

Artemisia: A Comprehensive Review of Phytochemistry, Medicinal Properties, and Biological Activities

Noorah Saleh Al-Sowayan*^{ID}, Fayafi Al-Harbi, Shouaa Abdulaziz Alrobaish

Department of Biology, College of Science, Qassim University, Buraydah, Saudi Arabia

Email: *nsaoiean@qu.edu.sa

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Abstract

This review provides a comprehensive overview of the phytochemistry, medicinal properties, and biological activities of the *Artemisia* species. *Artemisia* species exhibit a wide range of morphological and phytochemical diversity, showing promise for the treatment of various diseases in humans, plants, and animals. Phytochemicals found in *Artemisia* spp. include terpenoids, flavonoids, coumarins, caffeoylquinic acids, sterols, and acetylenes. Dietary flavonoids have been linked to reduced cell aging, lipid peroxidation, and cancer risks. Sterols, including plant sterols, play a significant role in reducing the plasma cholesterol levels. Essential oils from *Artemisia* plants contain volatile chemicals with antibacterial, antiviral, and antifungal properties that contribute to their biological activity. This study aimed to elucidate the effective compounds of *Artemisia* plants and their medicinal benefits and biological activities.

Keywords

Essential Oils, Artemisinin, Antimalarial, Bioactivity, Terpenoids, Flavonoids, Coumarins, Sterols, Acetylenes

1. Introduction

Medicinal plants are natural gifts to humans and help them lead disease-free and healthy lives. They also play a crucial role in health maintenance. They are believed to be considerably safer and more effective in the treatment of various ailments. Herbs are abundant worldwide. There is strong evidence of an increase in the demand for medicinal plants as a result of the worldwide trend toward improved “quality of life”. Plants have been used to treat various ailments in both

humans and animals as long as humanity exists. These plants are widely used by all segments of society, whether directly as folk medicines or indirectly as pharmaceutical preparations in modern medicine. *Artemisia* is one of the largest and most extensively distributed genera in the Asteraceae family (composite). It is a widespread genus with over 500 species and is largely found in temperate regions of Europe, Asia, and North America. These include perennial, biennial, and annual herbs or tiny shrubs [1]. In 1972, a Chinese research team discovered a chemical in the leaves of plants, artemisinin or qinhaosu. This chemical and its derivatives have been used for the first time as monotherapies for malaria. However, after 30 years of use, considerable drug resistance has been observed. The WHO recommends combining artemisinin with other long-acting antimalarials such as lumefantrine, mefloquine, and amodiaquine. These combinations are known as artemisinin combined treatment (ACTs). The discovery of *A. annua* was a significant milestone in the fight against malaria [2]. This study revealed that the aqueous solution extracted (cold and hot) from the wormwood plant is acidic in nature because it contains many glycosidic and phenolic compounds, tannins, resins, flavonoids, alkaloids, and terpenes, and can activate the SGOT enzyme at a rate of 15% for the cold aqueous extract and 48% for the hot aqueous extract. Careful analysis of the mineral elements of the *Artemisia* fruit powder also proved that it contains some elements, especially (Cd, Zn, Ni, Cu, Cl, and Pb) at different concentrations, and the presence of these elements led to an increase in the process of enzyme activation (SGOT), which plays an important role as an indicator of the work, effectiveness, and activity of some body organs (liver, kidneys, pancreas, etc.) [3]. This study aimed to shed light on the effective compounds of the *Artemisia* plant and its medicinal benefits and biological activities.

