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Review Article

Jusan (*Artemisia* L.) in the flora of Kazakhstan: a brief overview of its botanical characteristics, biologically active compounds and medical significance

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Abstract: The genus *Artemisia* L. (Asteraceae), commonly known as jusan, represents one of the most taxonomically diverse and pharmacologically significant groups of medicinal plants, widely distributed across arid and semi-arid regions of the Northern Hemisphere. Kazakhstan is a major center of diversity for *Artemisia*, where numerous species play essential ecological, ethnobotanical, and medicinal roles. This review provides a comprehensive overview of the botanical characteristics, phytochemical composition, and pharmacological potential of *Artemisia* species occurring in the flora of Kazakhstan, with particular emphasis on *A. absinthium*, *A. terrae-albae*, *A. cina*, *A. pauciflora*, *A. vulgaris*, and *A. schrenkiana*. The genus is characterized by a rich spectrum of biologically active compounds, including essential oils, sesquiterpene lactones (notably artemisinin and santonin), flavonoids, phenolic acids, coumarins, saponins, amino acids, vitamins, and mineral elements. These constituents underpin a wide range of pharmacological activities, such as antioxidant, anti-inflammatory, antidiabetic, antimicrobial, antiparasitic, and anticancer effects. Special attention is given to artemisinin and its derivatives, whose unique peroxide structure has led to groundbreaking advances in antimalarial therapy and has demonstrated promising anticancer and immunomodulatory properties. In addition, the review highlights emerging research trends, including the use of *Artemisia* extracts in green synthesis of metallic nanoparticles, which exhibit enhanced biomedical activity and environmental compatibility. Despite extensive experimental evidence from in vitro and in vivo studies, the clinical translation of *Artemisia*-based preparations remains limited, emphasizing the need for standardized phytochemical profiling, mechanistic studies, and well-designed clinical trials.

Keywords: Jusan; *Artemisia* L.; sesquiterpene lactones; artemisinin; antidiabetic activity; anticancer potential.

1 Introduction

The genus *Artemisia* L. is a taxonomically complex and ecologically adaptable group of plants belonging to the Asteraceae family. This genus includes about 500 – 600 species, distributed mainly in the Northern Hemisphere, and is characterised by morphological and chemical diversity [1]. Members of the genus *Artemisia* are usually described as perennial herbaceous plants adapted to a variety of ecological conditions in arid steppe, desert and mountain regions. They are characterised by deeply dissected leaves, a grey-green tomentose covering and small capitate inflorescences [2].

Jusan (Kazakh name for *Artemisia* species) is one of the most common plant species in the world, often playing a key role in the formation of the vegetation cover of the steppe community of Kazakhstan [3]. Members of the *Artemisia* L. genus are valuable medicinal plants in traditional medicine, widely used to treat wounds, vitamin deficiency, tuberculosis, nervous disorders, regulate blood pressure, relieve joint swelling, and alleviate headaches and toothaches [4]. Some species of jusan are widely used in traditional medicine in Central Asia, China and Europe for various therapeutic purposes, but the areas of application vary depending on regional medical traditions and local species composition. In Central Asia, including Kazakhstan, *Artemisia absinthium, A. vulgaris* and *A. scoparia* are used to treat digestive disorders, liver and biliary tract diseases, and parasitic infections. In traditional Chinese medicine (TCM), *Artemisia annua* and *A. argyi* occupy a special place; these plants have been used to reduce fever, suppress inflammation, improve blood circulation, and treat infectious diseases, and the antimalarial properties of artemisinin, isolated from *A. annua*, provide scientific justification for its historical use. In European traditional medicine, *A. absinthium* and *A. vulgaris* were used as appetite stimulants, cholagogues, and antiseptics, as well as in herbal preparations to stimulate the nervous system [5] – [7].

Since the 1950s, synthetic drugs have been causing various pathologies in living organisms. Synthetic drugs are ineffective not only from a biological point of view, but also from a production and economic point of view. Therefore, according to the World Health Organisation (WHO), in the next 10 years, herbal medicines will account for 60% of the total volume of medicines, while in Kazakhstan it will only be 17%. Developed countries are switching to traditional medicine systems that include natural products and medicines. The use of medicinal plants as a source of primary health care is safe and widely known, especially in developing countries [8].

The medicinal properties of medicinal plants are highly valued because they are safe, effective, environmentally friendly and have few side effects, which are the main advantages that increase demand for them [9]. According to the World Health Organisation (WHO), traditional medicine includes practices, methods and accumulated knowledge from human experience, including medicinal substances of plant, animal and mineral origin, traditional medical therapy and various methods of treating diseases [10].

Currently, herbal medicines are widely used for the treatment and prevention of various diseases, and their types and quantities are constantly growing [11], [12]. Medicinal plants have obvious advantages over synthetic drugs, including beneficial effects and low toxicity. However, the potential of medicinal plants of the domestic flora of Kazakhstan and their importance in the production of important medicines, cosmetics and food supplements from them have not yet been sufficiently studied [13].

Humanity has long recognised the importance of plants not only for their nutritional value, but also for their medicinal properties, which have been used to treat illnesses for thousands of years. Many wild plants are rich in natural resources. However, the rapid depletion of forests due to anthropogenic pressure, unplanned development and overuse of cultivated plants has led to a decline in their numbers and the disappearance of many species in the wild. This has serious consequences for biodiversity loss and the extinction of endemic species [14] – [16]. Due to the increasing impact of humanity on nature, the global community faces the enormous and urgent task of preserving biological diversity.

Traditional natural products and phytopreparations based on plants of the genus *Artemisia* L. have made a significant contribution to the development of natural product chemistry and pharmacological research, their scientific and practical significance is clearly demonstrated by data from modern natural sciences and medical science. In the traditional medicine of the Kazakh people, *Artemisia* species are used for diseases of the respiratory system (bronchitis, bronchial asthma), gastrointestinal pathologies, increased acidity, diarrhoea, chronic inflammatory diseases, including rheumatoid arthritis, have been effectively used in the treatment of. Furthermore, sage plants are known to be used as a haemostatic agent, to reduce complications following bites from poisonous insects and snakes, and in traditional medicine for certain types of cancer [17]. A comprehensive geobotanical and resource-based study of the natural populations of jusan allows for the rational use of the medicinal raw material, whilst preserving the ecological stability of the natural plant resources. allows for the rational use of medicinal raw materials and paves the way for the development of scientifically based management measures aimed at the conservation of natural plant resources. Taking into account the high resource potential of the *Artemisia* genus, which is widespread in Kazakhstan, their in-depth pharmaceutical research, the in-depth pharmaceutical study of these species, the development of new effective phytopreparations and the advancement of domestic pharmaceutical production are among the priority scientific directions of the current era.

