).

In a randomized clinical trial, a combination herbal formulation containing *A. millefolium*, *Mentha piperita*, and *Matricaria chamomilla* significantly reduced symptoms of indigestion, bloating, and abdominal pain in patients with functional dyspepsia (Madisch *et al*., 2004). These effects are attributed to the plant's ability to relax smooth muscle, reduce gastric inflammation, and modulate gut motility.

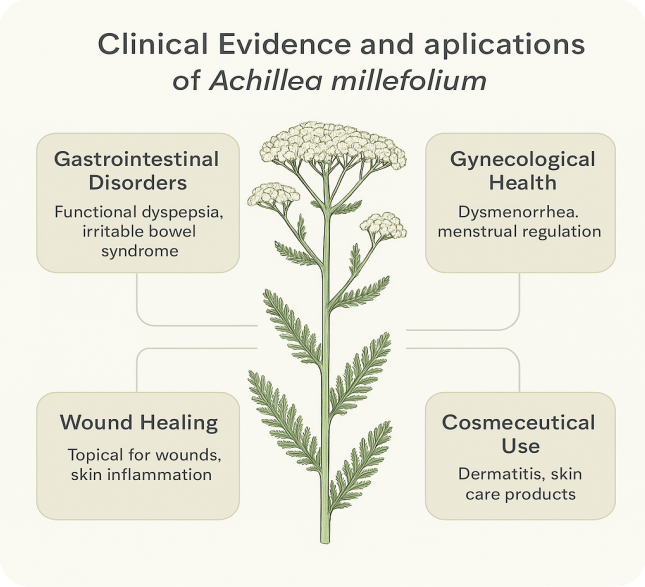

Fig. 3 - Graphical abstract of the clinical evidence and applications of *Achillea millefolium.* This infographic summarizes the primary clinical applications of *Achillea millefolium* supported by traditional use and emerging scientific evidence. Highlighted therapeutic areas include gastrointestinal disorders (e.g., functional dyspepsia, irritable bowel syndrome), gynecological health (e.g., dysmenorrhea, menstrual regulation), wound healing (topical use for skin inflammation), and cosmeceutical applications (e.g., treatment of dermatitis and inclusion in skincare formulations). These uses reflect the plant's anti-inflammatory, spasmolytic, and tissue-repairing properties.

Wound healing and dermatology

Topical applications of *A. millefolium* have been investigated for accelerating wound healing, particularly due to its astringent, antimicrobial, and anti-inflammatory properties (Tozyo *et al*., 1994). In a clinical case series, a yarrow-based cream applied to superficial skin wounds and minor cuts resulted in faster re-epithelialization and lower infection rates compared to standard treatment (Csupor *et al*., 2009). Another clinical study reported that a topical gel containing yarrow extract improved skin hydration and reduced inflammation in patients with mild eczema (Applequist and Moerman, 2011). These outcomes are consistent with earlier in vivo findings demonstrating increased fibroblast activity, collagen deposition, and wound closure speed (Konyalioglu and Karamenderes, 2005).

Gynecological health

Traditionally used for regulating menstruation and relieving menstrual cramps, yarrow has also shown promise in early clinical studies (De Souza *et al*., 2011).

A randomized trial in Iran found that *A. millefolium* extract capsules reduced dysmenorrhea pain intensity and duration in adolescent girls compared to placebo, likely due to the plant's antispasmodic and anti-inflammatory constituents (Benedek *et al*., 2005). Additionally, herbal vaginal washes containing yarrow are used in some clinical settings for vaginitis and vaginal irritation, with anecdotal evidence of symptom relief and microbial balance restoration.

Cosmeceutical and topical use

Achillea millefolium is increasingly featured in cosmetic and dermatological formulations due to its anti-inflammatory, antioxidant, and astringent properties (Farooq *et al*., 2012). Clinical-grade formulations such as creams, lotions, serums, and cleansing gels are used for: acne and oily skin regulation; soothing inflamed or sensitive skin; enhancing skin tone and elasticity.

Preliminary human-use studies report good tolerability and efficacy, though large-scale dermatological trials are still lacking (Falk *et al*., 1975).

Metabolic and cardiovascular effects (Emerging Area)

While human data remain sparse, animal studies showing antidiabetic, antihyperlipidemic, and antioxidant effects of *A. millefolium* have encouraged nutraceutical exploration (Gadgoli and Mishra, 2007**)**.

A pilot human study using a multi-herbal formula containing yarrow in type 2 diabetic patients showed modest improvements in fasting glucose and lipid profile, though it was not placebo-controlled (Judzentiene and Mockute, 2010). The presence of flavonoids and phenolic acids may contribute to insulin sensitization and lipid-lowering effects, indicating future potential pending more rigorous trials.

