REVIEW PAPER

Expanding Horizons of *Artemisia annua*: From Antimalarial to Multidimensional Therapeutic Applications

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ABSTRACT

Artemisia annua (*A. annua*) is best known as the natural source of artemisinin, a sesquiterpene lactone with potent antimalarial activity. Recent evidence, however, suggests that *A. annua* produces a diverse range of bioactive secondary metabolites, including arteannuin B, scopoletin, casticin, and chrysosplenetin, with pharmacological activities that extend far beyond malaria. This review critically summarizes current preclinical and clinical evidence supporting the anti-inflammatory, antibacterial, antiviral, anticancer, antioxidant, immunomodulatory, and neuroprotective effects of *A. annua* and its constituents. These activities are frequently associated with shared molecular mechanisms, such as the generation of reactive oxygen species, induction of ferroptosis, and modulation of key signaling pathways, including NF-κB and MAPK. Although robust in vitro and in vivo data are available, clinical validation remains limited, with only a small number of studies, including two randomized controlled trials, reported to date. Major challenges hindering clinical translation include poor oral bioavailability, rapid metabolism, and variability in phytochemical composition among extracts. Advances in formulation strategies, such as nanoemulsions and polymer-based delivery systems, together with synthetic biology approaches to enhance artemisinin production, offer promising solutions. This review integrates recent pharmacological findings, highlights current limitations, and identifies critical gaps to support the development of *A. annua* as a sustainable and versatile source of therapeutically valuable natural products.

Keywords: Artemisinin, *Artemisia annua*, therapeutic applications, bioactive constituents, pharmacological activities, sustainable therapeutics.

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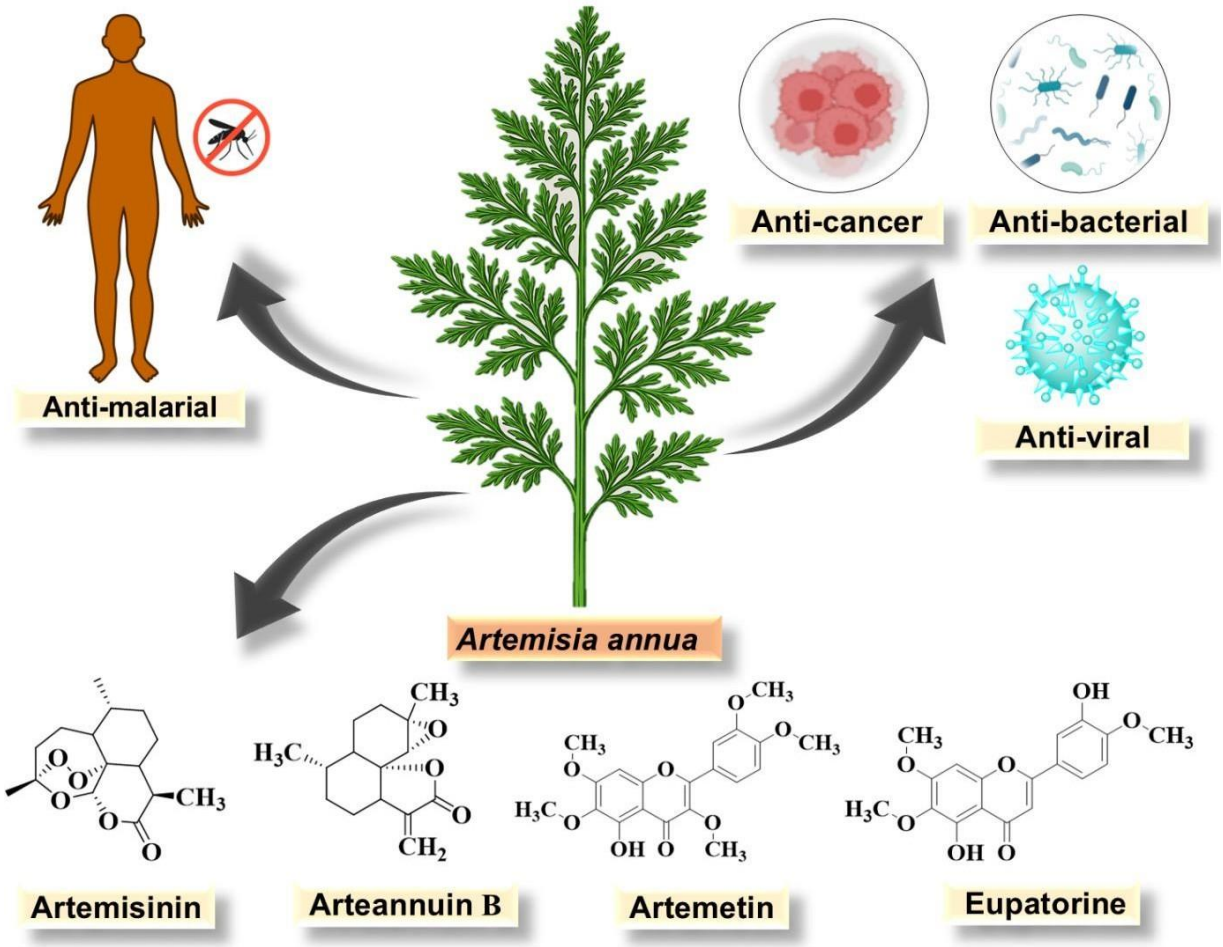


Fig. 1: A schematic overview of the phytochemical profile and therapeutic potential of *A. annua*, highlighting key bioactive constituents such as artemisinin, flavonoids, and essential oils, along with their pharmacological activities, including antimalarial, anticancer, antioxidant, and anti-inflammatory effects.

1. Introduction

The World Malaria Report (2020) estimated that approximately 229 million malaria cases occurred in 87 countries with high malaria prevalence. Approximately 95% of all malaria cases worldwide (Soni et al. 2022). Globally, the estimated number of fatalities attributable to malaria is approximately 409,000. In 2019, India recorded only 6.3 million malaria outbreaks. India holds the top spot on the list, accounting for 84% of all malaria-related deaths in Southeast Asia (WHO, 2020). Over the years, malaria-causing Plasmodium mosquitoes have developed resistance, rendering chloroquine- and sulfadoxine-pyrimethamine-based treatments ineffective. Consequently, the WHO guidelines recommend using Artemisinin-Based Combination Therapies (ACTs) as the first-line treatment for malaria (Dondorp et al. 2009). *A. annua* was first documented in the "52 Sickness Sides (Wu Shi Er Bing Fang)", a medical prescription discovered in the Mawangdui Han Tombs, intended for the treatment of haemorrhoids. The use of *A. annua* for addressing fever and chills associated with malaria was first recognized by Hong Ge (284–365 CE) in his work "Handbook of Prescriptions for Emergencies." Currently, *A. annua* is acknowledged as a medicinal plant and is included in the Chinese Pharmacopeia. Historical medical texts indicate that *A. annua* has been suggested for various ailments, including intermittent fever caused by malaria, heat or fever resulting from exhaustion, and bone steaming. It was also noted for its potential benefits in treating lice, wounds, tuberculosis, dysentery, scabies, hemorrhoids, acute convulsions linked to pollution from contact with the deceased pus in the ear, rhinopolyp, swelling, and pain around teeth, and it was recognized for its analgesic, summer-heat relieving, eyesight improving, and hemostatic properties.

