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Narrative Review

# The role of *Achillea millefolium* in traditional medicine: A review of its use in different cultures

**Maryam Jangjoo[1], Amirhosein Joshaghani[2], Fatemehzahra Tahernejadgatabi[2*]**

[1]Department of Nursing, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran
[2]Department of Nursing, University of social welfare and rehabilitation sciences, Tehran, Iran

***Corresponding Author:**
Fatemehzahra Tahernejadgatabi,
Email: tahernezhad76@gmail.com

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**Abstract**

**Background and aims:** The *Achillea* genus, part of the Asteraceae family, is native to the Northern Hemisphere, from Europe to Asia. These plants thrive in temperate climates and are often found in dry or semi-dry conditions. This research aimed to examine the therapeutic uses of *Achillea* plants, drawing from traditional medicine texts and laboratory and clinical studies.

**Methods:** This narrative review involved a comprehensive search of major scientific databases to gather information on *Achillea* and its extracts from native or endemic species within the *Achillea* genus. The review spanned several decades and utilized sources such as Google Scholar, Scopus, PubMed, Institute for Scientific Information Web of Science, and botanical and local books (1990 - present).

**Results:** *Achillea* is a medicinal plant used for the treatment of gynecological problems, diabetes control, gastrointestinal disorders, side effects of cancer such as mucositis caused by chemotherapy and radiotherapy, skin reactions caused by radiotherapy, treatment of prostate cancer, breast cancer, cervical cancer, and human gastric cancer.

**Conclusion:** Considering the role of medicinal herbs in improving the side effects of cancer, treating certain types of cancer, controlling diabetes, and treating gastrointestinal problems, it is recommended to use this plant as a complementary medicine alongside routine treatments.

**Keywords:** *Achillea* plants, *Achillea millefolium*, Yarrow, Medicinal, Cancer

## Introduction

The *Achillea* genus comprises 130 plant species, is part of the Asteraceae family, and is distributed across Europe and Asia in the northern hemisphere. These plants typically thrive in moderate climates and are commonly found in dry or semi-dry environments (1). The predominant species within this genus, *Achillea millefolium* L. (commonly known as yarrow or milfoil), has a history of traditional medicinal use spanning over 3000 years (2). This plant is called Yarrow in English, and in India, it is known by different names, including Biranjasipha, Gandana, Gandrain, Puthkanda, and Bhut Kesi (Hindi). *Achillea millefolium* L. contains a range of chemical compounds, such as essential oils, sesquiterpenes, and phenolic compounds, which contribute to its various therapeutic effects, including hepatoprotective, antioxidant, antimicrobial, antifungal, anti-inflammatory, analgesic, and antispasmodic properties (3-5).

The most important part of this plant is its upper flowers (6,7), which contain essential oil and are mainly used to treat influenza, bleeding, menstrual pain, and diarrhea (8). Tea from *A. millefolium* is also used for gastrointestinal problems like indigestion, gas, stomach pain, diarrhea, and stomachache. In a recent clinical trial, where participants were randomly assigned, neither the researchers nor the participants knew who received the treatment. This demonstrated that *A. millefolium* flower powder tea reduced pain intensity in primary dysmenorrhea. Additionally, millefolium tea alleviates chest pain, bloating, and diarrhea. Research from a clinical study has indicated that tea made from *A. millefolium* flower powder effectively reduces the severity of dysmenorrhea pain (9). This plant is available in herbal pharmacies as drops and capsules containing dried flowers. This plant is also used in industrial tea blends as one of the ingredients in phytotherapy, such as Amersan (10). *A. millefolium* can be used as an alcohol extract, essential oil, hydroalcoholic extract, methanol extract, water extract, beverage, and infusion (11). Therefore, in light of the above, this study aims to investigate the medicinal uses of *A. millefolium* plant in traditional medicine, phytochemistry, and botany.

## Methods

This narrative review involved a comprehensive search of major scientific databases to gather information on *Achillea* and its extracts from native or endemic species within the *Achillea* genus. The review spanned several decades and utilized sources such as Google Scholar, Scopus, PubMed, Institute for Scientific Information Web of Science, and botanical and local books (1990 - present).