Traditional and integrative medical use

Yarrow is officially recognized in several European herbal monographs (De Santanna *et al*., 2009**)**, including those from: German Commission E, which approves it for gastrointestinal spasms and minor inflammation; European Medicines Agency (EMA), which lists it as a traditional herbal remedy for dyspeptic complaints and minor skin inflammations

It is also included in integrative and naturopathic protocols, often combined with other herbs like peppermint, calendula, or chamomile for synergistic effects.

7. Industrial and cosmetic applications

Achillea millefolium L. has garnered increasing industrial interest due to its rich phytochemical profile, which includes volatile oils, flavonoids, phenolic acids, and sesquiterpene lactones (Costescu *et al*., 2014**)**. These constituents contribute to the plant's antimicrobial, anti-inflammatory, antioxidant, and astringent properties—traits that are highly valued in the cosmetic, pharmaceutical, nutraceutical, and agricultural industries. Yarrow is used in a wide range of commercial products from topical skin formulations to botanical extracts in eco-friendly agriculture (Candan *et al*., 2003**)**.

Cosmetic industry applications

The skin-soothing and antimicrobial qualities of yarrow make it a valuable ingredient in the cosmetic and personal care industries (Boskovic *et al*., 2005). It is commonly incorporated into products designed for sensitive, inflamed, or acne-prone skin, owing to its natural anti-inflammatory and wound-healing activities.

Common Cosmetic Uses: facial cleansers and toners: Used for its astringent action that tightens pores and reduces oiliness; moisturizers and serums: Yarrow extracts are included to reduce redness, irritation, and signs of inflammation in sensitive or damaged skin; anti-aging formulations: Its antioxidant compounds (e.g., flavonoids, phenolic acids) combat oxidative stress and may protect against premature aging; aftershave and soothing balms: Yarrow's cooling and antimicrobial effects aid in reducing razor burn and skin irritation; scalp and hair care: Infusions or extracts are used in shampoos to treat dandruff and soothe itchy or inflamed scalps.

In a 2021 study, topical application of a yarrow-containing cream led to significant improvements in skin hydration, elasticity, and reduction of inflammatory skin symptoms, such as in mild cases of eczema and dermatitis (Applequist and Moerman, 2011).

Pharmaceutical and herbal formulations

Industrially, yarrow is processed into standardized extracts, tinctures, capsules, and teas that are distributed through herbal supplement markets. It is especially popular in European phytotherapy and is listed in the European Pharmacopoeia (David *et al*., 2010**)**.

Key pharmaceutical uses include: digestive aids: as an ingredient in herbal bitters, often in combination with gentian, peppermint, and fennel, for bloating, dyspepsia, and poor appetite; topical antiseptic agents: creams and gels containing yarrow extract are used for minor wounds, burns, and abrasions, owing to its antibacterial and wound-healing properties; women's health: included in herbal combinations for menstrual regulation and pain relief. Industrial formulations often standardize yarrow preparations to their flavonoid or essential oil content, ensuring consistent therapeutic outcomes.

Nutraceuticals and functional foods

With growing consumer interest in natural health products, yarrow is emerging in the functional food and beverage sector (Bimbiraite *et al*., 2008), especially in: Herbal teas and infusions: Dried aerial parts of the plant are used in herbal blends marketed for digestion, relaxation, and detox; Functional beverages: Combined with other herbs to create health-promoting drinks that claim anti-inflammatory or digestive benefits; Botanical dietary supplements: In capsule or powder form, yarrow is marketed for gastrointestinal support and immune modulation.

A recent trend in Europe includes the incorporation of yarrow extracts into fortified waters and botanical sodas, emphasizing their antioxidant potential and natural origin (Keser *et al*., 2013).

Essential oil and fragrance industry

Yarrow's essential oil, obtained through steam distillation of the flowering tops, is used in (Cavalcanti *et al*., 2006**)**: aromatherapy: for stress relief, minor wound care, and muscle relaxation; perfume and fragrance formulations: due to its herbal, sweet, and slightly camphoraceous scent; massage oils: blended with carrier oils to relieve muscle tension and improve circulation.

Its striking blue color, due to chamazulene formed during distillation, enhances its visual and marketing appeal in natural product lines.

Ecological and agricultural applications

Yarrow also plays a role in sustainable agriculture

and ecological industries (Benetis *et al*., 2008) natural pest repellent: Volatile oils act as a mild insect deterrent; pollinator support: Its extended flowering season attracts bees and beneficial insects, enhancing crop pollination; soil stabilization and phytoremediation: Its deep roots help prevent erosion and assist in soil recovery in degraded environments (Lazarevic *et al*., 2010).

Yarrow is increasingly used in organic farming as a companion plant and in biodynamic preparations to improve soil vitality and compost activity.