A. annua belongs to the Asteraceae family, which falls under the division Magnoliophyta and the class Magnoliopsida, specifically the subclass Asteridae. This family is the largest among all flowering plant families, comprising approximately 25,000–36,000 known varieties (Mandel et al. 2019). Its global distribution primarily occurs in the Mediterranean, tropical, and temperate zones. A significant member of this genus, *A. annua*, is present in North America, Asia, Europe, and North Africa. The genus comprises approximately 600 taxa, spread across every continent except Antarctica (Soni et al. 2022). Diverse environmental conditions, including coastal areas, arid landscapes, and aquatic ecosystems, are home to species of this genus. This genus thrives across a wide range of climates, from sea level to high-altitude mountain regions, and in environments ranging from deserts to wetlands. The majority of the *A. annua* species are classified as decorative, non-woody plants that range from perennial to annual. These plants are also recognized for their medicinal and aromatic properties (Abad et al. 2012a). *A. annua*, also known as sweet wormwood, is native to China but is also found in various regions worldwide (Ekiert et al. 2021). The shoots of the plant contain a higher quantity of artemisinin, a compound with a variety of medicinal properties. This compound, a member of the terpene subclass, is found in various plants and functions as a deterrent to herbivores and parasites.

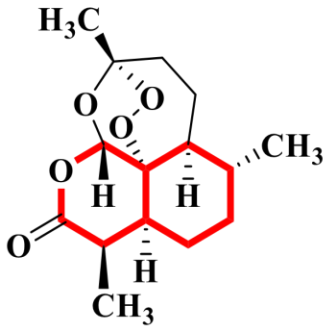
A. annua is well known for its bioactive compounds, particularly artemisinin, which is highly effective against malaria (Morua et al. 2025). Artemisinin plays a crucial role in ACTs, which are employed to combat multidrug-resistant (MDR) strains of Plasmodium. Recent research has revealed that flavonoids present in *A. annua* exhibit anticancer and antiparasitic properties. Fig. 1 illustrates the major bioactive components and their corresponding pharmacological effects (Ferreira et al. 2010b). In 2023, *Zhou et al.* reported a study of *A. annua* extract. They found that it could improve cognitive problems and changes in Alzheimer's disease (AD) by activating the AKT signaling pathway. The results of their study indicated that the *A. annua* extract could serve as a novel, multifaceted medication for AD, with promise for both prevention and management (Zhou 2023). Artemisinin was first isolated from the trichomes of flowers and leaves in China in 1971 and has been used for centuries to treat malaria. The historical significance of *A. annua* in malaria treatment is primarily attributable to the isolation of the compound artemisinin from plant sources in the 1970s. Artemisinin is a potent antimalarial compound that has revolutionized malaria treatment worldwide (Guo 2016). The WHO recommends ACTs as the standard treatment for malaria. ACTs play a significant role in reducing the burden of malaria and saving countless lives, particularly in regions heavily affected by the disease. Artemisinin is classified as a secondary metabolite in the sesquiterpene category and is synthesized by *A. annua* (Misra and Saema 2016). The worldwide demand for ACTs is growing due to a substantial supply chain gap. Extraction of artemisinin from naturally growing plants serves as a primary source and is safe for application (Weathers et al. 2011). The advancement of cultivars with enhanced artemisinin content using diverse methodologies is the primary focus of plant botanists worldwide. Artemisinin,

the active compound in *A. annua*, is highly effective in treating malaria, and its derivatives are now the cornerstone of global malaria treatment. However, a growing body of research suggests that *A. annua* and its derivatives may have potential therapeutic applications beyond malaria, such as anticancer potential against breast, lung, and colon cancer. The active sites of the isolated compounds from the *A. annua*-specific plant interact with the amino acid residues of the uncontrolled cell, consequently inhibiting cancer cells (Sharma and Dubey 2021).

According to the literature, artemisinin and its derivatives exhibit anticancer properties. It can selectively inhibit tumor growth in various types of cancers, including colon, breast, and lung cancers, induce apoptosis, and target cancer cells. *A. annua* is also a lactone-ring-containing sesquiterpene. Fig. 2 depicts the chemical structure of artemisinin, highlighting its unique sesquiterpene lactone framework. a phytochemical compound that fights bacterial, viral, and fungal infections by killing microbes, reducing inflammation, and protecting cells from damage, reported the ability of artemisinin to modulate the immune system, potentially impacting autoimmune diseases and conditions requiring immune function regulation. *A. annua*, in combination with other drugs or therapies, may reveal synergistic effects and enhance its therapeutic potential across a range of medical conditions. Therefore, the need to explore the potential therapeutic applications of *A. annua* beyond malaria is significant and holds promise for addressing various health challenges. Further research and clinical trials are required to fully understand the diverse therapeutic roles of this plant (Ahamd et al. 2023).

2. Bioactive Compounds of *A. annua*

Artemisinin, the key bioactive compound of *A. annua*, reported antifungal activity of *A. annua* (Artemisinin derivatives) against two opportunistic pathogens, *Candida albicans*, and *Cryptococcus neoformans*. Furthermore, *A. annua* possesses multiple therapeutic properties, including anti-fungal, anti-inflammatory, anti-protozoal, anti-oxidant, anti-tumor, and cytotoxic effects (Ćavar et al. 2012; de Magalhães et al. 2012). The antibacterial properties of artemisinin have been investigated against a wide range of bacteria, including *E. coli*, *S. aureus*, *P. aeruginosa*, *Mycobacterium intracellulare*, *Bacillus subtilis*, *Bacillus thuringiensis*, and *Salmonella sp*. *However*, *A. annua* remains largely unexplored (Appalasamy et al. 2014; Lal et al. 2020). However, artemisinin is exclusive to *A. annua* as it is



3,6,9-trimethyloctahydro-12*H*-3,12-epoxy dioxepino[4,3-*i*]isochromen-10(3*H*)-on

Fig. 2 Chemical structure of artemisinin (drawn using ChemDraw Professional 15.0)

absent in the majority of other *Artemisia* species (Soni et al. 2022). Several flavonoids derived from *A. annua* include eupatorin, chrysosplenetin, artemetin, casticin, cirsilineol, and chrysosplenol D (Fu et al. 2020a, 2021). A wide range of bioactive constituents have been isolated from *A. annua*, including sesquiterpenoids, flavonoids, coumarins, lipids, phenolics, purines, steroids, terpenoids, and aliphatics (Kim et al. 2016; Mishra et al. 2024a, b). Even with vast geographic variation, *A. annua* showed almost no morphological variation. However, the chemical composition and pharmacological properties of *A. annua* vary significantly depending on its geographical origin. It is important to note that water or alcoholic extracts of *A. annua* can have very different biological effects and chemical compositions, depending on how the plant was harvested, its origin, and how it was processed. However, essential oils exhibit only minor variations in their properties. Various parts of *A. annua* have been utilized for the extraction of bioactive compounds, with approximately 600 reported secondary metabolites extracted for formulation preparations, whereas only 37 molecules have been identified in tea or cold-water extracts (Debnath et al. 2011; Weathers and Towler 2012). Table 1 summarizes the key phytochemical constituents of *A. annua*, highlighting their pharmacological activities and structural features. The table includes major compounds such as artemisinin, flavonoids, and essential oils, along with their reported therapeutic properties, including antimalarial, anticancer, antioxidant, and anti-inflammatory activities.

2.1 Terpenoids

Terpenoids are an important category of bioactive compounds in *A. annua*. Terpenoids are the largest category of bioactive compounds found in plants, with

more than 40,000 distinct structures. The basic components of this class are five-carbon isoprene units. Terpenes are classified based on the number of isoprene units in their structures. Monoterpenes represent a category of terpenes composed of two isoprene units, characterized by the molecular formula $C_{10}H_{16}$. The remarkable chemical diversity of these molecules enables the plant to protect itself from both biotic and abiotic stressors while also serving as chemical signals that facilitate communication between the plant and its surroundings, including other plants and organisms. *A. annua* essential oil primarily consists of monoterpenes, which contribute to the plant's potent and aromatic scent. The essential oil is comprised of several key components, including camphene, borneol, camphor, carvone, limonene, α-terpinene, 1,8-cineole, α-and-β-pinene, and myrtenol. Sesquiterpenes represent another category of terpenes composed of three isoprene units, characterized by the molecular formula $C_{15}H_{24}$. Similar to monoterpenes, sesquiterpenes can have acyclic or cyclic structures, and their oxidation or rearrangement can lead to the formation of related sesquiterpenoids. Sesquiterpenes serve as defense agents and act as biocides against external organisms that pose a threat to plants. *A. annua* contains over 30 sesquiterpenes, primarily found in its aerial parts. The primary components were artemisinin, arteannuin B, and artemisinic acid. Artemisinin and its precursor, artemisinic acid, are most concentrated in the glandular trichomes on the plant's surface, which are found on the leaves and flower buds. Biosynthesis peaks just before or during flowering, mostly in the upper parts of the plant. Table 1 enlists the structure and biological functions of some of the key sesquiterpenes (Abad et al. 2012b).