2. Plant Appearance

The genus *Artemisia* has a wide variety of morphological and phytochemical diversity, which is linked to the geographical origin of the samples. The genus has remarkable ecological adaptability, with species ranging from sea level to high mountains and from dry zones to wetlands. Polyploidy is frequent, with varying cytotypes affecting outward appearance, anatomy, fertility, and phytochemicals [4]. The general morphological features of the genus *Artemisia* are as follows: alternate leaves, capitula small, usually racemose, paniculate or capitate, inflorescence, rarely solitary, involucre bracts in few rows, receptacle flat to hemispherical, without scales, and sometimes hirsute; florets all tubular, achenes obovoid, pappus absent, or occasionally a small scarious ring [5] (see **Figure 1** and **Figure 2**). In *Artemisia annua*, the natural presence of dimers or trimers of artemisinin molecules was not observed. Instead, these compounds are synthetic derivatives designed to enhance the antimalarial, antileukemia, and antiviral properties of artemisinin [6] [7]. While *Artemisia annua* is rich in artemisinin and various other sesquiterpenoids, artemisinin dimers and trimers are created through scientific

processes aimed at improving their potency and efficacy against various diseases [6] [8].



Figure 1. An image showing the full appearance of the *Artemisia* plant in the Qassim region.

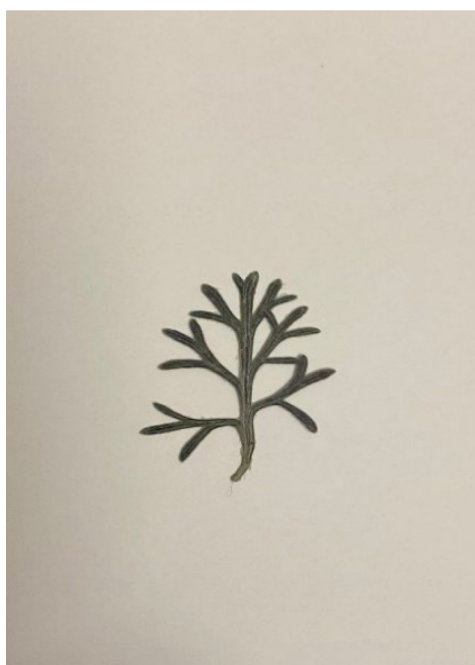


Figure 2. External appearance of an *Artemisia* plant leaf in the Qassim region.

3. Phytochemistry

According to a comprehensive literature review, the phytochemistry of the

Artemisia species includes terpenoids, flavonoids, coumarins, caffeoylquinic acids, sterols, and acetylenes. *Artemisia* species include dAbsinthium, Afar, Annua, Maritima, and Scoparia. A comprehensive analysis revealed that terpenoids, flavonoids, coumarins, caffeoylquinic acids, sterols, and acetylenes are among the phytochemicals found in the *Artemisia* species. *Artemisia* species include Absinthium, Afar, Annua, Maritima, and Scoparia [1]. Secondary metabolites found in over 260 *Artemisia* species include terpenoids, flavonoids, coumarins, glycosides, sterols, and polyacetylenes [9] (see Figure 3).

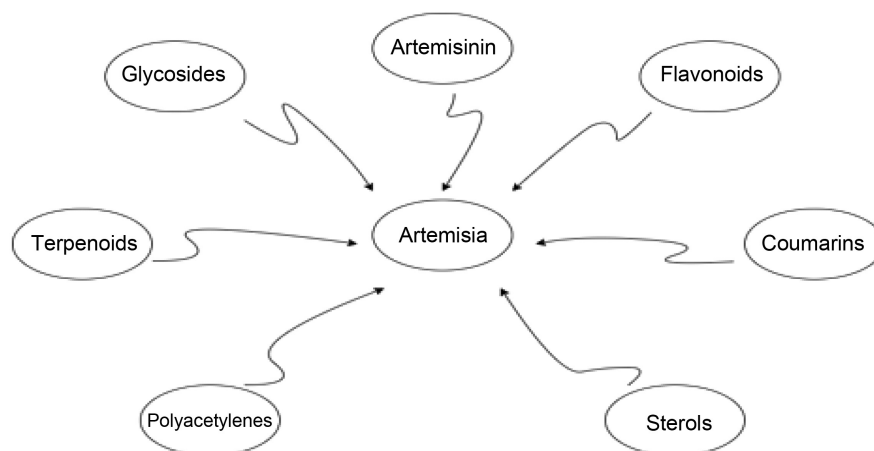


Figure 3. Active compounds in the *Artemisia* plant.