2 Taxonomic and botanical description of *Artemisia* L.

The genus *Artemisia* L. is a taxonomically complex and ecologically adaptable group of plants belonging to the Asteraceae family. This genus is characterised by morphological, ecological and chemical diversity, which has made it an important subject of research in modern botany, phytochemistry and pharmacognosy. The wide geographical distribution, species richness and adaptation to extreme natural conditions of the genus Artemisia testify to its evolutionary flexibility and serve as the basis for the formation of a diverse spectrum of biologically active compounds [18].

The genus *Artemisia* includes more than 500 species worldwide, and about 80 species are found in the border areas of Kazakhstan and neighbouring countries. Representatives of the genus are annual, biennial and perennial herbaceous plants, sometimes in the form of semi-shrubs. Some of them were studied directly under the guidance of Professor S. Adekhenov [19].

Morphological characteristics typical of species of the genus *Artemisia* include pinnate or deeply lobed leaves, grey-green felt-like hairs, apical inflorescence consisting of small tubular flowers, and the presence of a single-seeded fruit. These characteristics are the result of the plant's adaptation to environmental factors and play an important role in taxonomic diagnosis. Members of the genus *Artemisia* are mainly distributed in the Northern Hemisphere and are found in various natural zones of Eurasia, North America, and North Africa. The greatest species diversity is characteristic of arid and semi-arid climatic zones, especially in Central Asia. This region is considered one of the important centres of evolutionary formation and distribution of the genus *Artemisia*. In addition, jusan species play an important ecological and biogeocenotic role in the vegetation cover of Central Asia. They prevent soil erosion, serve as a natural barrier against desertification processes, and provide habitat and food sources for a number of animals. In addition, jusan communities are considered one of the key elements in the formation of the region's natural landscapes [20].

The widespread distribution and ecological success of the *Artemisia* genus is closely linked to their high level of adaptation to unfavourable environmental conditions. *Artemisia* species are characterised by their resistance to drought, high temperatures, soil salinity and nutrient deficiency. These properties have made them the dominant plants in desert and semi-desert regions [21].

The main morphological features of ecological adaptation include deeply lobed leaves, a pubescent surface, and a greyish colour. Such structures reduce evaporation and increase the plant's ability to retain water. In addition, a well-developed root system allows moisture to be absorbed from deep soil layers [22].

Physiologically, *Artemisia* species increase the synthesis of secondary metabolites under stress conditions. Essential oils, sesquiterpene lactones, flavonoids, and phenolic compounds are important components of the plant's biochemical defence system. These compounds provide the plant with ecological stability, acting as a defence against herbivores, microorganisms, and abiotic stress factors [23].

Artemisia schrenkiana Ledeb. (in kazakh - Шренк жусаны). The plant contains many biologically active substances, including essential oils, saponins, tannins, vitamins, amino acids, organic acids, enzymes, absinthin and santonin. In addition, this plant has been found to contain 9 different macro- and microelements, including lead, cadmium, zinc, copper, iron, manganese, sodium, and potassium. The study of jusan species is of particular importance due to the presence of many biologically active substances with enormous potential for agriculture and the pharmaceutical industry. However, excessive use of these resources not only depletes plant resources but also threatens to destroy ecosystems [24].

Artemisia absinthium L. (in kazakh - ащы жусан) is one of the most well-studied medicinal plants from a pharmacological point of view. The plant contains essential oils (thujone, thujol, camphor), sesquiterpene lactones, flavonoids, bitter glycosides, tannins, organic acids and vitamins. The combination of these compounds gives *A. absinthium* digestive stimulant, choleretic, antiseptic and anti-inflammatory properties. In addition, the plant contains macro- and microelements such as iron, zinc, copper, manganese, potassium and sodium, which increases its biological value. *A. absinthium* is widely used in traditional medicine to treat gastrointestinal diseases, parasitic infections and general weakness [25].

Artemisia terrae-albae L. (in kazakh - ақ жусан) is a plant species that grows in arid and semi-arid regions of Kazakhstan and Central Asia. Its chemical composition has been found to contain essential oils, flavonoids, phenolic compounds, tannins, saponins and organic acids. In addition, this plant accumulates important trace elements such as calcium, magnesium, potassium, iron, zinc and manganese. *A. terrae-albae* is used in traditional medicine as an anti-inflammatory, antimicrobial agent and digestive system regulator. Its high adaptability to arid climatic conditions indicates the high ability of this species to accumulate biologically active substances [26].

Artemisia cina (in kazakh - дәрмене жусан) is a medicinal plant rich in biologically active compounds. The main active component of the plant, santonin, is characterized by antiparasitic properties and has been widely used in medicine historically. In addition, essential oils, bitter substances, flavonoids, tannins and organic acids have been identified in *A. cina*. The mineral content includes trace elements such as iron, copper, zinc and manganese. This plant has been used mainly in tradional medicine against helminthiasis and its pharmacological potential is of interest in modern research [27].

Artemisia pauciflora (in kazakh - сирек гүлді жусан) is a species ecologically adapted to arid steppe and semi-desert environments. The plant contains essential oils, phenolic compounds, flavonoids, saponins, and tannins. In addition, macro- and microelements such as potassium, calcium, magnesium, iron, and zinc have been identified in its composition. *A. pauciflora* has been traditionally used in traditional medicine as an anti-inflammatory, analgesic, and general tonic remedy. However, since its chemical composition and pharmacological properties remain insufficiently studied, this species can be considered a promising object for further scientific investigation [28].

Artemisia vulgaris L. (in kazakh - кәдімгі жусан) is a perennial medicinal plant widely distributed across Eurasia. Its chemical composition includes essential oils, flavonoids, coumarins, saponins, tannins, vitamins, and organic acids. The plant is also rich in mineral elements such as iron, calcium, potassium, magnesium, and manganese. In traditional medicine, *A. vulgaris* has been used for the treatment of respiratory disorders, gastrointestinal dysfunctions, nervous system weakness, and inflammatory conditions. The diversity of biologically active compounds present in this species indicates its high pharmacological potential [29].

Despite the long-standing use of *Artemisia absinthium, A. terrae-albae, A. cina, A. pauciflora, A. vulgaris*, and *A. schrenkiana* in traditional medicine across Kazakhstan and Central Asia, comprehensive and comparative studies of their phytochemical composition and biological activities remain highly relevant. The pronounced pharmacological potential of these species supports their consideration as promising natural sources for the development of novel phytopharmaceuticals. However, the industrial utilization of *Artemisia* species requires scientifically justified resource assessments and continuous ecological monitoring to ensure the conservation of natural populations.