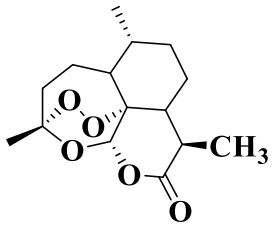
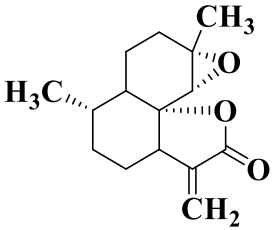
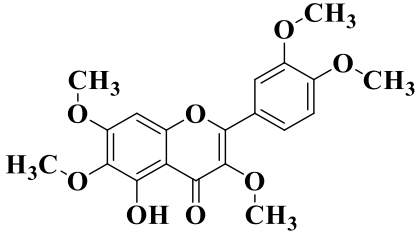
2.2 Phenolic and flavonoids:

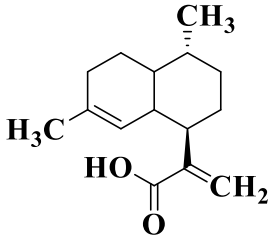
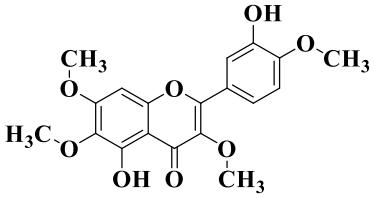
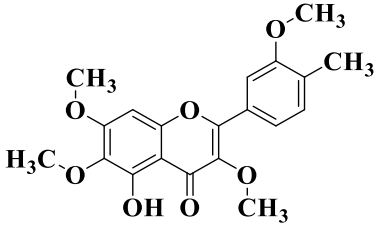
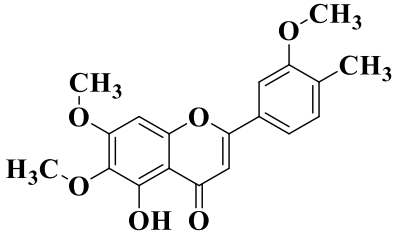
Phenolic compounds are organic molecules found extensively in plants, ranging from their roots to their fruits. The role of these molecules does not directly contribute to the fundamental processes of plant life, including growth or reproduction. These are compounds generated by plants as a defense mechanism against ultraviolet radiation and herbivorous animals, frequently acting as repellents because of their bitter taste (Carvalho et al. 2011). Phenolic compounds consist of molecules that have at least one aromatic ring (benzene) along with an alcohol group, with the fundamental structure known as phenol. On the other hand, flavonoids represent a remarkably varied class of phenolic compounds and stand out as the most significant category of phytonutrients. Fig. 3 represents, within the flavonoid category, various subclasses encompassing flavones, isoflavones, flavanols, flavonols, dihydroflavonols, flavanones, bioflavonoids, aurones, and chalcones. *A. annua* contains various classes of phenolic compounds in its alcoholic and aqueous extracts, like cyclitol, quinic acid, phenolic acid, and caffeic acid (Ferreira et al. 2010a). Flavonoids included luteolin, quercetin, rutin, apigenin, isorhamnetin, kaempferol, mearnsetin, artemetin, casticin, chrysosplenetin, chrysosplenol D, cirsilineol, and eupatorine. Various studies have highlighted that the antioxidant potential of *A. annua* is due to its rich flavonoid content and the variety of compounds present. The predominant flavonoids present in *A. annua* include eupatorine, cirsilineol, artemetin, casticin, chrysosplenetin, and chrysosplenol D (Brisibe et al. 2009).

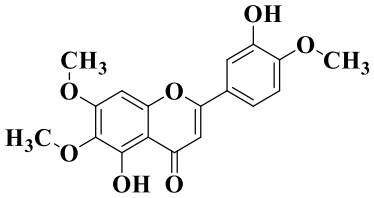
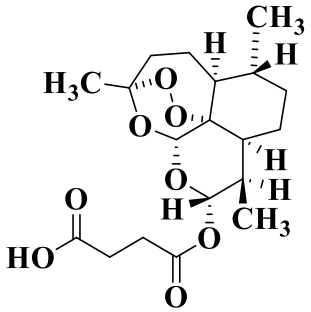
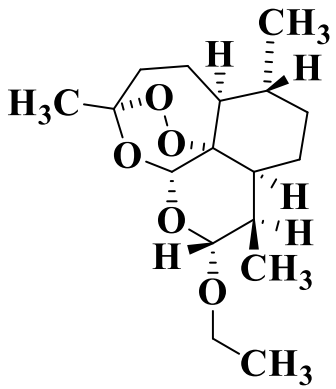
2.3 Coumarins:

Coumarins are organic compounds that originate from benzo-α-pyrone. These compounds possess one or more phenolic functions. Coumarins are found extensively throughout the plant kingdom. These substances develop within the leaves and tend to accumulate, particularly in the roots and bark, along with older or injured tissues. Coumarins serve as defense mechanisms against herbivores and harmful microorganisms. Their primary locations are on the surface and in the organs that are most vulnerable to predation, such as young leaves, fruits, and seeds, as a strategy to conserve metabolic energy. The primary coumarins identified in the alcoholic extracts of *A. annua* were scopolin and scopoletin. Table 1 shows the chemical structures and biological activities of several coumarins found in the extracts of *A. annua* (Fu et al. 2020b).

Table 1. *A. annua's* Phytochemistry, Pharmacological Characteristics, and Structural Information

S.No	Phytochemical classification	Molecules	Pharmacological Properties	Structures	References
1.	Sesquiterpene	Artemisinin	Anti-malarial, Anti-parasitic, Anti-inflammatory, Antiviral, Anti-fibrotic, and Anti-tumor		(Wang et al. 2020; Kshirsagar and Rao 2021)
2.	Sesquiterpene	Arteannuin B	Anti-viral, Anti-tumor, Anti-inflammatory, larvicidal		(Septembre-Malaterre et al. 2020a)
3.	Flavonoid	Artemetin	Hypotensor, Anti-tumor, Anti-oxidant, Anti-inflammatory		(Lv et al. 2023; Patel and Patel 2024)

4.	Sesquiterpene	Artemisinic acid	Allelopathy effect, and Anti-adipogenesis effect, can regulate adipocyte differentiation.		(Kong et al. 2013)
5.	Flavonol	Casticin	Anti-oxidant, Anti-aging, Anti-tumor, Anti-inflammatory		(Jan et al. 2020; Gan et al. 2024)
6.	Flavonoid	Chrysosplenetin	Anti-viral		(Lalani and Poh 2020; Ahmed et al. 2022)
7.	Flavonoid	Cirsilineol	Immunosuppressive, Anti-tumor		(You et al. 2022)

8.	Phenolic	Eupatorine	Anti-tumor		(Abd Razak et al. 2020)
9.	Terpenoids	Artesunate	Anti-malarial, Anti-cancer		(Khanal 2021)
10.	Terpenoids	Arteether	Anti-malarial, Anti-cancer		(Pirali-Hamedani et al. 2022)

