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COMPARATIVE STUDY ON THE VALORIZATION AND PHYTOTHERAPEUTIC POTENTIAL OF *ARTEMISIA ANNUA* L. IN CAMEROON AND ROMANIA

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Abstract. *Artemisia annua, commonly known as sweet wormwood, is a medicinal plant of considerable pharmacological importance, mainly due to its content of artemisinin, the key compound in modern antimalarial therapy. The objective of this study is to provide a comparative analysis of the current uses and future perspectives of this plant in two contrasting regions: Cameroon and Romania. For a better field identification of species of phytotherapeutic interest, a concise dichotomous key was developed. The study also examines the geographical distribution, phytochemical composition, and therapeutic applications of the species. The research methodology involved an extensive review of scientific literature, focusing on the comparative assessment of uses in scholarly and traditional phytotherapy, cultivation technologies, and phytochemical characteristics. Findings indicate that in Cameroon, A. annua is primarily cultivated for artemisinin extraction, used in malaria prevention and treatment programs, while in Romania the plant is not yet fully exploited from a phytotherapeutic perspective. Phytochemical data reveal a complex composition of bioactive metabolites, such as artemisinin, flavonoids, terpenoids, and phenolic compounds, whose concentrations vary depending on environmental, genetic, and agronomic factors. This work contributes to a better understanding of A. annua as a strategic medicinal resource, highlighting the need for sustainable valorization of spontaneous populations. Its originality and relevance derive from the integration of ethnopharmacological knowledge with modern scientific and economic perspectives, supporting the sustainable use of A. annua in Cameroon and Romania.*

Keywords*: Artemisia annua, artemisinin, phytochemical composition, antimalarial activity, phytotherapeutic potential, cultivation technology*

INTRODUCTION

Artemisia annua L., a species of the Asteraceae family, is an annual herbaceous plant with a wide geographical distribution, used in natural medicine for multiple therapeutic applications and recognized for its antimalarial role (KLAIMAN, 1985). *Artemisia annua* is an annual, glabrous species. The stem is straight, up to 1.5 m branched. The leaves are simple, pinnately lobed, triangular in appearance, accompanied by bracts. The anthodia are small, pedunculate, up to 3 mm in diameter, grouped in inflorescences with an elongated panicle appearance. The calatidium has two types of flowers, the central ones being bisexual, fertile, with a tubular corolla, stamens joined by anthers and inserted on the corolla tube, and the marginal flowers being unisexual, female, with a reduced corolla and an exserted stigma. The receptacle of the flowers, the involucral bracts, and the corolla are covered with numerous glandular trichomes, which are the site of artemisinin biosynthesis (WETZSTEIN *et al*., 2014; SÂRBU I. *et al*., 2013; CIOCÂRLAN V., 2009; NYÁRÁDY *et al*., 1964).

In Cameroon, *Artemisia annua* is a relatively recently introduced species, cultivated mainly for its antimalarial potential and economic value, reflecting the adaptation of global medical and agricultural practices to local challenges related to infectious diseases. The distribution of *A. annua* is active in several agro-ecological zones of the country, with the plant being widely cultivated within community structures known as "Artemisia houses" (WILLCOX *et al*., 2004). In addition to *Artemisia annua*, another species of interest cultivated in Cameroon is *Artemisia Afra* Jacq. ex Willd (SHINYUY, *et al*., 2025). The cultivation of *Artemisia annua* in Cameroon is widespread in several regions of the country, including the northwest, center, coast, Adamawa, southwest, and west, and is mainly coordinated by non-governmental organizations such as CIPCRE (International Center for Promotion and Creation). These structures ensure quality plant material by supplying certified seeds from MEDIPLANT (Research Center for Aromatic and Medicinal Plants, Conthey, Switzerland) (ANYINKENG *et al*., 2023).

