



## REVIEW: Pharmacological and Biological Activities of *Artemisia persica*: A Review

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### ARTICLE INFO

**Submitted:** 24 Feb 2023  
**Accepted:** 23 Apr 2023  
**Published:** 01 Jun 2023

#### Keywords:

Artemisinin;  
Asthma;  
Cancer;  
Central nervous system diseases;  
Depression

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#### Citation:

Hosseinzadeh MH, Arab A, Emad N, Bodaghabadi F, Boroughani M, Rajabzadeh F, Sheikhy M, Taghipour A, Shourabi B, Eghbali M, Zahedi P, Ebrahimzadeh MA. Pharmacological and Biological Activities of *Artemisia persica*: A Review. Tabari Biomed Stu Res J. 2023;5(1):25-32.

10.32598/tbsrj.v5i1.10527

## Introduction

Among several medically significant creatures, plants stand out, and *Artemisia* is one of the beneficial

plant genera. The name is said to have been derived from the Greek goddess Artemis (goddess of forests, childbirth and hunt).

### ABSTRACT

*Artemisia* is a beneficial plant genus from the Asteraceae family with about 500 species. Species of this genus are resistant herbs and shrubs, and its essential oil is renowned for its chemical value. *Artemisia* plants are often found in dry and semiarid locations, especially in Asia, Europe, and North America. Considering the importance of the *Artemisia* genus in treatment procedure of diseases, in this study, we have reviewed the pharmacological and biological activities of *Artemisia persica*. In traditional medicine, *A. persica* is often used in treating gastrointestinal, skin, and general diseases. In addition, its extract and essential oil have significant antioxidant, anti-bacterial, anti-fungal effects, anti-parasitic, anti-neoplasm, antinociceptive, anti-epileptic, anti-anxiety, etc. activities.

*Artemisia* is a member of the Asteraceae (Compositae) family, species of this genus are resistant herbs and shrubs, and its essential oil is renowned for its chemical value. *Artemisia* plants are often found in dry and semiarid locations in both the northern and southern hemispheres' temperate climates. This genus has about 500 species, the majority of which are widespread throughout Asia, Europe, and North America (1). Considering the importance of *Artemisia* genus in the treatment of diseases, in this study we have reviewed pharmacological and biological activities of *Artemisia persica*.

## Results

### The role of *Artemisia persica* in traditional medicine

Traditional medicine, based on ancestors' knowledge and experiences, has always led to discovery of herbal medicines effects. In traditional medicine, dry and fine powder of *A. persica* is used as wound healing (2) and antiparasitic agent (3). The *A. persica* decoction is effective in treating headache (2, 4), common cold (2), fever, gastrointestinal problems (5-7) and inflamed itchy rashes. Pressed juice of *A. persica* is used to prevent skin dryness of hands and face against cold winds (2). Also, antiseptic, anthelmintic, sedative (7) and memory-enhancing activity have been reported from different parts of the plant (4).

### Antioxidant

Multiple redox processes that normally occur in aerobic cells produce oxidants and radicals that are highly reactive and cytotoxic for healthy cells. They can cause damage in DNA and proteins structure if they are not eliminated. Antioxidants, which eliminate free radicals and detoxify body, can counteract detrimental effects of free radicals. Plants and plant-derived products contain a vast array of phytochemicals, including antioxidants, which are believed to reduce the risk of oxidants and oxidative stress-related diseases (8, 9).

In Ahmadvand *et al.* study, hydroalcoholic

extract and essential oil of *A. persica* aerial part (during its flowering stage) significantly inhibited oxidants in radical scavenging activity and total antioxidant capacity tests. The hydroalcoholic extract was more potent than essential oil due to the amount and type of antioxidant compounds (alpha-terpinene, thymol, nerolidol, and phenol)(10). Also, the significant antioxidant potential of *A. persica* leaf and stem methanolic extract, and aerial parts essential oil has been confirmed in DPPH and ABTS tests (11, 12).

### Infectious and parasitic diseases

#### • Anti-bacterial

Although impressive progress has been made in controlling bacterial diseases, frequent epidemics caused by drug-resistant bacteria and the appearance of new pathogenic strains have necessitated the discovery of new antibiotics. Since ancient times, plants have been used to treat infectious diseases. Scientific research has proven the therapeutic effects of plants in treating infectious diseases. Therefore, investigating medicinal plants is a practical approach for discovering new anti-bacterial agents to solve widespread public health problems (13, 14).