Note: The chemical structures were drawn using ChemDraw Professional 15.0

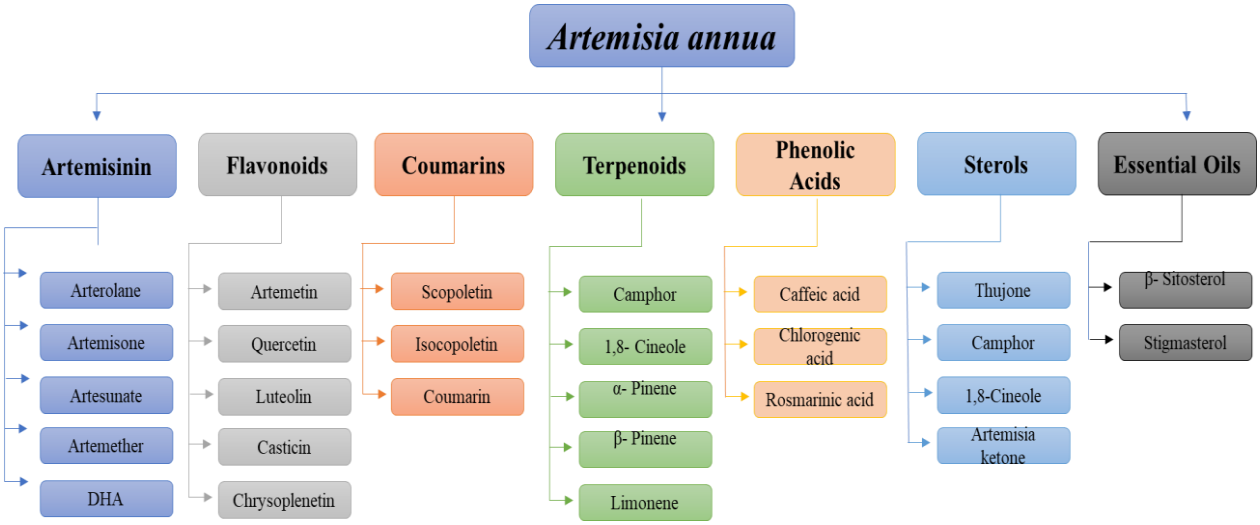


Fig. 3 Secondary metabolites present in *A. annua* (Zeng et al. 2023)

3. Pharmacological properties of *A. annua*

A. annua (commonly known as sweet wormwood) is a medicinal plant renowned for its diverse pharmacological properties, primarily attributed to its bioactive compound artemisinin. This plant exhibits potent antimalarial activity, with artemisinin and its derivatives serving as the cornerstones of modern malaria therapy. In addition to its antimalarial, *A. annua* has demonstrated significant anti-inflammatory, antioxidant, antiviral, and anticancer properties. These activities are linked to their rich phytochemical profile, including flavonoids, sesquiterpenes, and phenolic acids, which help to mitigate oxidative stress and inflammation (Feng et al. 2020a). Fig. 4 shows a graphical representation of the pharmacological properties of *A. annua*, *which* is presented below. Studies have also highlighted its potential for managing diabetes and cardiovascular disorders by improving lipid profiles and glucose metabolism. Furthermore, *A. annua* exhibits antimicrobial activity against a broad spectrum of pathogens. Owing to its therapeutic versatility and minimal side effects, this plant continues to be explored for novel drug development and the treatment of various diseases.

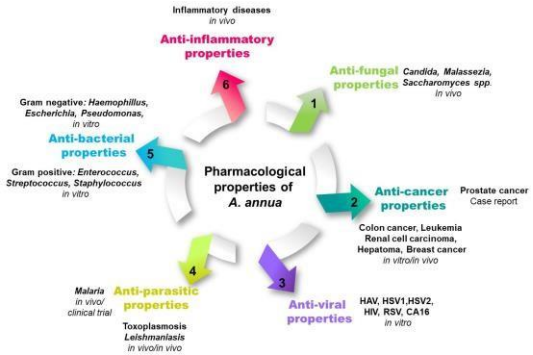


Fig. 4 Pharmacological properties of *A. annua*

3.1 Anticancer Properties of *A. annua*

Cancer continues to be a prominent cause of mortality alongside cardiovascular and respiratory disorders. With the increase in the population, there is growing concern regarding the rising risk of cancer. The ongoing search for novel chemotherapeutics to combat cancer continues. Primarily, individuals with highly metastatic and aggressive cancers gain advantages from alternative medications compared with standard chemotherapeutics, as cancer cells often develop resistance to these conventional treatments. *A. annua* has been recognized and utilized for a long time for the treatment of cancer, offering a significant reservoir of active compounds.

3.1.1 Mechanisms of *A. annua* in cancers

Mechanisms through which *A. annua* constituents act against various types of cancers (e.g., apoptosis induction, inhibition of metastasis, anti-angiogenesis).

With the rigorous efforts of scientists, various mechanisms have been identified for the anticancer activities of *A. annua* constituents. Fig. 5 illustrates the anticancer mechanisms of action of artemisinin, showing key signaling pathways involved in cancer cell inhibition and apoptosis, with symbols indicating activation (+), inhibition (–), downregulation (↓), and upregulation (↑). The outcome of their results has revealed that the oxidative stress response plays a significant role in inducing cell death, as evidence shows that the endoperoxide moiety is essential for the bioactivity of constituents in *A. annua*. This cleavage results in the formation of ROS, which likely contributes to oxidative stress. Together, ROS and oxidative DNA damage significantly impact cellular integrity, resulting in disruption of the processes of cellular replication and division, which ultimately leads to cell cycle arrest and cell death. It has been found that cell cycle arrest can take place at the G1 or G2 checkpoints, likely influenced by specific defects in the cell cycle machinery of different tumor cell lines. This sequence of events ultimately results in apoptosis. Depending on the cell model, *A. annua* constituents can induce both mitochondrial and extrinsic apoptotic pathways, characterized by upregulated Fas/CD95 expression, breakdown of the mitochondrial membrane potential, cytochrome C release, PARP cleavage, and activation of caspases 3 and 9. In addition to apoptosis, *A. annua* compounds are capable of triggering several non-apoptotic modes of cell death, including necrosis, autophagy, necroptosis, anoikis (anchorage-dependent cell death), oncosis (ischemic cell death), and ferroptosis, a distinct form of regulated cell death that is strictly dependent on intracellular iron and driven by ironcatalyzed lipid peroxidation, setting it apart from apoptosis and other programmed cell death pathways (Chen et al. 2020b). Ferroptosis is mechanistically characterized by the accumulation of ferrous iron (Fe^{2+}), excessive ROS generation via Fenton chemistry, and uncontrolled peroxidation of membrane lipids, leading to catastrophic membrane damage and regulated necrotic cell death (Chen et al. 2020b). Importantly, artemisinin and its derivatives derived from *A. annua* have been shown to enhance ferroptotic sensitivity in cancer cells by disrupting iron homeostasis, promoting ferritin degradation, increasing the intracellular labile iron pool, and amplifying iron-dependent oxidative stress, thereby selectively sensitizing tumor cells to ferroptotic death (Carbone 2020a).

This ferroptosis-mediated cytotoxicity is particularly pronounced in cancer cells with elevated iron requirements or compromised antioxidant defenses, highlighting ferroptosis as a promising therapeutic vulnerability in oncology (Chen et al. 2024). Moreover, the presence of ferrous iron has been demonstrated to significantly potentiate the cytotoxic effects of *A. annua* compounds, further supporting ferroptosis as a key iron-dependent mechanism contributing to their anticancer activity (Carbone 2020b). Table 2 summarizes notable findings from studies employing diverse cancer cell lines and highlights the probable molecular mechanisms involved.