3 Phytochemical structure of *Artemisia* L.

Medicinal plants are well known as rich sources of phytochemical compounds that exhibit significant biological activity, particularly antioxidant properties, by inhibiting free radicals. According to the World Health Organization (WHO), approximately 60% of the world's population relies on medicinal plants for primary healthcare. Both traditional medicine and modern scientific research indicate that the medicinal potential of the genus *Artemisia* is exceptionally high.

Species of the genus *Artemisia* are considered among the most important medicinal plants due to their high content of essential oils and flavonoids and have been extensively investigated. Numerous studies have demonstrated that *Artemisia* species possess anti-inflammatory, antioxidant, antihypertensive, hypolipidemic, and anticancer properties. In traditional medicine, these plants are widely used for the treatment of gastrointestinal disorders, and several reports indicate their effects on the urinary system, including antispasmodic activity. Phytochemical investigations have revealed that *Artemisia* species contain flavonoids, acetylenic compounds, coumarins, and terpenoids, particularly sesquiterpene lactones (Figure 1). Although extensive scientific research has been conducted on many species of the genus *Artemisia*, population characteristics and distribution patterns of some medicinal species remain insufficiently studied to date [30].

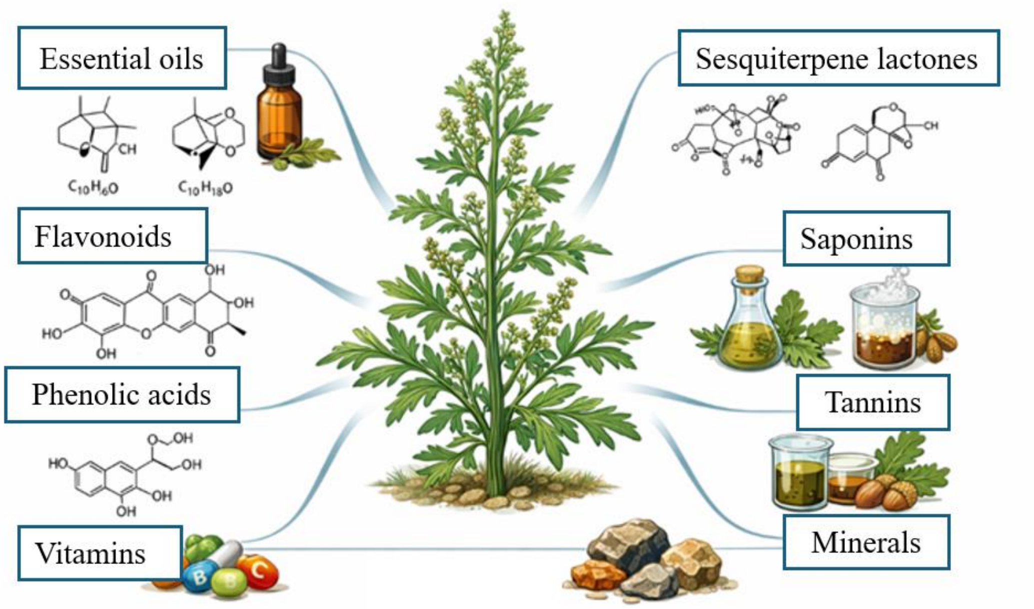

Figure 1. Phytochemical composition of *Artemisia* L.

According to the literature, more than 260 species of the genus *Artemisia* L. have been investigated, and the results indicate pronounced pharmacological activity and a complex chemical composition involving multiple classes of secondary metabolites. The primary biologically active constituents of *Artemisia* are essential oils (EOs), while additional active components include organic acids, fatty acids, and tannins [31].

Essential oils of *Artemisia* species consist mainly of mono- and sesquiterpenes, including thujone, camphor, 1,8-cineole, borneol, pinene, and camphene. These compounds are responsible not only for the characteristic aroma and taste of the plants but

also for their antimicrobial, anti-inflammatory, and antiparasitic activities. The qualitative and quantitative composition of essential oils varies considerably among different *Artemisia* species [32].

Studies focusing on the ability of *Artemisia* essential oils to reduce microbial resistance and effectively inhibit microbial growth represent an important and relevant research direction. As early as 1881, De la Croix was the first to evaluate the antibacterial properties of essential oils [33].

Another important group of biologically active compounds characteristic of the genus *Artemisia* is sesquiterpene lactones, including absinthin, artabsin, santonin, and artemisinin. Artemisinin, an endoperoxide sesquiterpene lactone isolated from the Chinese medicinal plant *Artemisia annua*, led to the development of a new class of highly effective antimalarial drugs. Artemisinin-based combination therapies are currently regarded as the most effective modern treatment for uncomplicated *Plasmodium falciparum malaria*. In addition, the essential oil of *A. annua* exhibits antioxidant activity, reaching approximately 18% of the activity of the reference compound α-tocopherol. A lactone-enriched fraction obtained from the ethanol extract of *A. annua* demonstrated anti-ulcerogenic activity in rat models of ethanol- and indomethacin-induced gastric ulcers. Beyond its antimalarial effects, *A. annua* has also been reported to possess anti-inflammatory, antipyretic, antiparasitic, and cytotoxic properties [34].