In Ramak *et al.* study, methanolic extract of *A. persica* aerial parts inhibits the growth of *Staphylococcus aureus* and *Bacillus subtilis* through destroying cell wall and preventing the release of anti-bacterial agents (by inhibiting the efflux protein)(12). In another study, significant synergistic effects were observed in inhibiting the growth of *Escherichia coli* and *Listeria monocytogenes* in food products by adding *A. persica* aerial parts essential oil (in flowering stage) to the *Lactobacillus paracasei* (probiotic bacteria)(15). essential oil of *A. persica* aerial parts inhibits the growth of *E. coli*, *Pseudomonas aeruginosa*, *Enterobacter* Sp, *Enterococcus* and *Staphylococcus saprophyticus* in microdilution test (16). In contrast, in Jeppesen *et al.* study, the methanolic extract of *A. persica* had no significant effects on *S. aureus*, *E. coli*, *B. subtilis* and *P. aeruginosa* (17). Also, Owliaa *et al.* reported that *A. persica* essential oil did

not show any anti-pseudomonal activity against *P. aeruginosa* (18).

#### • Anti-fungal

Fungal infections cause a wide range of human problems, from superficial skin diseases to fatal systemic diseases. The involvement and severity of infection depend on the fungal type and patient's immune system strength. Although there has been made significant progress in discovering novel effective drugs in recent years, but drug resistance and challenges are still stable in treatment procedures. So far, various herbal compounds have been interrogated in treating fungal infections (19, 20). *A. persica* is one of them.

*A. persica* aerial parts essential oil has strong anti-fungal activity against *Aspergillus ochraceus*, *Aspergillus parasiticus*, *Aspergillus flavus*, *Aspergillus nidulans*, *Aspergillus fumigatus* and *Aspergillus niger*. Anti-fungal activity of essential oil has been attributed to the presence of 1,8-cineole, artedouglasia oxide C and pinene. Penetration disorder and cell wall disruption proposed as the main mechanism of anti-fungal activity, which ultimately leads to cell death (21). Another study confirmed the anti-fungal activity of *A. persica* aerial parts essential oil on *Aspergillus niger*. Irreversible membrane disorder and inhibition of cellular energy production were considered as possible mechanisms. Borneol and 1,8-cineole were considered as main compounds in essential oil in this study (22). Ramak *et al.* reported the anti-fungal activity of *A. persica* aerial parts essential oil (extracted by water distillation and supercritical fluid extraction methods) against *Microsporum canis*, *Trichophyton rubrum*, *Trichophyton mentagrophytes* and *Epidermophyton floccosum* strains. Davanone and lincantafuran H were predominant compounds in supercritical fluid extraction and davanone in the water distillation method (12).

#### • Anti-parasitic

Using herbal compounds to treat parasitic diseases has always been of interest. Herbal

compounds have been used in various studies, both as adjuvant and anti-parasitic compounds, with positive effects (23). Artemisinin, isolated from *Artemisia annua*, is a well-known antimalarial compound (24). Therefore, several studies have investigated the anti-parasitic properties of *A. persica*.

In Najm *et al.* study, ethanolic extract of *A. persica* aerial parts significantly inhibited amastigotes and promastigotes of *Leishmania major* in an *in vivo* model. Cytotoxicity assay showed no toxicity for host cells (mouse macrophages) in this study (25).

Moradi-Afrapoli *et al.* reported anti *Plasmodium falciparum* activity of ethanolic extract of *A. persica* aerial parts. Antimalarial activity of the extract is attributed to bisabolol oxide sesquiterpene diesters. However, the ethanolic extract caused cytotoxicity in skeletal rat cells (26). Weaker antimalarial activity was reported from methanolic extract of *A. persica*. Davanone was recognized as the major compound of the extract (24).

#### Anti neoplasm

One of the main causes of cancer in living tissues is oxidants. Herbal compounds, a very rich source of antioxidants, have always been considered as one of the prominent options in cancer treatment (27).

The hydroalcoholic extract of *A. persica* aerial parts induces apoptosis in AGS cells (gastric cancer cells) in a dose-dependent and time-dependent manner. This anti-cancer activity can be attributed to artemisinin compound which is presented in the plant (28). *A. persica* aerial parts ethanolic extract also inhibits proliferation of HepG-2 (human liver cancer cells) and Hep-2 (human larynx cancer cells) cell lines by activating caspases, depolarizing the mitochondrial membrane potential, reducing Bcl-2 expression and stopping the cell cycle (29). In addition, *A. persica* aerial parts essential oil demonstrated significant cytotoxicity on MCF-7 (human breast cancer cell) and HeLa cells (cervical cancer cells). While it only affects normal lymphocytes in very high doses (12, 30).

#### Antinociceptive

Until now, valuable antinociceptive activities have been reported from medicinal plants. In some cases, they have strengthened the drug effects or functioned more effectively than official drugs (31). Herbal compounds may affect cholinergic pathways, GABA receptors and opioid system as antinociceptive agents. Inhibition of the synthesis, and the release of arachidonic acid, prostaglandins, phospholipase, nitric oxide, and cyclooxygenase-2 have been reported as analgesic mechanisms of some herbs (32).

The hydroalcoholic extract of *A. persica* leaves and branches significantly improved capsaicin-induced dental pulp pain in rats, which increased meal time and frequency (temporomandibular joint pain reduces food intake). It seems that pain modulation may be related to the presence of sesquiterpenes, scoparone and flavonols in *A. persica* and its anti-inflammatory activity (33). In confirmation, an inhibitory activity on COX-1 has been reported from ethanolic extract of *A. persica*, which can be effective in treating pain, inflammation and fever (17).