3.1. Essential Oils of the *Artemisia* Plant

Essential oils are complex mixtures of volatile chemicals such as terpenes and aromatic phenol derivatives. They serve important roles in nature due to their diverse bioactivity, which includes antibacterial, antiviral, and antifungal properties. *Artemisia* is a source of essential oils such as pinene, thujyl alcohol, cadinene, phellandrene, and thujone, among others, and has been shown to be effective for a variety of biological activities, including analgesic, anti-coccidial, anti-diabetic, antifungal, antiviral, anti-herpes virus, and many others [10].

3.2. Artemisinin

Artemisia annua, a member of the Asteraceae family, is renowned for its production of artemisinin, a sesquiterpene lactone that exhibits potent antimalarial properties against *Plasmodium falciparum*, primarily because of its crucial endoperoxide structure. This compound has gained global recognition as an effective treatment for malaria because it disrupts the life cycle of the parasite [11]. In addition to its antimalarial effects, *Artemisia* extract has demonstrated significant efficacy against coccidiosis in young rabbits. A dose of 1200 mg/kg resulted in a remarkable 96.36% reduction in oocyst shedding and improved weight gain, indicating its potential as a viable alternative to conventional treatments for parasitic infections [12]. Thus, the therapeutic benefits of *Artemisia annua* extend beyond malaria, highlighting its versatility for combating various parasitic diseases.

Artemisinin contains an endoperoxide moiety that reacts with iron to produce harmful free radicals. Cancer cells have considerably more intracellular free iron than normal cells, and it has been demonstrated that artemisinin and its analogs preferentially induce death in many cancer cell lines [13].

Furthermore, artemisinin compounds have been demonstrated to exhibit anti-angiogenic, anti-inflammatory, anti-metastatic, and growth-inhibitory properties. These features make artemisinin a promising candidate for cancer chemotherapy [14].

In contrast, simple artemisinin analogs are less powerful than standard cancer chemotherapeutic drugs and have short plasma half-lives, necessitating high doses and frequent administration for cancer treatment. More powerful and target-specific artemisinin molecules are currently being developed [15].

These include artemisinin dimers and trimers, artemisinin hybrid compounds, and the tagging of artemisinin compounds with molecules implicated in intracellular iron transport. These chemicals show promise as effective anticancer medicines, with fewer adverse effects than standard chemotherapeutics [16].

3.3. Flavonoids

The redox capabilities of flavonoids render them as effective antioxidants. Research suggests that a diet high in flavonoids may reduce cell aging, lipid peroxidation, and cancer risks. The mechanism of action of flavonoids is unclear, and the most effective antioxidants such as quercetin may not always have the highest bioavailability, stability, or biological activity. Humans who consume highly hydroxylated quercetin (from onions and apples) and naringin (from white grapefruit) have a lower risk of developing lung cancer [17].

3.4. Terpenoids

Are much more important in the pharmaceutical industry. Terpenoids are used as ointments and creams to treat itching and pain. It also showed antimicrobial activity, which offered resistance to microorganisms in wards. Terpenoids act as natural agricultural pesticides by forming resins and rubbers. Fontanellar gun, a mechanism by which termites use terpenoids to kill harmful insect termites, belongs to the subfamily Nasutitermitinae. Although terpenoids are beneficial, they also have harmful effects such as respiratory problems, central nervous system effects, vomiting, and nausea. Most children are also affected by terpenoid indigestion [11].