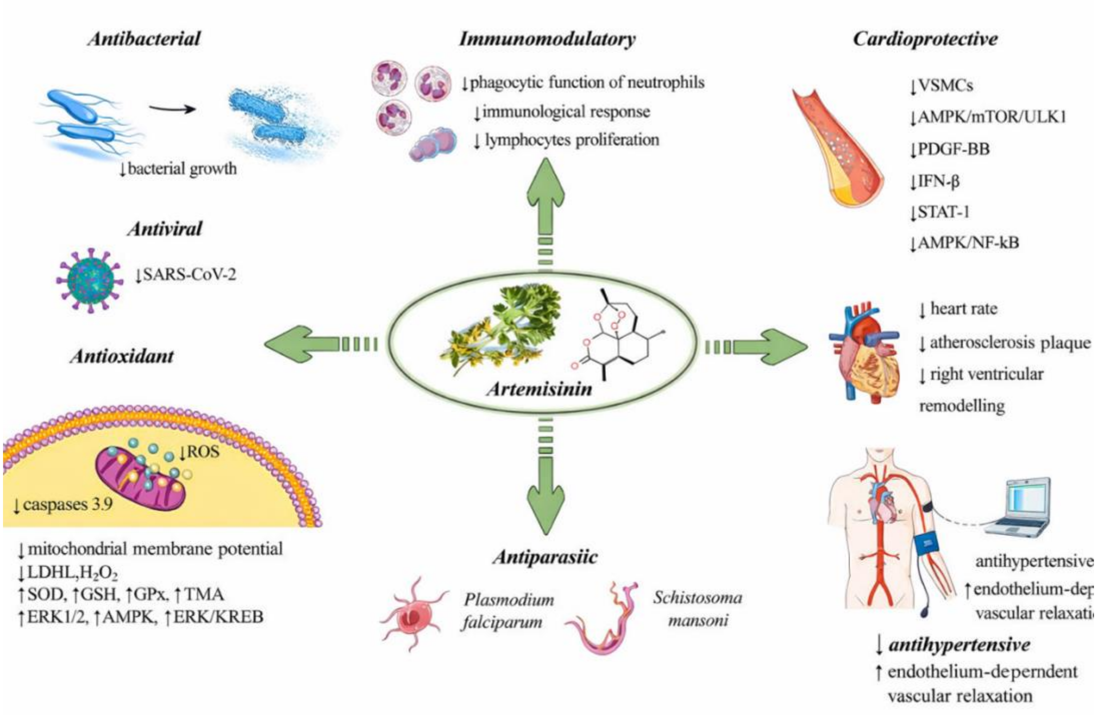

Figure 2. The most important pharmacological properties and mechanisms of artemisinin

Artemisinin (ART) and its semi-synthetic derivatives constitute a group of antimalarial drugs used for the treatment of uncomplicated malaria caused by *Plasmodium falciparum, Plasmodium malariae, Plasmodium vivax, Plasmodium ovale,* and *Plasmodium knowlesi* [35]. Artemisinin was discovered in 1972 by the Chinese pharmacologist Tu Youyou, who was awarded the Nobel Prize in Physiology or Medicine in 2015 for this breakthrough [36]. The discovery and application of ART derived from *Artemisia annua* L. represents a classic example of how traditional knowledge and medicine, in this case, Traditional Chinese Medicine - can lead to the development of novel pharmaceutical agents [37].

Artemisinin has been traditionally used in China as an antimalarial remedy and is obtained from the medicinal plant *Artemisia annua* L. Alternatively, its precursor compounds can be produced through genetically engineered yeast, a method that is considerably more productive than plant-based extraction. However, clinical evidence has indicated the emergence of ART-resistant malaria strains, first reported in Southeast Asia in 2008. Beyond its antimalarial activity, ART exhibits strong anti-inflammatory and immunomodulatory properties [38], as well as the ability to regulate oxidative stress (Figure 2). Therapeutic effects of ART and its derivatives in kidney diseases have also been confirmed.

Another important pharmacological property of ART is its anticancer potential (Figure 3). In China, *A. annua*, commonly known as Qinghaosu, has demonstrated proven efficacy against *P. falciparum malaria*, and several ART derivatives are currently available in various pharmaceutical formulations, including intravenous, rectal, and oral preparations. These natural secondary metabolites of *A. annua* include artemether, artesunate, artemisinin, artemelin, dihydroartemisinin (DHA), and artemotil (β-artemether), as well as artemisinic acid (qinghao acid), a biosynthetic precursor of ART, which is present in the plant at concentrations up to ten times higher than artemisinin itself [39].

Artemisinin is a highly oxygenated sesquiterpene containing a unique 1,2,4-trioxane ring structure. Its antimalarial activity is attributed to the presence of a peroxide bridge associated with this distinctive structure, which differentiates ART from most other known antimalarial compounds that typically contain heterocyclic nitrogen atoms. Several semi-synthetic ART derivatives are synthesized from DHA. The biosynthetic pathways of artemisinin in *A. annua* have been extensively investigated. However, artemisinin is naturally produced in low amounts in the plant, and extraction from cultivated sources alone is insufficient to meet global demand. Consequently, current approaches focus on advances in genetic and metabolic engineering to enhance ART production in *A. annua* and other plant systems [40].