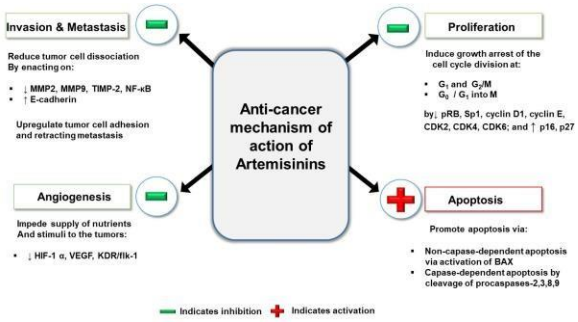


Fig. 5 Anti-cancer mechanism of action of artemisinin, (+ activation; – inhibition; ↓ regulation and ↑ upregulation)

The anticancer activity of the *A. annua* extract against human breast cancer was investigated by *Lang et al*. The findings of their study indicated that the extract significantly reduced the viability of various cancer cell lines, including breast (MDA-MB-231 and MCF7), pancreatic (MIA PaCa-2), prostate (PC-3), and non-small cell lung cancer (A459) cells. In contrast, normal mammary epithelial cells, lymphocytes, and PBMC exhibited notable resistance to the extract treatment. Similarly, the predominant compounds in the extract, arteannuin B, chrysosplenol D, and casticin, while excluding arteannuic acid, demonstrated an inhibitory effect on the viability of MDA-MB-231 breast cancer cells. The extract led to the accumulation of multinucleated cancer cells within 24 hours of treatment, increased the number of cells in the S and G2/M phases of the cell cycle, activation of caspase 3, followed by a loss of mitochondrial membrane potential, and the formation of an apoptotic hypodiploid cell population (Lang et al. 2019a). The anti-cancer potential of *A. annua* has been documented not only in human cell studies, but also in animal research. For instance, one study assessed the cytotoxic effects of *A. annua* on two canine

osteosarcoma (OSA) cell lines, OSCA-40 and OSCA8, with an emphasis on the potential role of ferroptosis. OSCA-40 and OSCA-8 were subjected to various dilutions of the extract to calculate the EC50. Subsequently, the uptake of artemisinin by the cells was assessed, along with its effects on the cell cycle, intracellular iron levels, cellular morphology, and state of lipid oxidation. The extract exhibited a concentration of artemisinin of 63.8 ± 3.4 µg/mL. Interestingly, in OSCA-40, modifications in the cell cycle and a notably elevated intracellular iron concentration were detected. The treatment with the extract in both cell lines was linked to lipid peroxidation and the emergence of a "ballooning" phenotype, indicating the activation of ferroptosis (Salaroli et al. 2022). Table 2 presents the anticancer activities of key bioactive constituents isolated from *A. annua* against various human cancer cell lines. Compounds such as artemisinin, artesunate, scopoletin, and flavonoids (e.g., luteolin and quercetin) are listed along with their respective target cell lines, IC_{50} values, and reported mechanisms of action, including induction of apoptosis, cell cycle arrest, and reactive oxygen species (ROS) generation.

Table 2 Anticancer potential of *A. annua* constituents against various cell lines

S.No.	Source Compound	Type of Cancer	Mechanism of Action	References
1.	Artemisinin	Breast Cancer	Induces apoptosis via ROS generation, disrupts mitochondrial membrane potential.	(Efferth et al. 2001)
		Leukemia	Alters cell cycle progression, promotes apoptosis through upregulation of p53 and Bax protein	(Lam et al. 2019)
		Prostate Cancer	Induces apoptosis and ferroptosis through iron-dependent lipid peroxidation	(Na et al. 2024)
		Ovarian Cancer	Enhances ROS production, leading to apoptosis, and interferes with DNA repair mechanisms.	(Yuan et al. 2020)
		Multiple Myeloma	Inhibits growth by triggering apoptosis through the endoplasmic reticulum stress response	(Wu et al. 2013)
		Oral Squamous Cell Carcinoma	Promotes apoptosis via JNK and p38 MAPK pathway regulation	(Chen et al. 2014)

		Bladder Cancer	Inhibits angiogenesis, reduces VEGF expression, and induces cell cycle arrest	(Wei et al. 2017)
2.	Luteolin	Cervical Cancer	Inhibits cell migration and invasion by MMP expression	(van Loggenberg et al. 2022)
		Colon Cancer	Induces apoptosis; inhibits PI3K/Akt and Wnt/β-catenin signaling pathways	(Pandurangan 2013)
3.	Artesunate	Colorectal Cancer	Inhibits cell proliferation, induces apoptosis via caspase activation, and DNA damage	(Demir et al. 2024)
4.	Scopoletin	Liver cancer (Hepatocellular)	Suppresses NF-κB pathway, reduces cell viability, and inhibits proliferation	(Xu et al. 2018)
5.	Caffeic Acid	Melanoma	Induces apoptosis by activating caspase-3, and downregulates survival pathways like Akt	(Lee et al. 2012)
6.	Dihydroartemisinin	Lung Cancer	Inhibits tumor growth by regulating Wnt/β-catenin signaling pathway, and induces autophagy	(Chen et al. 2020a)
7.	Artemether	Pancreatic Cancer	Triggers apoptosis through oxidative stress and MAPK pathway activation	(Wang et al. 2016)

8.	Quercetin	Glioblastoma	Reduces tumor cell viability via PI3K/Akt and MAPK signaling pathways	(Pappalardo et al. 2016)
9.	Artemisinin	Bladder Cancer	Inhibits angiogenesis, reduces VEGF expression, and induces cell cycle arrest	(Wei et al. 2017)
10.	Scoparone	Gastric Cancer	Reduces tumor growth by modulating immune response and inducing apoptosis	(Li et al. 2020)

Note: ROS–Reactive Oxygen Species; **MMP**– Modulating Matrix Metalloproteinase; DNA- Deoxyribonucleic Acid; **NF-Kb**- Nuclear Factor kappa-light-chainenhancer of activated B cells: **JNK**- c-Jun N-terminal Kinase; **MAPK** Mitogen-Activated Protein Kinase; **WNT**-Wingless/Integrated ***PI3K/AKT*** Phosphoinositide 3-Kinase/Protein Kinase B Pathway; **VEGF**- Vascular Endothelial Growth Factor