3.5. Coumarins

Natural coumarins are phytochemicals that have antiviral, antimicrobial, biological, and therapeutic properties. These include antihypertensive, antiparasitic, antioxidant, antiproliferative, anti-worm, and anti-inflammatory effects. Numerous coumarin compounds such as umbelliferone, scopoletin, visniadin, bergapten, fraxetin, and marmin have been shown to have anti-inflammatory activities.

Umbelliprenin has been shown to reduced carrageenin-induced paw edema by approximately 39% [18].

3.6. Glycosides

Glycosides are strong antihyperglycemic drugs that increase insulin production by directly affecting β -cells without affecting K^+ -ATP channel function or the amount of cAMP in the islets. Patients with diabetes and obesity are the greatest candidates for this weight reduction strategy because they eliminate sugar from their diet. Steviol glycosides have been employed as cancer chemopreventive drugs, and steviosides have shown strong anticancer activity in a mouse model experiment [19].

3.7. Steryls

Steryl esters are abundant in vegetable oils. Nuts, vegetables, and grains are less significant sources of sterol. The ability of sterols to reduce plasma and LDL cholesterol and their structural resemblance to cholesterol give them nutritional significance. The possibility of using plant sterols as a natural preventative dietary supplement has drawn attention because cholesterol-lowering medications, such as statins, significantly decrease morbidity and mortality from cardiovascular disease. Unlike sterols, which are detectable in plasma, stanols (saturated at C-5) are found in small amounts in food and are efficient in reducing plasma cholesterol without raising plasma levels [20].

4. Medical Uses of the *Artemisia* Plant

A. annua is recognized for its superior medicinal value. This species is particularly esteemed for its high artemisinin content, a compound that plays a crucial role in the effective treatment of malaria. Additionally, *Artemisia annua* demonstrates significant antibacterial properties, especially in leaf extracts, making it a valuable resource for herbal medicine [21].

4.1. Antioxidant

Artemisia, which exhibits the most potent antibacterial activity, is found in the leaf. Specifically, extracts from the leaves of *Artemisia nilagirica* demonstrate a broad spectrum of antibacterial effects, with hexane and methanol extracts proving to be particularly effective against a variety of bacterial strains [22].

Numerous therapeutic plants, such as *Artemisia* spp., contain phenolic compounds that can act as antioxidants [23]. This lowered the WBC count by a percentage. It increases the percentage of glutathione (GSH), catalase (CAT), and superoxide dismutase (SOD) while decreasing the percentage of lipid peroxidation [24]. This genus contains a number of coumarins, flavonoids, phenylpropanoids, sterols, and terpenoids (particularly sesquiterpenes and monoterpenes), together with their glycosides, which have been demonstrated to have antioxidant properties [25]. The antioxidant properties of the essential oils were also measured,

revealing antioxidant properties similar to those of thymol [26]. Numerous studies have shown that the ability of phenolic compounds to scavenge free radicals results in their antioxidant activity. Phenolic substances can also function as antioxidants by blocking the production of radicals, chelating metal ions, and enhancing the body's natural antioxidant defence mechanisms. Consequently, several naturally occurring antioxidants derived from plants have recently been reported [1]. Antioxidants present in food can strengthen cellular defenses and prevent oxidative damage to cellular constituents [27]. *A. annua* is well known for its therapeutic characteristics, which help to avoid a variety of illnesses. The bioactive components of *A. annua* are excellent resources for pharmacological development. The defensive ability of *A. annua* as a potent antioxidant against free-radical damage has been previously described [28].