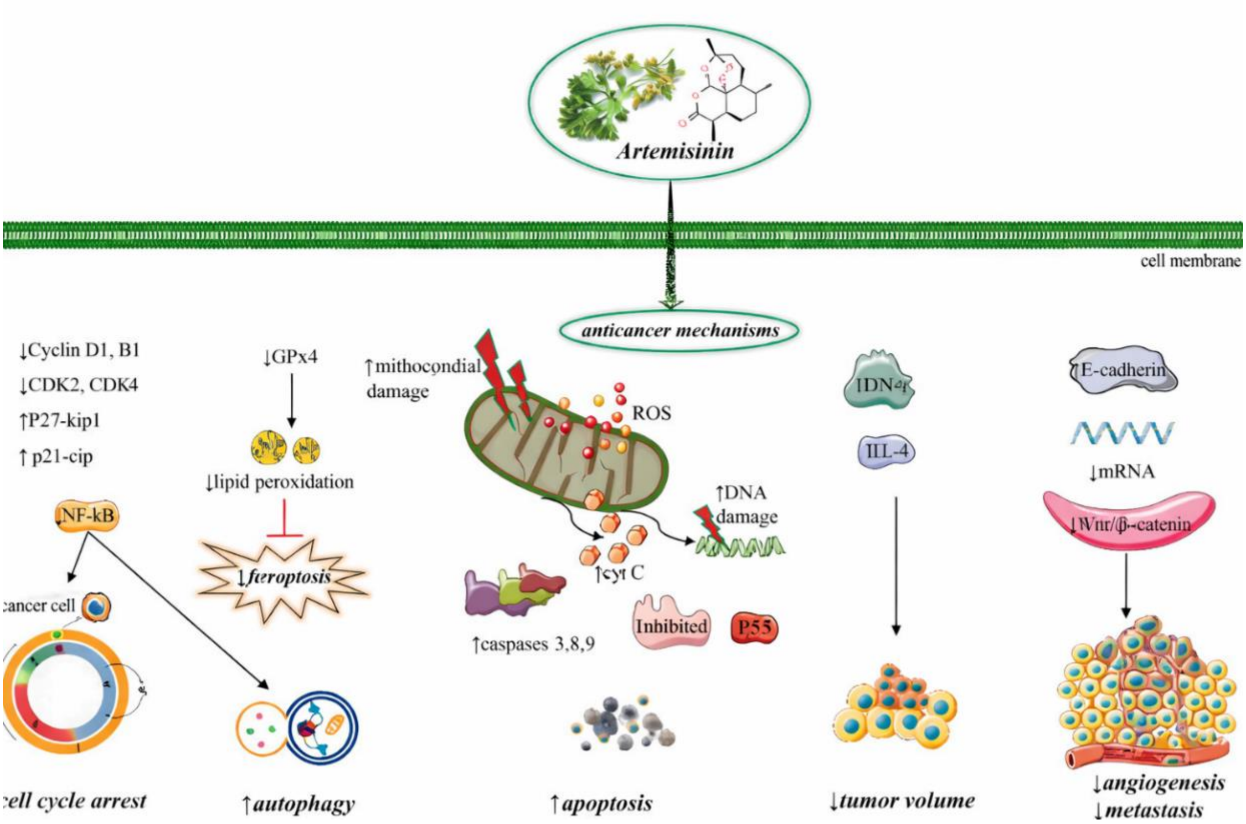

Figure 3. Schematic diagram with the anticancer potential of ART

Artemisinin (ART) is a lipophilic compound with poor water solubility (Figure 4). A study by Bhakuni et al. reported that the leaves of *Artemisia annua* contain approximately 1.4% essential oils. The presence of essential oils in the leaves may partially explain the improved solubility of ART and its higher bioavailability when administered as dried *A. annua* leaves. Titulaer et al. demonstrated that ART is rapidly but incompletely absorbed following oral administration [41]. When ART was formulated in oil, it exhibited a rapid absorption profile with relatively high peak plasma concentrations, whereas its aqueous suspension showed a slower onset of absorption and lower plasma concentrations, resulting in a more sustained release profile. It has been reported that oil-based ART administered intramuscularly achieves a bioavailability of approximately 32%, with a mean absorption time of 0.78 h. In one study, the pharmacokinetics of ART were evaluated in healthy adults following single oral doses of 250, 500, and 1000 mg. A satisfactory correlation ($r^2 = 0.92$) was observed between the areas under the plasma concentration–time curve (AUC) and plasma ART concentrations measured 5 h after administration of the 500 and 1000 mg doses. In another study, the pharmacokinetics of ART were assessed in ten healthy Vietnamese adult males following oral administration of 500 mg daily for seven consecutive days. The results demonstrated an unusual time-dependent pharmacokinetic profile. ART AUC values decreased by up to 34% on day 4 and by 24% on day 7, which was attributed to auto-induction of ART metabolism. Consistently, incubation of liver microsomes from rats pretreated with oral ART (60 mg/kg/day for 5 days) showed an accelerated rate of ART elimination. Following oral administration, the bioavailability of artesunate, ART, and artemether is approximately 30% due to extensive first-pass metabolism. Artesunate reaches peak plasma concentrations within approximately 3 minutes, whereas artemether achieves peak levels within 2–6 h. Plasma protein binding of these compounds ranges from 43% to 81.5%. Both drugs undergo extensive metabolism and are rapidly converted to dihydroartemisinin (DHA), with a plasma elimination half-life of approximately 1–2 h [42].

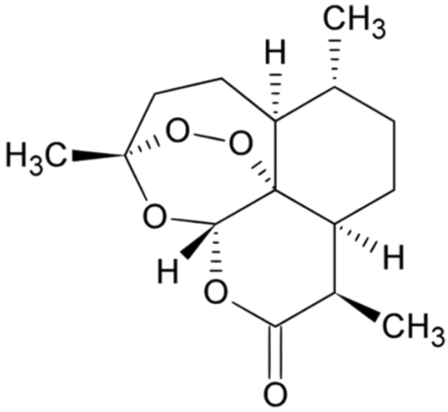

Figure 4. Structural formula of artemisinin

In addition, flavonoids (quercetin, luteolin, apigenin and their glycosides), phenolic acids (chlorogenic, caffeic, ferulic acids), coumarins, saponins and mucilage are widely distributed in *Artemisia* species. These compounds have antioxidant, anti-inflammatory, hepatoprotective and immunomodulatory effects, which comprehensively determine the pharmacological activity of jusan.

Jusan plants also contain organic acids, amino acids, enzymes and vitamins (especially vitamins C and B). Amino acid analysis of *Artemisia schrenkiana* Ledeb. (Table 1) was performed by capillary electrophoresis using a "Capel 105M" system (Russia). Dried plant material (1.0 g) was extracted with 10 mL of 0.1 M HCl in an ultrasonic bath for 15 min, followed by centrifugation at 10,000 rpm for 10 min and filtration through a 0.45 µm membrane. Separation was conducted in a fused silica capillary (50 µm i.d., 60 cm length) at 25°C with 20 mM sodium tetraborate buffer (pH 9.3) as background electrolyte, under 20 kV voltage. Detection was performed at 200 nm. Amino acids were identified by comparing migration times with reference standards and quantified using external calibration curves. All samples were analyzed in triplicate, with results expressed in mg/L and percentage (Table 2). The detection limit ranged from 0.5 to 1.0 µg/mL (S/N = 3:1).

In addition, many studies show that jusan species contain macro- and microelements (potassium, sodium, calcium, magnesium, iron, zinc, copper, manganese, cadmium, lead, etc.). These elements play an important role in the physiological function of the plant and enhance its biological and medicinal properties [43]

Table 1. Amino acids identified from plant extract of *Artemisia schrenkiana* Ledeb.

№	Time	Component	Height	Start	End	Area	Conc, mg/l	% of amino acids
1	6.198	arginine	0.505	6.167	6.233	22.02	25.0	0.103 ± 0.041
2	8.522	lysine	0.157	8.483	8.563	3.495	1.70	0.007 ± 0.002
3	8.652	tyrosine	0.102	8.570	8.697	3.948	4.10	0.017 ± 0.005
4	9.025	phenylalanine	0.140	8.945	9.087	6.859	6.50	0.027 ± 0.008
5	9.243	histidine	0.396	9.123	9.335	24.95	23.0	0.095 ± 0.047
6	9.493	Leucine+ isoleucine	9.190	9.335	9.590	524.5	190.0	0.781 ± 0.203
7	9.632	methionine	0.468	9.590	9.708	14.29	12.0	0.049 ± 0.017
8	9.802	proline	0.198	9.708	9.838	8.101	5.00	0.021 ± 0.005
9	9.893	threonine	0.711	9.843	9.967	22.44	15.0	0.062 ± 0.025
10	10.237	serin	0.051	10.198	10.302	2.143	1.10	0.005 ± 0.001
11	10.367	alanine	0.316	10.302	10.443	10.7	4.50	0.018 ± 0.005
12	10.867	glycine	0.204	10.832	10.918	3.677	1.30	0.005 ± 0.002