3.2 Anti-Inflammatory and Antimicrobial Activities

Mechanisms through which *A. annua* compounds reduce inflammation, relevant biomarkers, and pathways involved (e.g., NF-kB inhibition and cytokine modulation). The anti-inflammatory effects of artemisinin have been extensively studied in various disease models, including autoimmune disorders, allergic reactions, and sepsis (Septembre-Malaterre et al. 2020a). Research suggests that these effects are due to the suppression of key inflammatory pathways, such as mitogen-activated protein kinase (MAPK) and PI3K/Akt signaling cascades, as well as the inhibition of NF-κB activation and the expression of Toll-like receptors 4 and 9 (Acosta-Martinez and Cabail 2022). Although artemisinins have been well documented for their anti-inflammatory properties, studies on the whole plant, *A. annua*, remain limited. One of the earliest investigations in 1993 assessed the effects of plants on mice and rats subjected to inflammation induced by yeast powder, dimethylbenzene, and egg whites. Oral administration of *A. annua* water extract (at doses of 15, 30, and 60 g/kg for four to six days) led to a significant reduction in inflammation (Guo et al. 2022). Furthermore, we compared the antiinflammatory potential of different *A. annua* extracts (water, methanol, ethanol, and acetone) through in vitro experiments (Kim et al. 2016). Among these, acetone extract, which had the highest artemisinin content, was the most effective in suppressing the production of inflammatory mediators such as nitric oxide (NO), prostaglandin E2 (PGE2), and cytokines (IL-1β, IL-6, and IL-10) in lipopolysaccharide (LPS)stimulated macrophages. Similar findings were reported by Chougouo et al. (2016), in which ethanol extracts and five isolated compounds (artemisinin, scopoletin, chrysosplenetin, eupatin, and sitosterol glucoside) demonstrated inhibitory effects on NO production in LPS-induced macrophages at varying concentrations (Chougouo et al. 2016). In another study, *A. annua* tea infusion was tested for its ability to reduce intestinal inflammation using Caco-2 cells at a concentration of 3300 μg/ml(de Magalhaes et al. 2012). Although no anti-inflammatory effects were observed in normal Caco-2 cells, the infusion significantly lowered IL-6 and IL-8 secretion in inflamed cells. This study also indicated that the observed anti-inflammatory effects were not solely due to artemisinin but were likely attributed to rosmarinic acid, the primary phenolic compound in *A. annua*. Other compounds found in *A. annua*, such as casticin and chrysosplenol-d, have also demonstrated strong anti-inflammatory activity in both animal models and cultured macrophages (Li et al. 2015). In mice, topical application of casticin and chrysosplenol-d reduced croton oil-induced skin swelling, while oral administration suppressed systemic inflammation by downregulating NF-κB and c-JUN signaling pathways. Overall, these findings suggest that *A. annua* may have potential as a therapeutic agent for inflammatory conditions. However, studies indicate that high doses and prolonged administration (15–60 g/kg in animals and 100–3000 μg/mL in vitro) may be necessary for significant effects. The key bioactive components contributing to these properties include artemisinin, scopoletin, chrysosplenetin, eupatin, sitosterol glucoside, rosmarinic acid, casticin, and chrysosplenol D. Clinical studies have also explored the antiinflammatory effects of *A. annua* in humans. Fig. 6 presents the proposed mechanism by which artemisinin modulates key signaling pathways underlying its anti-inflammatory, anti-allergic, and antioxidant activities, with symbols denoting pathway activation (+) and inhibition (–). A randomized placebo-controlled trial involving 42 patients with osteoarthritis found that taking 150 mg *A. annua* extract twice daily improved pain, stiffness, and functional mobility without adverse effects (Trendafilova et al. 2020). However, increasing the dosage to 300 mg twice daily resulted in gastrointestinal issues in 28.6% of participants and did not provide significantly better outcomes than the placebo. In another clinical trial, *A. annua* was tested alongside standard treatments for rheumatoid arthritis (Yang et al. 2017). Patients were divided into two groups: one received leflunomide and methotrexate, whereas the other received the same treatment plus *A. annua* extract (30 g/day). Although no significant effects were observed at 12 weeks, improvements in pain, joint inflammation, and overall treatment effectiveness were observed at 24 and 48 weeks. These results suggest that *A. annua* may enhance long-term management of rheumatoid arthritis when used as a complementary treatment. Despite these encouraging clinical observations, the translational evidence supporting the anti-inflammatory efficacy of *A. annua* remains limited. The available clinical studies, including the randomized placebo-controlled trial in osteoarthritis, are constrained by small sample sizes, relatively short intervention durations, and heterogeneity in extract composition and dosing

regimens. Moreover, the evaluated outcomes primarily focused on symptomatic improvement rather than validated inflammatory biomarkers or diseasemodifying endpoints, limiting mechanistic interpretation of the observed effects. The occurrence of gastrointestinal adverse effects at higher doses further highlights challenges related to tolerability and dose optimization. Collectively, these limitations underscore the gap between robust preclinical antiinflammatory evidence and consistent clinical translation, emphasizing the need for larger, wellcontrolled clinical trials employing standardized formulations and biomarker-driven endpoints to substantiate the therapeutic potential of *A. annua* in inflammatory disorders.

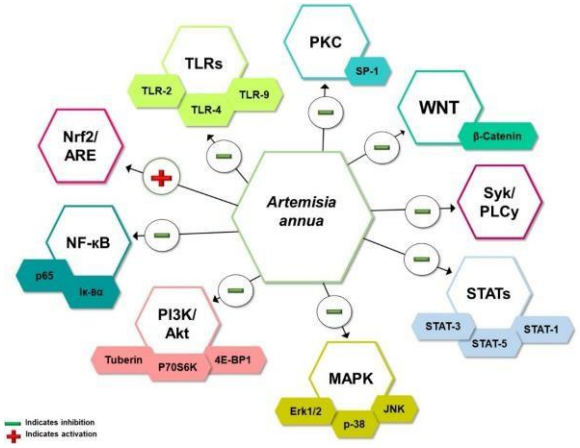


Fig. 6 Proposed mechanism of action of artemisinin in modulating signaling pathways underlying their antiinflammatory, anti-allergic, and antioxidant activities. (+ Activation; -Inhibition)

3.2.1 The effectiveness of *A. annua* against various pathogens, including bacteria, fungi, and viruses, with an emphasis on resistant strains

In recent times, researchers have concentrated on the antifungal and antibacterial properties of *A. annua*, with a particular emphasis on its essential oils. Studies have been conducted on a variety of fungi and bacteria, including those that are gram-positive (*Enterococcus, Streptococcus, Staphylococcus, Bacillus, Listeria spp.*), gram-negative bacteria (*Haemophilus, Escherichia, Pseudomonas, Klebsiella, Acinetobacter, Salmonella, Yersinia spp.)*, and fungi (*Candida, Malassezia, Saccharomyces spp.*). The essential oil of *A. annua* exhibits both antifungal and antibacterial properties. According to reports, the French variant of the oil did not demonstrate any antibacterial effects against Escherichia coli and Staphylococcus aureus. Conversely, the oils from Romania, Italy, and China demonstrated antibacterial properties against these two strains. This discrepancy might be attributed to variations in the strains and the chemical makeup of the oils utilized in these investigations. The chemical profiles of the essential oil differed significantly, with camphor, artemisia ketone, and 1,8-cineole being the primary constituents in the oil derived from the aerial parts of *A. annua*. In contrast, for essential oils extracted from *A. annua* seeds, trans-3(10)-caren-4-ol was the predominant component, and camphor was absent. (Habibi et al. 2013). The vapor-phase of the oil and the spike oil demonstrated greater antimicrobial effectiveness due to their higher terpenoid content compared to the total oil and the stem oil, respectively(Li et al. 2012; Santomauro et al. 2016, 2018). The primary isolated components have been extensively researched and have demonstrated impressive antimicrobial properties(Bilia et al. 2014; Marinas et al. 2015; Donato et al. 2015). Nevertheless, the overall oil exhibited more potent antimicrobial properties, indicating that the essential oil's antimicrobial effects were at least partially due to the synergistic interactions among its components. Additionally, the antimicrobial efficacy of the primary components might be influenced by other minor constituents. Besides the essential oil of *A. annua*, both the leaf powder and crude extracts from the entire plant demonstrated antimicrobial properties, positioning *A. annua* as a promising source for developing new antimicrobial agents (Gupta et al. 2009; Pawar et al. 2015). Nonetheless, there is a lack of *in vivo* research evaluating the antimicrobial properties of *A. annua*, and its advantages and disadvantages compared to current antimicrobial agents remain unclear. Additional research is necessary to thoroughly assess the potential of *A. annua* for antimicrobial use in clinical settings.

3.3 Antidiabetic Properties

A. annua has been explored for its capacity to enhance insulin sensitivity and reduce blood sugar levels. Studies have demonstrated the effectiveness of waterbased extracts of *A. annua* in mitigating hyperglycemia and hypoinsulinemia in patients with diabetes, with significant decreases in blood glucose levels observed in those treated with 28.5 mg/kg twice daily. The potential mechanisms behind these effects include stimulation of insulin secretion from beta cells, inhibition of pancreatic alpha cells, and amplification of insulin action (Winkelman 1989). Additionally, a critical link among oxidative stress, inflammation, and

insulin function has been increasingly acknowledged. This is attributed to the role of antioxidants in defending the adverse effects of hyperglycemia and in improving glucose metabolism (Woerdenbag et al. 1991). Typically, these antioxidants are flavonoids, which have been found to target biological mechanisms linked to type 2 diabetes mellitus, such as α-glycosidase, glucose cotransporter, and aldose reductase (Helal et al. 2014).

3.4 Cytotoxic and Anti-tumor Properties

A. annua demonstrates a broad range of biochemical activities, suggesting its potential as a source for developing novel herbal treatments for cancer. In an *in vitro* and *in vivo* study conducted by (Lang et al. 2019b). It was found that *A. annua* plant extract, devoid of artemisinin, exhibited antitumor properties. The researchers identified the active components and validated them through the study conducted in two *in vivo* cancer models, namely the chick chorioallantoic membrane assay, commonly known as CAM assay, and orthotopic breast cancer xenografts in nude mice.(Taleghani et al. 2020).