4.2. Antimicrobial

It is advisable to use essential oil as an antibacterial ingredient because it can produce an inhibition zone that is larger than that of a typical medication. (mugwort) essential oil possesses strong antibacterial properties owing to the presence of 1,8-cineole, camphene, and α -thujone, whereas artemisinin is responsible for its antineoplastic properties. It is well established that the diethyl ether extract of *A. nilagirica* leaves exhibits antimicrobial properties against the soil-borne plant pathogen, *Phytophthora capsici*. The disc fusion method was used to evaluate antimicrobial activity. The results showed that mycelial development of *P. capsici* was entirely suppressed by a concentration of 100 ppm oil in carrot agar vehicle [29]. A variety of pathogens, such as *Bacillus subtilis*, *Candida krusei*, *Enterococcus hirae*, *Enterococcus faecalis*, *Escherichia coli*, *Haemophilus influenzae*, *Pseudomonas aeruginosa*, *Saccharomyces cerevisiae*, and *Staphylococcus aureus*, have been shown to exhibit antimicrobial activity in *Artemisia annua* extracts [27].

4.3. Antifungal

The oil from *Artemisia* sp. possesses antifungal properties. Lignans and coumarins of *A. annua* exhibit antifungal properties [27]. This oil also showed fungicidal activity against *Colletotrichum fragariae*, *C. gloeosporioides*, *C. acutatum*, and *Artemisia caerulescens* subsp. *densiflora* (Viv.) oil against *Aspergillus*, *Alternaria* and *Fusarium* species. This oil also showed fungicidal activity against *Colletotrichum fragariae*, *C. gloeosporioides*, and *C. acutatum* and *Artemisia caerulescens* subsp. *densiflora* (Viv.) oil against *Aspergillus*, *Alternaria*, and *Fusarium* species [30]. Other *Artemisia* species, such as *Artemisia abrotanum* and *Artemisia pallens*, contain ethanolic extracts that are effective against *Bacillus stearothermophilus* and *Pseudomonas cepacia*. In addition to their antibacterial properties, the plant extracts exhibited maximal antifungal efficacy against *Saccharomyces cerevisiae* and *Trichosporon beigelii*. This implies that these two unique plant ethanolic extracts may possess antibacterial and antifungal properties [31]. Sesquiterpene ketone vulgarone B, which was isolated from the volatile fraction of

Artemisia douglasiana, had antifungal properties against *Botrytis cinerea*, *Colletotrichum acutatum*, *Colletotrichum fragariae*, and *Colletotrichum gloeosporioides*. Based on research analyzing structure and activity, it was shown that the α -unsaturated carbonyl function is necessary for the antifungal activity. Therefore, vulgarone B might serve as a Michael-type acceptor for biological nucleophiles. In vitro, *Pneumocystis carinii* was susceptible to the antifungal effects of artemisinin and its derivatives [32].

4.4. Antibacterial

Antioxidant and antimicrobial aqueous extracts may be produced from the aerial parts of the plants. The prepared herbal tea possesses antibacterial, analgesic, and anti-spasmodic properties. This shrub is also utilized as cow feed in the plateau regions of Algeria [25]. Plant extracts and chemicals derived from *Artemisia* spp. are potent inhibitors of parasites and bacteria. Certain phytochemicals have been shown through mechanistic investigations to possess bactericidal activity against both Gram-positive and Gram-negative bacteria. These capabilities involve the disruption of the bacterial membrane. Among the phytochemicals, Antiretrovirals are noteworthy since they belong to a novel family of antibacterial medications [33]. In 2006, Blagojević *et al.*, from Serbia and Montenegro, investigated the effects of *A. vulgaris* essential oil on several bacteria. Steam distillation was used to separate the oil from the aboveground and subterranean parts of the plant [34]. The zones of pathogen growth suppression on the paper filters were investigated 10 and 30 times. *Salmonella enteritidis*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, and *Escherichia coli* are among the microorganisms against which oil derived from aerial parts showed inhibitory effects [35]. A previous study showed that the *A.* oil extract has a synergistic antibacterial action against both Gram-positive and Gram-negative bacteria [36].