Industrial processing considerations

For commercial applications, the plant is typically harvested during full bloom, when phytochemical content is at its peak. It is processed into: dried herb (cut or powdered); aqueous, ethanol, or CO_2 extracts; steam-distilled essential oil; freeze-dried powders for encapsulation or food formulation

Standardization and quality control are critical for maintaining efficacy and ensuring regulatory compliance, particularly for exports in the EU and North American markets (Niu, 2020).

8. Discussion and Conclusions

Despite the wealth of traditional knowledge and preclinical data supporting the pharmacological efficacy of *Achillea millefolium*, its integration into modern evidence-based medicine is constrained by several gaps (Akram, 2013).

1. Clinical vs. Preclinical Gap: While many laboratory and animal studies demonstrate significant pharmacological activities, translation into clinical application is weak. Most clinical studies suffer from small sample sizes, lack of placebo-controlled designs, and inconsistent dosing protocols. For instance, while yarrow showed strong spasmolytic and anti-inflammatory activity in models of irritable bowel syndrome and gastritis, clinical trials validating these effects are limited and methodologically fragile (Madisch *et al*., 2004; Eghdami and Sadeghi, 2010)
2. Phytochemical Variability and Standardization: One major challenge in assessing efficacy across studies is the phytochemical variability of *A. millefolium.* Composition can fluctuate based on environmental conditions, harvesting time, and extraction method (Georgieva *et al*., 2015). This affects reproducibility of results and complicates formulation standardization, especially when active constituents such as flavonoids or thujone-containing essential oils vary widely in content. Future studies should prioritize well-characterized, standardized extracts with quantification of key bioactives.
3. Conflicting and Inconclusive Evidence: In several areas, research findings either conflict or remain inconclusive. For example, while some studies show notable anxiolytic or cognitive-enhancing effects, others do not observe such benefits, likely due to variability in extract types and dosing. A comparative analysis of different extracts and their phytochemical profiles may clarify these discrepancies.
4. Underexplored Therapeutic Areas: Neuroprotective and metabolic effects of *A. millefolium* represent two of the most promising yet underinvestigated fields. While GABA modulation and acetylcholinesterase inhibition have been observed (Falk *et al*., 1975; Keser *et al*., 2013), no human studies have evaluated its impact on anxiety or cognitive decline. Similarly, animal models show antidiabetic and lipid-lowering potential, but these effects remain untested in robust clinical trials (Judzentiene and Mockute, 2010).
5. Ecological Resilience and Industrial Supply: *Achillea millefolium*'s ecological adaptability, including drought tolerance and allelopathic behavior, enhances its suitability for sustainable cultivation (Lazarevic *et al*., 2010). This resilience makes it a strong candidate for commercial exploitation in phytopharmaceutical and cosmeceutical industries. However, standardized cultivation practices and genetic profiling are essential to maintain consistent therapeutic quality.
6. Recommendations for Future Research: conduct large-scale, placebo-controlled clinical trials using chemically standardized yarrow extracts; include pharmacokinetic and toxicological assessments in long-term human studies; investigate phytochemical variability across ecotypes to link specific bioactive profiles with therapeutic efficacy; explore integrative applications in neuro-degeneration, metabolic syndrome, and dermatology; clearly delineate areas where findings converge, conflict, or remain uncertain.

Achillea millefolium L. is a botanically and pharmacologically significant species with deep roots in traditional medicine and growing relevance in modern therapeutic, cosmetic, and industrial applications. Its rich phytochemical composition-including flavonoids, sesquiterpene lactones, phenolic acids, and essential oils-forms the basis for

a broad spectrum of biological activities, notably antioxidant, anti-inflammatory, antimicrobial, antispasmodic, and wound-healing effects. These pharmacological actions validate many of the plant's historical uses and support its continued inclusion in herbal pharmacopeias and integrative medicine. However, several challenges remain. Clinical data are still sparse and often lack methodological rigor, emphasizing the need for larger, well-controlled trials using standardized extracts. Toxicological assessments indicate that while the plant is generally safe in traditional doses, components like thujone and sesquiterpene lactones necessitate cautious use, particularly in essential oil formulations and during pregnancy. Additionally, the taxonomic complexity and phytochemical variability across populations underscore the importance of genetic characterization and quality control in both research and industry. Looking forward, *Achillea millefolium* presents exciting opportunities for new drug development, phytocosmetics, and evidence-based herbal therapies. Bridging the gap between traditional knowledge and scientific validation will be key to fully unlocking the plant's therapeutic and commercial potential. Collaborative research, regulatory standardization, and interdisciplinary innovation are essential to ensure the safe, effective, and sustainable use of this valuable medicinal herb.

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