A. annua appears to hold significant potential as a cancer therapeutic agent because of its cytotoxic and antitumor properties, which include its ability to induce apoptosis, generate ROS, inhibit cell proliferation and angiogenesis, and modulate the immune response. Although further clinical trials are necessary to fully understand its safety and efficacy in humans, existing research suggests that this plant-based treatment could be a valuable addition to conventional cancer therapies (Hou et al. 2012).

3.5 Immunomodulatory properties

A. annua exhibits significant immunomodulatory properties, making it a valuable treatment choice for immune-related diseases and conditions. Its potential to manage cytokine production, regulate immune cell activity, decrease oxidative stress, and block inflammatory pathways highlights its potential as a natural remedy to enhance immune function and reduce inflammation (Kawai and Akira 2009). Despite the need for further research, particularly clinical trials in humans, to fully comprehend its potential efficacy and safety, the available evidence underscores its potential as a versatile and beneficial medicinal plant. Numerous studies have focused on artemisinin and its derivatives with respect to their Immunoregulatory characteristics (WojtkowiakGiera et al. 2019).

In vitro Studies, scientists have conducted lab experiments on immune cells, which revealed that *A. annua* extracts can regulate the formation of cytokines and boost the efficiency of immune cells. (Septembre-Malaterre et al. 2020b). *In Vivo* Studies have demonstrated that *A. annua* regulates immune responses in conditions such as autoimmune diseases, infections, and cancer. These studies have indicated that the plant can decrease inflammation and enhance immune function, and clinical studies in humans have suggested that *A. annua* may have potential advantages in regulating immune responses under various conditions, but additional research is needed to confirm these findings(Feng et al.
2020b).

3.5 Anti-viral properties

Studies have shown that *A. annua* extracts, artemisinin, and its derivatives possess potent *in vitro* and *in vivo* antiviral activities against a broad spectrum of viruses, including both DNA and RNA viruses (Efferth 2018).

A. annua is a natural remedy with significant antiviral properties, making it a promising treatment for various viral infections. Its ability to inhibit viral replication, directly inactivate viruses, modulate the immune system, and prevent viral entry into host cells highlights its potential as an antiviral agent (Chang and Woo 2003). Although existing research provides a solid foundation for its antiviral effects, more comprehensive clinical studies are essential to fully understand its efficacy and safety in humans (Reiter et al. 2015). However, *A. annua* remains a valuable plant with potential applications in the inhibition and treatment of viral diseases. *A. annua* extracts can impede the replication of numerous viruses such as influenza, herpes simplex virus, and hepatitis B and C viruses (Dai et al. 2016). Amidst the COVID-19 pandemic, *A. annua* has gained recognition for its purported antiviral properties against SARS-CoV-2, the disease-causing pathogen. While some studies and anecdotal evidence indicate that it may help lower viral load and alleviate symptoms, additional rigorous clinical trials are essential to validate its efficacy (Zulhendri et al. 2021).

3.6 Anti-oxidant Properties

Numerous studies have demonstrated the significant antioxidant capabilities of *A. annua*, which have been attributed to its phenolic compounds(Iqbal et al. 2012; Lang et al. 2019b).

Messaili (2020) identified specific compound families, including terpenes, flavonoids, and coumarins, as key contributors to the antioxidant activity of this plant(Messaili et al. 2020). The flavonoid chrysoprenol D (molecular formula: $C_{18}H_{16}O_8$) also has antioxidant properties. However, the alcoholic extract of the plant exhibited stronger antioxidant effects than its individual components, highlighting the synergistic effects of the plant compounds(Ćavar et al. 2012).

4. Anti-malarial properties of artemisinin and its derivatives

In 2015, You you Tu was awarded the Nobel Prize in Physiology and Medicine for her significant contributions in discovering artemisinin and its effective application in malaria treatment. Artemisinin is a valuable discovery in traditional Chinese medicine, distinguished by its unique sesquiterpene lactone that has evolved through phytochemical processes (Tu 2011). The emergence of chloroquine resistance in *P. falciparum* during the early 1960s marked a significant challenge for malaria treatment. Beginning in the 1960s, resistance to chloroquine emerged in *P. falciparum*, prompting the search for a novel antimalarial drug, artemisinin. Artemisinin was discovered by Chinese scientist You you Tu in the 1970s during a research project, she aimed to find a cure for malaria, where she came across Chinese texts that mentioned the utilization of *A. annua* for treating fevers, she was successful in isolating the artemisinin from the plant. It functions by targeting Plasmodium parasites at various stages of their life cycle. provides detailed information on the secondary metabolites present in *Artemisia spp.*

The association of You you Tu with the "523 project" commenced in the year 1969 examine over 10,000 herbal formulations, a secondary metabolite having antimalarial properties of *A. annua* was evaluated against malaria in mice; however, an inconsistent success rate ranging from 12% to 68% was attained. The extract of *A. annua* in heated water was determined to exhibit the least efficacy in combating malaria, which prompted You you Tu to hypothesize that this phenomenon can be used as a phytochemical to treat malaria, as it is susceptible to heat and undergoes rapid decomposition at elevated temperatures in aqueous or alcoholic solutions (Kong and Tan 2015). When *A. annua* was extracted with chilled ethyl ether, the efficacy of inhibition against the malarial parasite reached 100%. Subsequently, multiple investigations have substantiated the decomposition of the endoperoxide ring of plants at temperatures exceeding 60 ℃ (Li et al. 2013). Numerous studies have examined other aspects of this sesquiterpene chemical, since artemisinin was found to be the most efficient antimalarial medication (Meshnick 2002; Bridgford et al. 2018; Liu et al. 2019; Wang et al. 2019; Ma et al. 2020). Many research teams have extensively documented the antimalarial qualities of additional artemisinin derivatives, including dihydroartemisinin (Han and Lee 2017; Heller et al. 2018; Chu et al. 2019; Ounjaijean and Somsak 2020). Artemisinic acid, a precursor, has also been reported to be converted into artemisinin (Lenihan et al. 2008; Kung et al. 2018; Ikram et al. 2019). However, the potential significance of artemisinin acid as an important sesquiterpene at the clinical level is under investigation (Bhowmick et al. 2020; Tian et al. 2021). Researchers also reported the antimalarial property of arteether, a sesquiterpene through in vitro studies which shows its potential in binding to human plasma protein(Brossi et al. 1988; Wanwimolruk et al. 1992; Sissoko et al. 2020). Additionally, artesunate was also examined for its efficacy with variety of other antimalarial compounds against both chloroquineresistant and sensitive strains of *P. falciparum.* It was observed that between all endoperoxide-bridgecontaining sesquiterpenes, artesunate in combination with artemisinin has the maximum effectiveness against malaria(Gopalakrishnan and Kumar 2015; Organization 2015; Feng et al. 2017; Naing et al. 2019). They are particularly effective against the asexual stages of the parasite in the red blood cells. Artemisinin is known for its rapid onset of action, such as reduction of number of parasites in the blood stream and providing rapid relief from malaria symptoms. This speed is crucial in cases of severe diseases. Artemisinin and its derivatives are highly effective at reducing the number of parasites in the body, which helps prevent the development of drug resistance (Tayyab Ansari et al. 2013). Owing to concerns regarding the development of drug-resistant strains of the malarial parasite, artemisinin is typically administered in combination with other antimalarial drugs. This synergistic approach ensures the effectiveness of treatment and reduces the likelihood of resistance. ACTs have become a cornerstone of malaria treatment worldwide. They are recommended by the

WHO Health Organization as first-line treatment for malaria. (White 1998). Despite its effectiveness, challenges remain associated with the production and distribution of artemisinin. The primary source of artemisinin is *A. annua*, which requires specific growth conditions and extraction processes. Ongoing research is focused on identifying alternative sources of artemisinin, developing more efficient synthetic methods, and investigating new potential derivatives with enhanced properties(Daily 2006). Artemisinin and its derivatives continue to play a crucial role in malaria control. Additionally, they are being explored for potential applications in the treatment of other diseases such as cancer. Overall, the discovery and development of artemisinin as a potent antimalarial compound represents a significant milestone in the fight against malaria, and continues to be a key component of malaria control strategies worldwide (Dai et al. 2017).