### *Plant occurrence*

Asteraceae plants are found worldwide, particularly in dry and semi-dry areas of subtropical and slightly cooler latitudes. *Achillea*, which consists of about 130 types of flowering and perennial plants, is mainly located in Europe and the temperate regions of Asia and the Americas. In Turkey, there are 46 *Achillea* species, 25 of which are specific to that region, while Iran is home to 19 species, including seven unique to the area (12). Originating from Europe and western Asia, *A. millefolium* is also prevalent in many temperate areas, including North America, and encompasses around 85 species, mainly located in Europe, Asia, and North America (13). *A. millefolium* is commonly found in grasslands and open forests and typically grows at altitudes of 3500 meters. The plant usually undergoes active growth in the spring and blooms from May to June (11).

### *Botanical description*

*Achillea millefolium* is a member of the Asteraceae family, the largest family of vascular plants. It is a tall, upright herbaceous perennial that can reach heights up to 50 cm. The plant has a slender underground stem that produces numerous roots and stolons, each with a thick, fleshy scale at every joint. The leaves, which are 5–20 cm long, have a feathery appearance and can be bipinnate or tripinnate, with varying degrees of hairiness (pubescence). They are spirally arranged near the middle and bottom of the stem. The flowers are typically white but can also be pink or pale purple and are clustered in flat-topped heads at the ends of stems and branches. The fruits are shiny, oblong achenes, approximately 2 mm in size, with broad-winged margins and no pappus (14).

### *Taxonomy*

*Achillea millefolium*, which originates from Europe, comprises three subspecies: subsp. millefolium, known for its small white flowers; subsp. alpestris (Wimm. & Grab.) with pink flowers; and subsp. ceretanum Sennen, distinguished by its large white flowers is exclusively found in Spain and southern France (15). The *A. millefolium* species complex includes several closely related species or microspecies, such as *Achillea collina* J. Becker ex Reichenb. Moreover, *Achillea pannonica* Scheele, previously considered a subspecies of *A. millefolium*, is now commonly not included. Differentiating between these species involves examining their ploidy levels; for example, *A. millefolium* is a hexaploid, *A. collina* is a tetraploid, and *A. pannonica* is generally identified as an octoploid (15).

### *Chemical constituents*

It contains a variety of compounds, including alkaloids, glucosides, choline, volatile oil, azulene, chamazulene, salicylic acid, sesquiterpenoids, dicaffeoylquinic acids (DCCAs), luteolin-7-O-beta-D-glucuronide, borneol, camphor, eucalyptol, beta-pinene, alpha-terpineol, diphenylpicrylhydrazyl radical, artemetin, dihydrodehydrodiconiferyl alcohol 9-O-beta-D-glucopyranoside, and apigenin (16,17).

### *Gynecological problems and disorders*

Jenabi et al investigated the effect of *A. millefolium* on relieving dysmenorrhea pain. The intervention group received *A. millefolium* tea bags for two menstrual cycles over three days. The findings of this study showed that the average pain scores in the intervention group were significantly lower than the control group in both the first and second cycles ($P < 0.001$). Therefore, *A, millefolium* can be used as a complementary method to reduce the severity of primary dysmenorrhea pain (9).

Pereira (2018) demonstrated in an interventional study on primiparous women that *A. millefolium* ointment reduced pain, redness, ecchymosis, and edema of episiotomy wounds. Thus, this ointment may be beneficial for relieving pain caused by episiotomy wounds (18).

In laboratory experiments, Aljancić et al discovered that the flavonoids found in *A. millefolium* demonstrate a notable inhibitory impact on *Candida albicans, Bacillus subtilis*, and *Aspergillus niger* (19).

### *Diabetes*

The findings of the study by Rezaei et al showed that administration of *A. millefolium* extract at doses of 25 mg/kg/d and 100 mg/kg/d in streptozocin-induced diabetic rats resulted in a reduction in blood sugar, lipids, and liver enzymes in diabetic rats. The effects above were more pronounced at the 100 mg/kg dose than the 25 mg/kg dose (20).