The diverse ecological landscapes of Kazakhstan, spanning from the Caspian lowlands to the Altai mountain range, create varying environmental conditions that profoundly affect the accumulation of secondary metabolites in *Artemisia* species. Soil characteristics, particularly increased salinity in areas like the Balkhash basin, together with the harsh continental climate of the Ustyurt plateau, are key determinants of chemotypic variation within the genus. Under saline conditions, *Artemisia* plants typically respond by synthesizing higher levels of osmoprotective compounds and phenolic substances, which serve as adaptive mechanisms against osmotic stress and may contribute to enhanced radical-scavenging activity. In contrast, populations inhabiting the hyper-arid zones of the Ustyurt plateau frequently accumulate greater quantities of volatile terpenoids and sesquiterpene lactones, compounds that provide protection against intense ultraviolet exposure and moisture loss. Such ecological adaptability leads to pronounced intraspecific phytochemical heterogeneity, whereby geographically isolated populations of the same species exhibit distinctive metabolic profiles. As an illustration, *Artemisia terrae-albae* collected from saline substrates in the Balkhash region may demonstrate flavonoid patterns differing substantially from those found in individuals growing in the non-saline environments of the Tien Shan foothills. Recognition of this chemotypic variability is critical for informed selection of plant materials yielding optimal concentrations of bioactive constituents for pharmaceutical development. Moreover, it emphasizes the necessity for population-specific conservation approaches and continuous ecological assessment, given that shifts in environmental parameters could significantly modify chemical composition and, by extension, the therapeutic potential of these valuable plant resources.

4 Antidiabetic activity of *Artemisia* L.

At present, diabetes mellitus is one of the most widespread chronic metabolic diseases worldwide. The adverse side effects associated with synthetic antidiabetic drugs have increased interest in identifying alternative natural therapeutic sources. In this context, plants belonging to the genus *Artemisia* have attracted considerable scientific attention in recent years due to their potential antidiabetic activity. In traditional medicine, various *Artemisia* species have long been used to regulate carbohydrate metabolism, reduce blood glucose levels, and improve overall metabolic function.

Evidence supporting the antidiabetic effects of *Artemisia* has been obtained from both *in vitro* and *in vivo* experimental studies. *In vitro* assays have demonstrated that *Artemisia* extracts are capable of inhibiting the activity of key carbohydrate-hydrolyzing enzymes, including α-amylase and α-glucosidase, thereby slowing carbohydrate digestion and reducing intestinal glucose absorption. In *in vivo* studies, aqueous and alcoholic extracts derived from different *Artemisia* species significantly lowered blood glucose levels and improved insulin sensitivity in experimentally induced diabetic animal models [44]–[47].

The mechanisms underlying the glucose-lowering effects of *Artemisia* appear to be multifactorial. Several studies suggest that flavonoids, phenolic acids, and sesquiterpene lactones present in *Artemisia* protect pancreatic β-cells and stimulate insulin secretion. Additionally, these bioactive compounds enhance glucose uptake in peripheral tissues, thereby contributing to reduced insulin resistance. It has also been reported that extracts of certain *Artemisia* species may increase hepatic glycogen storage while suppressing gluconeogenesis.

The antidiabetic activity of *Artemisia* is closely associated with its antioxidant and anti-inflammatory properties. Oxidative stress and chronic low-grade inflammation play key roles in the pathogenesis of diabetes mellitus. Polyphenols and flavonoids present in *Artemisia* effectively scavenge free radicals, inhibit lipid peroxidation, and reduce the production of inflammatory mediators. These effects may attenuate pancreatic tissue damage and help prevent the development of diabetic complications [48].

Currently, the antidiabetic potential of the genus *Artemisia* is considered a promising direction for clinical application. However, the number of clinical studies remains limited, and comprehensive randomized controlled trials are required to fully assess the efficacy and safety of *Artemisia* based preparations. Furthermore, issues related to the standardization of active compounds, optimal dosage regimens, and long-term safety remain unresolved. Therefore, the development of antidiabetic phytopharmaceuticals based on *Artemisia* species necessitates integrated phytochemical, pharmacological, and clinical investigations.

5 Antitumor effects of *Artemisia* and green synthesis

The key feature underlying the anticancer activity of *Artemisia* compounds, particularly artemisinins, lies in their pronounced sensitivity to iron availability. Cancer cells accumulate and metabolize iron at significantly higher levels than normal cells in order to sustain their rapid proliferation and division. The endoperoxide bridge (C–O–O–C) present in the artemisinin molecule undergoes cleavage upon interaction with iron ions, especially Fe^{2+}. This reaction leads to the generation of highly reactive oxygen-centered and carbon-centered free radicals, as well as reactive oxygen species (ROS). These radicals directly damage intracellular macromolecules, including lipids, proteins, and DNA. Lipid peroxidation compromises membrane integrity, while DNA damage induces cell cycle arrest and genomic instability. As a result, excessive intracellular oxidative stress ultimately triggers cell death. Since healthy cells generally contain lower intracellular iron concentrations, they are considerably less affected, thereby increasing the therapeutic index of artemisinins [49].

Artemisinins induce programmed cell death (apoptosis) in cancer cells through multiple interconnected molecular pathways, which can be broadly categorized into three major mechanisms.

First, the intrinsic (mitochondrial) pathway. Artemisinin-induced oxidative stress directly alters mitochondrial inner membrane permeability. This process is regulated by changes in the balance between pro- and anti-apoptotic members of the Bcl-2 protein family, such as Bax and Bcl-2. Consequently, mitochondrial permeability transition pores open, leading to the release of apoptogenic factors, including cytochrome c, into the cytoplasm. Cytochrome c associates with Apaf-1 and procaspase-9 to form the apoptosome complex, which activates caspase-9. Activated caspase-9 subsequently triggers the effector caspase-3, initiating a proteolytic cascade that degrades key structural and functional proteins, such as poly(ADP-ribose) polymerase (PARP), ultimately leading to apoptotic cell death [50].

Second, the extrinsic (death receptor-mediated) pathway. Artemisinin has been shown to enhance the expression of death receptors, such as Fas/APO-1/CD95, or stimulate the production of their ligands (FasL) in certain cancer cell types. Ligand binding promotes receptor trimerization and recruitment of adaptor proteins, including FADD, which in turn activate procaspase-8. Activated caspase-8 either directly activates caspase-3 or cleaves the BH3-only protein Bid, thereby linking the extrinsic pathway to mitochondrial apoptosis and amplifying the apoptotic signal.