In Ebrahimi *et al.* studies, *A. persica* essential oil significantly reduced the duration of licking and biting, leg limping, and leg lifting in formalin test. Also, the use of *A. persica* essential oil in the hot plate and tail immersion tests significantly increases the pain threshold time. It seems that *A. persica* essential oil reduces inflammatory mediators levels or affects opioid receptors in relieving pain (34, 35).

### Central nervous system diseases

Nowadays it is claimed that CNS disorders affect a large number of people every year which leads to a significant rise in disability and mortality rate. Such ailments form a vast proportion of neurological diseases which cause very high financial costs for communities. Toxicity, metabolic disorders, inflammation, genetic defects are some of the main factors (36). Although the therapeutic capabilities of medicinal plants in treating CNS disorders have been known for centuries, few concentrated efforts have been made to identify and develop CNS herbal

medicines. Currently, herbal medicines are considered as one of the therapeutic hopes for developing psychotherapeutic drugs. Especially since several trials have shown clinical effectiveness of herbal compounds in treating CNS-related diseases (37).

#### • Anti-epileptic

*A. persica* Hydroalcoholic extract decreases MDA levels in serum and prefrontal cortex of mice by increasing antioxidant capacity and reducing the expression of NMDA receptors, thus significantly increases the seizure threshold (38). Also, synergistic effects on diazepam and inhibitory effects on flumazenil from *A. persica* hydroalcoholic extract have been reported, which may confirm its effects on benzodiazepine receptors. The extract significantly reduces tonic convulsive movement frequency but does not affect seizure onset (39). Treatment with the essential oil of *A. persica* whole plant significantly delays seizure onset (at a dose of 50 mg/kg). It decreases the frequency of tonic attacks, movements and head tics (at a dose of 100 mg/kg). It may be related to the modulation of GABA receptors, inhibition of oxidative stress and brain inflammation markers by increasing antioxidant capacity and decreasing MDA levels (40). Also, essential oil reduces the seizure threshold (41).

#### • Anti-anxiety

The hydroalcoholic extract of *A. persica* leaves and stems has significant anti-anxiety effects compared to diazepam, which seems to be due to the antioxidative properties of its phenolic compounds (chlorogenic acid and gallic acid) that increase antioxidant capacity and reduce malondialdehyde (MDA) levels. Although the plant extract in high doses functioned as pro-oxidants and caused an increase in oxidative stress that decreases or reverses anti-anxiety activity in some tests (38). *A. persica* leaves ethanolic extract modulates cholinergic activity and neuritis in rat hippocampus that improves anxiety disorder. However, the treatment with extract did not significantly reduce serum and brain

MDA levels (42). Also, *A. persica* essential oil can effectively improve epilepsy anxiety (41).

#### • Memory impairment

In an *in vitro* study, *A. persica* hydroalcoholic extract improved memory impairment caused by pentylentetrazol by reducing MDA levels and increasing antioxidant capacity (39). *A. persica* leaves ethanolic extract moderated cognitive damage and memory impairment in passive avoidance memory and rotarod tests, which seems to be due to the antioxidant activity of its phenolic and flavonoid compounds (42). Also, *A. persica* essential oil can effectively improve epilepsy memory impairment (41).

#### Other

In an *in vivo* study, *A. persica* essential oil was used to treat depression recognized as one of the most common psychiatric disorders in epilepsy. But the treatment with different doses of essential oil had no significant effects on duration of immobility in the tail suspension test (41).

A clinical trial investigated the acute effects of *A. persica* inhalation formulation on pulmonary function of asthmatic patients aged 6-18 years. Although the FEV1/FVC, PEF75, PEF50 and PEF25 indices decreased significantly in *A. persica* inhalation group, the FEV1, FVC and PEF25 indices did not change significantly. Finally, it was concluded that the spirometry index did not improve in asthmatic patients after *A. persica* inhalation (43).

#### Conclusion

In conclusion, *A. persica* is often used in treating gastrointestinal, skin, and general diseases in traditional medicine. In addition, its extract and essential oil have significant antioxidant, anti-bacterial, anti-fungal, anti-parasitic, anti-neoplasm, antinociceptive, anti-epileptic, anti-anxiety, etc. activity.

#### Conflicts of Interest

None has been declared.

#### Authors' Contribution

Design: M.H.H. and M.A.E.; Search: M.H.H.; Data extraction: M.H.H., A.A., N.E., F.B., M.B., F.R., M.S., A.T., B.S., M.E. and P.Z.; First draft: M.H.H., A.A., N.E., F.B., M.B., F.R., M.S., A.T., B.S., M.E. and P.Z.; Final revision: M.H.H. and M.A.E.; supervision: M.A.E. All authors read and approved the final version of the manuscript.

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