4.5. Antidiabetic

Diabetes is treated using the wormwood herb, *Artemisia alba*. Rats orally administered wormwood plant showed a decrease in sugar content owing to the activity of the MDH enzyme. These findings indicated that herbal extracts prepared from wormwood leaves can effectively reduce blood sugar levels. Furthermore, the additional apparent action of the isoform form of MDH on liver cells of rats with diabetes was eliminated using an alcoholic extract [37]. Additionally, artemisinin and its derivatives have been reported to increase insulin secretion, which has been shown in human islets as well as in rats and mice, thereby attenuating diabetes hyperglycemia [3].

4.6. Anti-Viral

Significant antiviral activity has been demonstrated using several phytochemicals extracted from different *Artemisia* species. With low micromolar activity against hepatitis B and C viruses, human herpes viruses HSV-1 and HSV-2, HIV-1, and

influenza virus A, antiretroviral therapy (ART) has emerged as the most promising antiviral medication option. The majority of the time, antiretroviral therapies (ARTs) blocked the host cell type and metabolic needs for viral replication by inhibiting the primary regulatory mechanisms of virus-infected cells (NF- κ B or Sp1-dependent pathways). Certain *Artemisia* species, such as *A. annua*, *A. absinthium*, *A. vulgaris*, *A. maritima*, and *A. indhiana*, are attracting more attention from researchers in light of the COVID-19 pandemic because of their strong potential for anti-infectious, antiviral, and anti-inflammatory properties. Owing to their strong antiviral and anti-inflammatory properties, recent research has highlighted the intriguing functions of artemisinin and its derivatives (ARTs) as potential therapeutic candidates against SARS-CoV-2. ARTs attach to ferrous iron (e.g., heme) and produce reactive oxygen species (ROS), which can have either cytotoxic or cytostatic effects. In addition to causing cellular damage, ROS generation can potentially lead to peroxide membrane lipids, activate pro-apoptotic pathways, or create instability in the mitochondrial and genomic DNA. The ability of diverse phytochemicals extracted from different species of *Artemisia* to modulate reactive oxygen species (ROS) underscores the significance of investigating the potential therapeutic applications of these substances in clinical situations involving oxidative stress [33].

4.7. Anti-Carcinogenic

Certain *Artemisia* species have been shown to inhibit the development of multiple cancer cell lines, including leukemia, colon cancer, renal cell carcinoma, and breast cancer. The phytochemical examination of the extracts revealed the presence of tannins, cardiac glycosides, anthocyanins, flavonoids, and coumarins. These phytochemicals and their derivatives alter cell migration, cause apoptosis or cell cycle arrest, and prevent angiogenesis, among other mechanisms by which they exhibit growth inhibitory properties [33]. Swiss albino mice were used to test the anticancer properties of *Artemisia nilagirica* (MEAN) methanolic extract of *A. nilagirica*. Mean survival time (MST) and percentage increase in lifespan were observed at doses of 150 and 250 mg/kg, respectively. In comparison with EAC control animals, they found that treatment with MEAN decreased tumor volume, packed cell volume, and viable tumor cell count in a dose-dependent manner 30 [24]. Compared to the common medication vincristine, the methanolic extract of *A. nilagirica* showed significant anticancer activity in Swiss albino mice. In contrast, the aqueous extract of *Solanum nigrum* combined with species of the genus *Artemisia*, such as *A. vulgaris*, *A. nilagirica*, and *A. parvi-fora*, has an inhibitory effect on colony accumulation and cell growth in human breast, prostate, and colorectal cell lines [29]. Since immune cells effectively eliminate apoptotic cells in vivo, drugs that induce apoptosis are particularly interesting for the treatment of cancer. According to available information, treating breast cancer cells with *M. annua* extract causes DNA breakage, loss of mitochondrial membrane potential, and other classic apoptotic symptoms. Additionally, treatment of xenograft

models with the Momundo extract activated apoptosis in vivo. These results unmistakably show that *Artemisia annua* possesses active components other than artemisinin, which has therapeutic potential [38].