Third, gene-level regulation and the p53-dependent pathway. Artemisinin may promote stabilization and activation of the tumor suppressor protein p53, often referred to as the "guardian of the genome." Upon DNA damage, activated p53 induces the transcription of pro-apoptotic genes such as Bax, PUMA, and Noxa, while simultaneously regulating cell cycle arrest through upregulation of p21. Thus, artemisinin-induced DNA damage triggers apoptosis via p53-mediated signaling pathways [51].

Beyond apoptosis and direct cytotoxicity, *Artemisia* compounds exert additional anticancer effects. Artemisinins can induce autophagy, a cellular recycling process mediated by lysosomes. Depending on the cellular context, autophagy may function as a protective mechanism or contribute to an alternative form of programmed cell death known as autophagic cell death. Furthermore, artemisinins inhibit angiogenesis by suppressing the formation of new blood vessels within tumor tissues, thereby limiting nutrient supply and metastatic potential. They may also downregulate the expression of proteins involved in tumor invasion and metastasis, such as matrix metalloproteinases (MMPs) [52].

Natural plant extracts play a crucial role in green synthesis processes due to their stability and environmental compatibility [53]. Unlike conventional chemical synthesis methods, green synthesis minimizes the use of toxic reagents and prevents the formation of hazardous by-products, thereby reducing environmental impact [54]. Silver nanoparticles synthesized using plant extracts are non-toxic and biocompatible, making them highly suitable for various biomedical applications, including wound healing, drug delivery, and bioimaging. In addition, these nanoparticles exhibit strong activity against a broad spectrum of pathogens, including viruses, bacteria, and fungi [38].

Recent studies have investigated the in vitro cytotoxic effects of silver nanoparticles synthesized via a green approach using *Artemisia* schrenkiana leaf extract (*A. schrenkiana*-AgNPs). The results demonstrated that these nanoparticles effectively inhibited the proliferation of liver (HepG2) and pancreatic (PANC-1) cancer cell lines (Figure 5). The primary mechanism underlying their biological activity involves nanoparticle penetration into the cell membrane and subsequent intracellular generation of reactive oxygen species, leading to oxidative stress, mitochondrial dysfunction, and ultimately apoptosis. Thus, green-synthesized *Artemisia* schrenkiana-AgNPs can be considered promising, environmentally friendly, and biocompatible anticancer agents whose activity is largely mediated through ROS-induced apoptotic pathways [55].

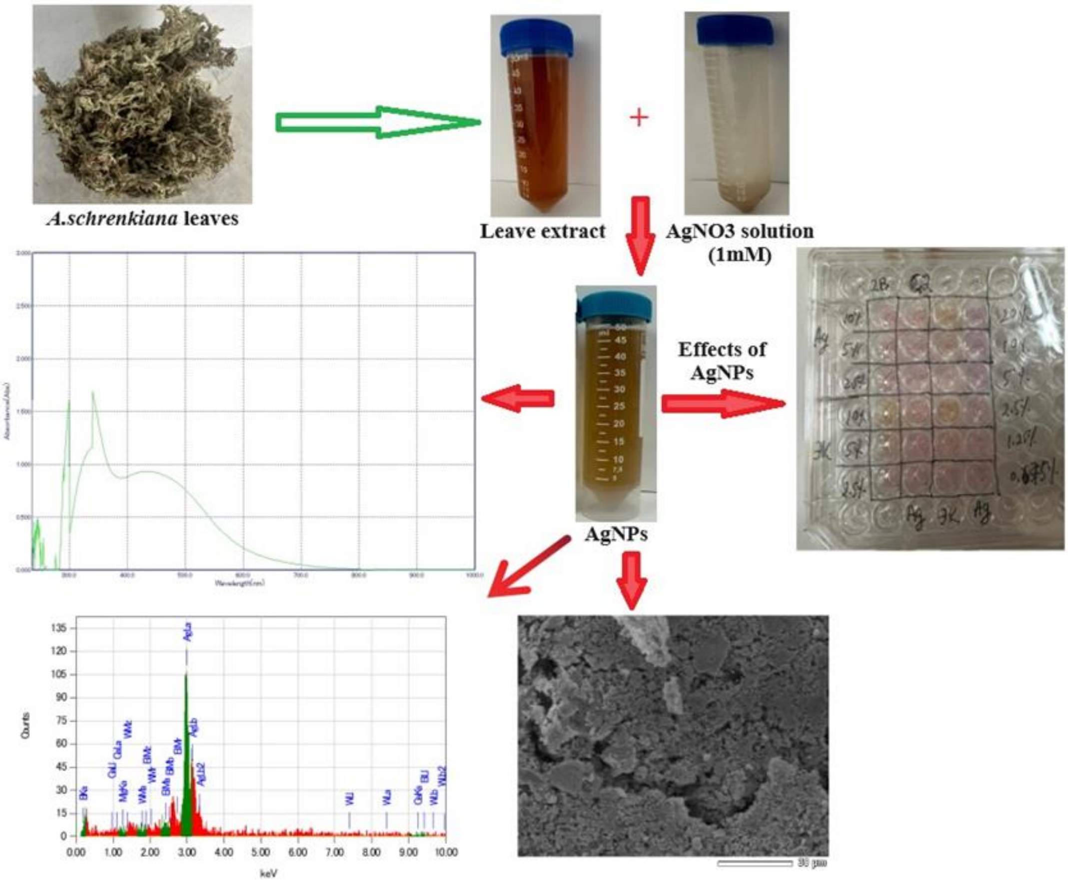

Figure 5. Synthesis of silver nanoparticles from *Artemisia schrenkiana* Ledeb. by green synthesis

6. Current trends and future perspectives

Over the past decades, research on plants belonging to the genus *Artemisia* L. has evolved into a multidisciplinary and integrative field, where traditional ethnopharmacological knowledge is increasingly combined with advances in molecular biology, phytochemistry, nanotechnology, and biomedicine. Contemporary scientific approaches are no longer limited to descriptive assessments of biological activity but are focused on elucidating the underlying mechanisms of action at the molecular and cellular levels.

One of the key directions in modern research involves comprehensive profiling of the phytochemical composition of *Artemisia* species using high-resolution analytical techniques such as LC–MS/MS, GC–MS, and NMR spectroscopy, as well as the standardization of biologically active compounds. This strategy enables the identification of pharmacological effects associated with specific active molecules rather than crude extracts. Moreover, comparative analyses of *Artemisia* species collected from different geographical regions provide insights into environmentally driven metabolic adaptations and chemical variability influenced by ecological factors [56].