Sadeghi and colleagues also reported that *A. millefolium* lowers blood sugar levels in male rats (21). Another study confirmed the role of *A. millefolium* in reducing blood sugar levels (22). Scientific evidence suggests that diabetes increases oxidative stress factors and decreases antioxidant levels, NADPH levels, and glutathione levels (23). Additionally, protein oxidation and the production of glycated proteins in this condition contribute to damage in various organs. It has been reported that antioxidants can mitigate these changes (24). Multiple studies have confirmed the antioxidant effects of *A. millefolium* (25-27). Therefore, it can be argued that using *A. millefolium* may benefit diabetic patients due to its antioxidant effects (28). Considering the antioxidant effects of *A. millefolium* extract, this plant can be used as a blood sugar-lowering agent and a reducer of sugar absorption from the gastrointestinal system (20).

### *Gastrointestinal disorder*

The results of the study by Abdi et al on patients with gastritis aged 12 and older demonstrated that the administration of *A. millefolium* at a dose of 5.0 mg per kilogram every 8 hours led to a significant reduction in the recovery period of the intervention group compared to the control group. This effect may be due to the anti-

spasmodic and anti-infective properties of the active compounds in *A. millefolium*, ultimately reducing intestinal movements. Findings from a study on rats also showed that *A. millefolium* can reduce smooth muscle contractions (29).

This impact could be ascribed to the antiseptic characteristics of *Achillea*'s active components and its ability to reduce bowel movements due to its antispasmodic effects. Additionally, a study on animals suggested that the alcoholic extract of *A. millefolium* could suppress the smooth muscle contractions of isolated ileums in rats (30). Bais et al also reported that the methanolic extract of *A. millefolium* exhibited antidiarrheal activity in rats (31). Previous studies have also suggested that *A. millefolium* has antiviral (32) and antibacterial (30) effects, contributing to the shorter recovery time of the patients in the intervention group.

### *Mucositis induced by chemotherapy*

Studies suggest that *A. millefolium* can effectively improve oral mucositis resulting from chemotherapy. In this regard, Miranzadeh et al demonstrated in a study on cancer patients that the administration of *A. millefolium* four times daily for 14 days led to a reduction in the severity of stomatitis and oral mucositis in the intervention group (33).

Hajisalem et al conducted a study comparing the effects of a standard solution (containing 1400 mg of Lidocaine, 224 mg of dexamethasone, and 35 000 mg of sucralfate per liter, in addition to a Diphenhydramine solution) with distilled *A. millefolium* in patients with oral mucositis. The control group received the standard mouthwash, while the experimental group received a combination of the standard mouthwash and *A. millefolium* distillate (50/50). The findings revealed that *A.millefolium* distillate demonstrated greater efficacy in treating oral mucositis than the standard solution (34).

Previous studies have suggested that flavonoids possess anti-ulcer properties and that plants containing saponins and tannins demonstrate anti-ulcer effects (35). The existence of flavonoids, tannins, and other bioactive elements in Yarrow may have significantly contributed to preventing and treating oral mucositis (36).

### *Skin complications*

Historical records, such as those from Pliny the Elder and Dioscorides dating back to the first century C.E., mention the use of *Achillea* for treating wounds and inflammation. Anecdotal evidence also suggests its common use for managing infectious diseases (37,38).

In a clinical randomized study from 2016 involving 75 breast cancer patients undergoing mastectomy and radiotherapy, the application of *A. millefolium* extract during radiotherapy for five weeks resulted in reduced skin reactions in the intervention group compared to the control group at the end of the third and fifth weeks of treatment (39).

Additionally, research has indicated that *A. millefolium* effectively alleviated atopic dermatitis-like skin lesions in NC/Nga mice, partly through anti-inflammatory mechanisms (40). Other studies have demonstrated the anti-inflammatory effects of the plant's oil extracts and their ability to enhance cutaneous wound healing (41). Traditionally, *A. millefolium*, also known as Yarrow, has been used to heal wounds and relieve rashes and itching. The essential oil derived from *A. millefolium* has been reported to exhibit potent antioxidant and antimicrobial properties (42). Furthermore, extracts of *A. millefolium* have shown cytotoxic or cytostatic effects against various malignant tumor cell lines, with flavonols identified as responsible for the plant's antitumor activity (43).