5. Areas for Further Investigation and Research Gaps

The absence of standardized preparations and dosages hinders comparisons between studies. Establishing standardized extracts or formulations would improve consistency and reliability. Further research is necessary to understand the precise mechanisms underlying the properties of *A. annua* under various environmental conditions. Elucidating these molecular pathways may aid the development of targeted therapies. Thorough long-term safety studies are required to determine potential side effects, interactions with medications, and optimal dosing in different populations. Larger, well-controlled clinical trials are crucial for validating the efficacy of *A. annua* under specific conditions. Rigorous study designs with extended follow-up periods can offer clearer insights into therapeutic benefits. Further investigations into particular diseases or conditions such as cancer or inflammatory disorders, for which primary evidence suggests potential benefits, may yield valuable insights. Examining *A. annua* in combination with conventional treatments or other natural compounds may offer synergistic effects and enhance therapeutic outcomes. The diverse potential of *A. annua* beyond malaria warrants further investigation. Robust and well-designed studies addressing these research gaps can better establish their therapeutic value for various health conditions.

6. Bioavailability

- **Artemisinin**: When delivered via dried *Artemisia annua* leaves (DLA/pACT), artemisinin's bioavailability is >40 times higher than pure artemisinin due to the plant matrix (flavonoids, terpenes) inhibiting CYP2B6 and CYP3A4 enzymes, reducing first-pass metabolism.
- **Combination Therapies**: Natural artemisinin-based combinations (nACTs) with compounds like arteannuin B and scopoletin enhance bioavailability ~10-fold, improving antimalarial efficacy.
- **Tea Infusions**: Artemisinin in tea absorbs faster (Cmax: 240 ± 75 ng/mL, AUC: 336 ± 71 ng/mL·hr) but delivers only ~19% of the recommended dose, limiting its therapeutic use.
- **Nanoformulations**: Artesunate and artemether in nanoemulsions (e.g., ARTNEs) improve solubility and bioavailability, with 62% drug release in 12 hours and enhanced plasma levels in rats.

Stability

- **Artemisinin**: Stable during drying and tablet formation, with levels slightly increasing post-drying. Cultivars (e.g., Hunan, China) yield >2% artemisinin, consistent across batches.
- **Other Compounds**: Flavonoids increase ~4fold during processing, while monoterpenes like camphor may decrease. Artesunate's poor water solubility is mitigated by nanoemulsions (60 nm droplet size).
- **Storage**: Artemisinin in dried leaves remains stable long-term, supporting cost-effective production.

7. Pharmacokinetic Profiles

- **Artemisinin**: In mice, oral DLA artemisinin has a half-life (T½) of ~51.6 min and an elimination rate of 0.80 h^{-1}. Infected mice show higher plasma levels due to plant matrix effects.
- **Combination Therapy**: Artemisinin with arteannuin B, arteannuic acid, and scopoletin increases AUC0→∞ (3.78-fold in healthy mice, 2.62-fold in infected), Cmax (3.47fold, 1.82-fold), and T½ (1.13–1.22-fold), with reduced clearance.

- **Derivatives**: Deoxyartemisinin has low bioavailability (1.6%), while 10deoxoartemisinin reaches 26.1%. Artesunate shows linear pharmacokinetics (1–400 ng/mL) but requires frequent dosing due to its short half-life.
- **Flavonoids/Coumarins**: Peak plasma levels in 1– 4 hours; some undergo glucuronidation. They interact with CYP450 enzymes, potentially causing drug interactions.

8. Clinical Applications, Challenges, and Prospects

Translating the potential for the therapeutic use of *A. annua*, particularly artemisinin, into clinical settings presents numerous obstacles. This plant, commonly known as sweet wormwood, has a long history of use in traditional Chinese medicine to treat fever and malaria. However, their incorporation into contemporary clinical applications is complicated by several limitations.

8.1 Standardization and Quality Control: Ensuring the consistent quality and potency of artemisinin and *A. annua* extracts poses a challenge due to variations in plant growth conditions, extraction methods, and geographical factors. Standardizing the active compounds is essential for achieving reliable clinical outcomes.

8.2 Resistance and Efficacy: There concerns about the possibility of developing resistance to artemisinin-based therapies, similar to the resistance observed with conventional antimalarial drugs. Therefore, it is essential to further explore and optimize their effectiveness against various strains of parasites or diseases.

8.3 Safety and Side Effects: Although artemisinin is typically regarded as safe, prolonged use or high doses may lead to toxicity or adverse effects. It is crucial to determine the optimal dosage and potential side effects in a clinical setting to avoid any negative consequences. Prospects for research on *A. annua* involve various avenues to address these challenges and expand their clinical applications.

8.4 Formulation Optimization: The purpose of this scientific investigation was to create innovative drug delivery systems or formulations that could improve the bioavailability and stability of artemisinin, thereby increasing its therapeutic effectiveness.

8.5 Clinical Trials and evidence-based medicine: Extensive clinical trials across different populations and diseases to assess the safety, efficacy, and dosage regimens of *A. annua* and its derivatives are essential for evidencebased medicine.

8.6 Combination Therapies and Synergistic Effects: Exploring the synergistic effects of artemisinin and other compounds, either from natural or synthetic sources, could enhance its therapeutic potential. Combinations may mitigate resistance issues and improve overall efficacy. **8.7 Mechanistic Studies:** Understanding the mechanisms of action of artemisinin at the molecular level and its interactions with biological systems can provide insights into its therapeutic applications and aid in targeted drug development.

8.7 Quality Control and Standardization: Developing robust quality control measures and standardized protocols for extraction, cultivation, and manufacturing can ensure the consistency and reliability of therapeutic outcomes. In conclusion, while *A. annua* and its active compound artemisinin hold promise for various therapeutic applications, overcoming challenges related to standardization, bioavailability, efficacy, and safety is essential for successful translation into clinical practice. Future research efforts focusing on optimization, combination therapies, mechanistic insights, and rigorous clinical evaluations will be pivotal for realizing the full potential of *A. annua*-based therapies.

9. Conclusion

A. annua plays an important role in antimalarial medications, particularly artemisinin, that significantly impact global efforts to combat malaria. In addition to artemisinin, *A. annua* contains various bioactive compounds with potential therapeutic applications, including flavonoids, terpenoids, and polyphenols. Recent studies have suggested that *A. annua* may hold promise beyond malaria treatment. Preliminary research has indicated its potential for combating other infectious diseases, such as bacterial and viral infections. Some compounds found in *A. annua* exhibit anti-inflammatory properties, suggesting their potential use in treating inflammatory conditions. There are ongoing investigations of plant compounds and their effects on cancer cells. Early results are promising, highlighting the need for further exploration in this area. Despite its potential, challenges such as standardization of extracts, dosage determination, and understanding of its mechanism of action remain. Further rigorous

research is imperative to fully harness the therapeutic potential of *A. annua*. In conclusion, *A. annua*, primarily known for its role in malaria treatment, holds promise as a therapeutic compound beyond its traditional use. Exploring its potential applications in treating various diseases such as inflammation, infections, and cancer could lead to groundbreaking advancements in medicine. However, to fully utilize its benefits, continued and extensive research is necessary to unravel its mechanisms, standardize its usage, and establish its efficacy and safety across different conditions.

Statements and Declaration

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Author Contribution:

NS contributed to writing the original draft preparation, **AR** contributed to writing the original draft preparation. **IZA** did Supervision, and **SS** did Supervision and formal analysis.

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