Another major research focus is the identification of molecular targets of *Artemisia*-derived compounds. Increasing evidence indicates that their antidiabetic, anti-inflammatory, and anticancer effects are mediated through key signaling pathways, including insulin signaling cascades, AMPK, NF-κB, MAPK, p53, and caspase-dependent systems. Such mechanistic studies allow for a systematic evaluation of the biological potential of the genus *Artemisia* and establish a scientific foundation for the development of evidence-based phytopharmaceuticals [10].

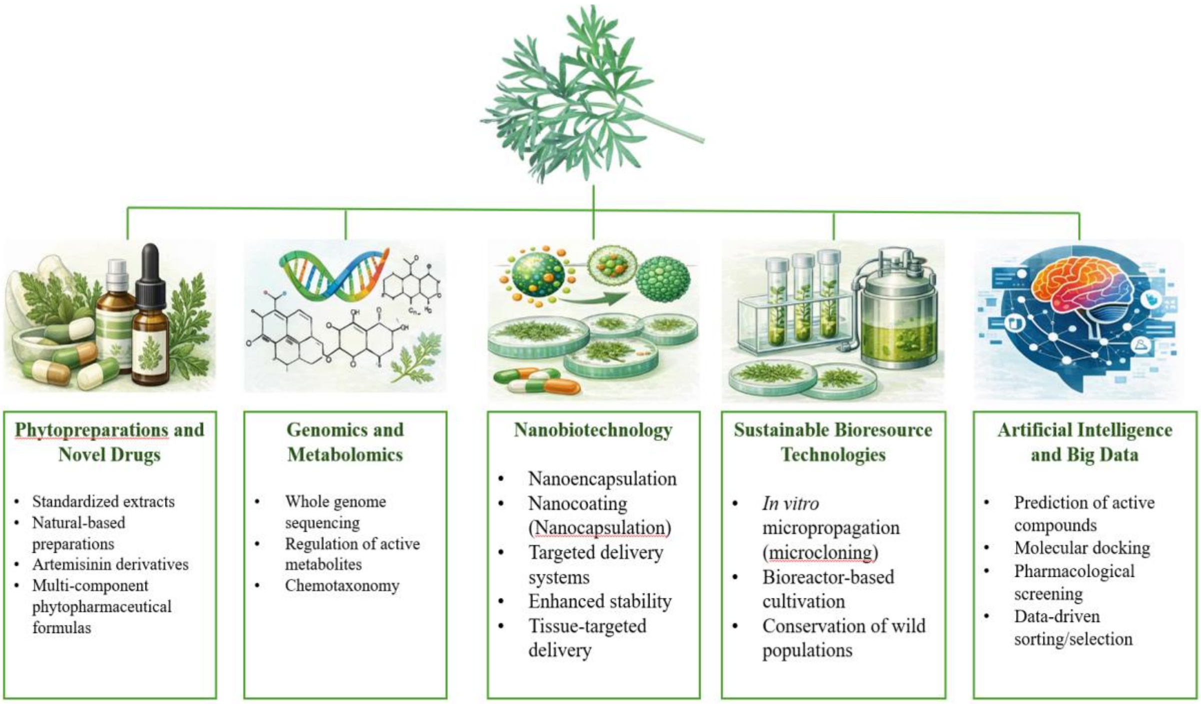

Figure 6. Future directions for research on the genus *Artemisia* L.

In recent years, particular attention has been directed toward the integration of *Artemisia* extracts with green nanotechnology approaches (Figure 6). The biosynthesis of metallic nanoparticles using plant extracts is recognized as an environmentally friendly, cost-effective, and biocompatible strategy. Silver nanoparticles synthesized from *Artemisia* extracts have demonstrated pronounced antimicrobial, antioxidant, and anticancer activities, significantly expanding their prospective applications in biomedicine.

An important direction for future research is the evaluation of the clinical potential of *Artemisia* species. At present, most available studies are limited to in vitro and in vivo experimental models, while the lack of clinical trials remains a major barrier to the translation of *Artemisia*-based products into medical practice. Therefore, well-designed clinical studies focusing on bioavailability, pharmacokinetics, toxicity, and long-term safety of active compounds are urgently needed.

In addition, the sustainable use of *Artemisia* resources and the conservation of biodiversity should constitute an integral component of future research efforts. The protection of natural populations, along with the development of introduction strategies and cultivation technologies under controlled conditions, will ensure the long-term and environmentally responsible utilization of *Artemisia*-derived phytomaterials.

7 Conclusion

The literature review shows that plants from the genus *Artemisia* L. have important phytochemical and pharmacological potential. Tannins, flavonoids, phenolic compounds, sesquiterpene lactones, and trace elements found in Artemisia species support their antioxidant, anti-inflammatory, antidiabetic, antimicrobial, and anticancer properties. These qualities make *Artemisia* valuable in traditional medicine and a promising source for modern pharmacology and biomedicine. The biological effects of compounds from *Artemisia* relate mainly to their ability to manage oxidative stress, inflammatory markers, cell cycle regulation, and processes tied to cell death. The importance of artemisinin and its derivatives highlights the global relevance of this genus.

In addition, combining *Artemisia* extracts with green synthesis methods increases their use in creating environmentally friendly biomedical products. The rich variety of phytochemicals in *Artemisia* species found in Kazakhstan opens up opportunities to shift from wild harvesting to sustainable large-scale farming. Creating specialized plantations would provide a reliable supply of raw materials for the pharmaceutical industry while helping protect natural populations. Setting up local processing facilities to extract bioactive compounds could boost a domestic phytochemical industry. This aligns with national goals for reducing imports and developing science-based exports.

Future research should aim to improve farming methods for important local *Artemisia* species and create cost-effective technologies for their large-scale growth and processing. However, to fully harness the biological activity of *Artemisia* species, we need more standardization of phytochemicals, deeper exploration of molecular mechanisms, and well-structured clinical trials. Thorough research on this genus could greatly help in creating new phytopharmaceuticals and improving the national pharmaceutical and biotechnology sectors.

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Ethics Approval and Consent to Participate
This study did not involve human participants or animals. Therefore, ethical approval and informed consent were not required.

Data Availability Statement
The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Supporting Information
Not applicable.

Conflict of Interest
The authors declare no conflict of interest.

AI Use Disclosure
The authors confirm that Artificial Intelligence (AI) tools were used only for language editing and improvement of readability. No AI tools were used to generate scientific results, data, figures, or interpretations. All analyses, conclusions, and scientific content were developed by the authors.

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