4.8. Antiulcer Activity

The antiulcer activity of freeze-dried ethanolic extracts of aerial sections of *A. nilagirica* was observed. Rats were used in this study. The extract was orally administered at a dose of 500 mg/kg, which prevented the animals from experiencing stomach ulcer effects caused by ethanol-hydrochloric acid. According to their study, a dose of 500 mg/kg provided the best degree of stomach protection. They discovered that the anti-ulcer effect resulted from an increase in mucus content followed by a corresponding increase in proteins. As a control, they used cimetidine, which has no effect on mucus secretion in animal models [24].

4.9. Antiasthmatic Activity

On healthy adult Wistar strain rats, aqueous extracts of *A. nilagirica* aerial parts and *Sesamum indicum* seeds were tested for their anti-asthmatic properties. Rats treated with ovalbumin suspension developed asthma, which is comparable to that of human asthma. When plant extracts were administered to sensitized Wistar rats, the number of white blood cells (WBCs), particularly neutrophils and monocytes, decreased significantly, indicating a strong therapeutic effect. Compared to the ovalbumin-treated group, it protected tissue proteins from neutrophils, prevented histamine-induced bronchospasm, reduced nitrate ion generation, reduced lung inflammation in asthmatic animal models, and relieved bronchial congestion. Comparison of aqueous plant extracts at 200 mg/kg with the positive control ketotifen, showed considerable efficacy in in vivo anti-asthmatic investigation [24].

4.10. Anti-Parasitic

Plant-parasitic nematodes are among the most damaging pathogens to food and fiber crops. Root-knot nematodes cause the vast majority of losses. An ethanolic preparation of *A. nilagirica* flowering meristems (1 mg/ml) effectively prevented *Meloidogyne incognita* from causing root-knot diseases in mulberry trees. The homeopathic medication *A. nilagirica* extract (Cina) decreased root-knot disease and improved the nutritional value of afflicted plant leaves. It lowers nematode populations in roots and soil. Silkworm larvae fed the leaves of Cina-treated plants exhibited improved growth, increased silk gland weight, shell weight, shell ratio (SR%), and effective rate of rearing (ERR%), resulting in increased silk production for commercial purposes, fewer feeding and number of feeding days, shorter starting time and span of spinning, shorter molting time to cocoon formation, and zero mortality rate. *A. nilagirica* possesses antihelminthic properties. The ethanolic extract of *A. nilagirica* blooming tips is effective against *Trichinella spiralis*, a gastrointestinal worm responsible for trichinellosis. Trichinellosis is a global

parasitic illness that affects humans, domestic animals, and wild animals [24].

4.11. Function in Neurodegeneration

Extracts from many *Artemisia* species exert neuroprotective effects against localized ischemia-reperfusion-induced brain damage, microglial cytotoxicity, and glutamate excitotoxicity. Furthermore, *Artemisia* protects neurons from mitochondrial potential loss, reactive oxygen species, and H₂O₂-induced mortality by activating the Nrf2 pathway. ARTs enhance learning and memory in Alzheimer's disease rats by inhibiting A β ₂₅₋₃₅-induced inflammatory cytokine levels (IL-1 β , IL-6, and TNF- α), restoring autophagic flux, and boosting A β fibril clearance [33].

5. Conclusion

Artemisia is a plant that has shown promising results in the treatment of many human, plant, and animal diseases, and studies are ongoing. *Artemisia* spp. have neuroprotective properties and can enhance learning and memory in rats with AD. The genus *Artemisia* has a wide variety of morphological and phytochemical diversity, with species such as *Artemisia annua* being significant in the fight against malaria. Artemisinin compounds are promising anticancer drugs with few adverse effects. The development of more powerful and target-specific artemisinin molecules such as dimers, trimers, and hybrid compounds is ongoing. Artemisinin analogs induce cell death in many cancer cell lines because of their interaction with intracellular iron. Flavonoids in the diet may reduce cell aging, lipid peroxidation, and cancer risks.

Conflict of Interest Statement

The authors have declared that no competing interests exist.

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