### *Prostate cancer cells*

Shahani et al conducted a study to evaluate the effects of the methanolic extract of *A. millefolium* (MEA) on the growth inhibition caused by bleomycin in human non-malignant fibroblast and prostate cancer cells. The results indicated that *A. millefolium* had a positive impact on suppressing the growth of prostate cancer cells, suggesting the potential use of plant-derived compounds combined with bleomycin to treat certain cancers. Furthermore, the study found that MEA demonstrated a synergistic effect when used with bleomycin, resulting in a 1.2 to 1.7-fold increase in prostate cancer cell killing. These findings suggest the potential of combining *A. millefolium* with bleomycin to enhance the effectiveness of cancer treatments while minimizing toxicity to normal cells (44).

### *Breast cancer cells*

Amini Navaie and colleagues conducted a study to explore the effects of aqueous, ethanolic, and methanolic extracts from the flowers and leaves of *A. millefolium* L. on the MCF-7 breast cancer cell line, focusing on their antioxidant and anti-proliferative-properties. The study revealed that *A. millefolium* exhibited significant antioxidant and cytotoxic effects against the MCF-7 cell line. Specifically, the ethanol extract of the leaves and the methanol extract of the flowers demonstrated the most potent radical scavenging activities, with IC50 values of 1.16 µg/mL and 7.4 µg/mL, respectively. These findings indicate that *A. millefolium* possesses properties that suggest it could be used as a natural antioxidant source or a potential supplement in the food and pharmaceutical industries (45).

### *Cervical cancer (HeLa) cells*

Abou Baker conducted a study in which they utilized HPLC quantitative analysis to comprehensively measure 20 bioactive compounds in fractions of *A. millefolium* L obtained through different solvents (petroleum ether, ethyl acetate, methanol, and water). The study found that the extract inhibited the growth of the tested cell lines, with the most notable inhibition observed in HCT-15 cells, followed by NCI-H460 cells. Treatment

with two different concentrations of the extract (75 and 100 µg/mL) led to changes in the cell cycle profile and increased levels of apoptosis in both HCT-15 and NCI-H460 cells. Furthermore, the extract enhanced the expression of p53 and p21 in NCI-H460 cells (which have wt p53) while reducing XIAP levels in HCT-15 cells (with mutant p53) (46).

### *Human gastric cancer cells*

Sofalian and colleagues conducted a research study investigating the influence of a hydroalcoholic extract derived from *Achilla millefolium* and *Salvia officinalis* on human gastric cancer cells. They extracted the aerial parts of the plants and exposed AGS cells to varying concentrations of the hydro-alcoholic extract (ranging from 50-1000 g/mL). The impact of the hydro-alcoholic extracts and cell toxicity was evaluated using the MTT assay at 24, 48, and 72 hours. At the same time, apoptosis induction was assessed through flow cytometry using the Annexin-V/PI staining method. The results from the MTT assay indicated that these extracts showed a dose and time-dependent effect on AGS cells, with the highest percentage of cell death observed at the highest concentration and after 72 hours of incubation ($P<0.05$) (47). The results of this study indicate that the hydroalcoholic extract of Achilla millefolium has anticancer effects, which can inhibit the growth of these cells.

## Conclusion

This narrative review provides the latest research in the *A. millefolium* field, enhancing accessibility to established experimental and clinical data. It is expected to encourage further research to validate the observed effects. Results from this review demonstrate that *A. millefolium* is effective as an inexpensive and compliment therapy with a diversity of pharmacological properties such as spasmolytic, anti-inflammatory, analgesic, hemostatic, antidiabetic, cholagogue, antitumor, antioxidant, antifungal, antiseptic and liver protective effect. Considering the role of medicinal herbs in improving the side effects of cancer, treating certain types of cancer, controlling diabetes, and treating gastrointestinal problems, it is recommended to use this plant as a complementary medicine alongside routine treatments.

### Authors Contribution

**Conceptualization:** Maryam Jangjoo.
**Data curation:** Amirhosein Joshaghani.
**Investigation:** Maryam Jangjoo.
**Methodology:** Amirhosein Joshaghani.
**Project administration:** Fatemehzahra Tahernejadgatabi.
**Resources:** Maryam Jangjoo.
**Supervision:** Fatemehzahra Tahernejadgatabi.
**Validation:** Fatemehzahra Tahernejadgatabi.
**Writing–original draft:** Fatemehzahra Tahernejadgatabi, Amirhosein Joshaghani.
**Writing–review & editing:** Amirhosein Joshaghani.

### Competing Interests

The authors declare that there is no conflict of interest.

### Ethical Approval

Not Applicable.

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