In the flora of Romania, Sârbu et al. (2013) recognize 17 spontaneous species, 2 cultivated and subspontaneous species, one probable species, and one species with uncertain presence. The spontaneous species ar: *A. annua* L. – sporadic; *A. scoparia* Waldst. et Kit. (syn. *A. capillaris* Thunb., *A. scoparioides* Grossh.) – frequent; *A. eriantha* Ten. (syn. *A. petrosa* (Baumg.) Jan) – frequent; *A. pedemontana* Balb. (syn. *A. lanata* Willd.) – rare, on rocky habitats; *A. vulgaris* L. – frequent; *A. santonicum* L. (syn. *A. monogyna* Waldst. et Kit.) – frequent; *A. lerchiana* Stechm. (*A. taurica* auct. roman., non Willd.) – rare, in dry places and on rocky substrates; *A. dzevanovskyi* Leonova – rare, in dry places and on rocky substrates; *A. alba* Turra (syn. *A. lobelii* All.) – rare, on calcareous rocky habitats; *A. absinthium* L. – frequent; *A. tschernieviana* Besser (syn. *A. arenaria* DC.) – rare, on coastal sands; *A. lancea* Vaniot – very rare, in the forest-steppe zone, ruderal, occurring in sunny places on skeletal soils; *A. lavandulaefolia* DC. – very rare, in the forest-steppe zone, ruderal, occurring in sunny places on skeletal soils; *A. argyi* H. Lév. et Vaniot – very rare, in the forest-steppe zone, ruderal, occurring in sunny places on skeletal soils; *A. austriaca* Jacq. – frequent; *A. pontica* L. – frequent; *A. campestris* L. – frequent (SÂRBU I. *et al*., 2013). The two cultivated and subspontaneous species are *A. dracunculus* L. and *A. abrotanum* L. Recent studies show that, under cultivation, *A. lancea* and *A. lavandulaefolia* are significantly more productive than *A. absinthium* and support the further development of research and cultivation technologies (PUIU *et al*., 2022).

MATERIAL AND METHODS

This paper is based on a comparative documentary analysis of the approach to the *Artemisia annua* species in two distinct agro-ecological contexts, corresponding to a tropical area such as Cameroon and a temperate area such as Romania. The method used consisted exclusively of analyzing the specialized literature in order to create a comparative framework that captures cultivation practices, therapeutic uses, as well as data on the chemical composition and medicinal properties of the plant in the two distinct areas of interest. The materials used included published scientific papers, articles from specialized journals, botanical books, as well as in vitro medical studies, agronomic and pharmacological studies. The sources analyzed were identified by consulting scientific databases and available academic literature, covering both botanical and agro-technical aspects, as well as medical and economic applications of the species.

RESULTS AND DISCUSSIONS

Artemisia annua cultivated in the Grass-field regions of Cameroon has a complex phytochemical profile dominated by artemisinin, along with other secondary metabolites such as scopoletin and a volatile fraction rich in monoterpenes and sesquiterpenes. The artemisinin content ranged from 0.4 to 19.2 mg/kg (average 11.1 mg/kg), with maximum values in

Bandjoun, Bafoussam, and Dschang and minimum values in Bafut. Scopoletin was identified in the range of 0.24–10.38 mg/kg (average 1.90 mg/kg). Analysis of the volatile fraction revealed 13 main compounds, including α-pinene, camphene, limonene, eucalyptol, camphor, and caryophyllene, with wide variations (e.g., α-pinene 0.6–21.2 mg/kg, eucalyptol 2.9–102 mg/kg). Compared to temperate European regions (Luxembourg, Germany, Belgium; 0.4–1.1 mg/kg), *A. annua* from Cameroon has higher artemisinin concentrations, comparable to those in Brazil and the Democratic Republic of Congo (NKUITCHOU-CHOUGOUO *et al*., 2014).

Other separate investigations report that the sesquiterpene lactone artemisinin is consistently reported as the main antiplasmodial marker of *Artemisia annua* in Cameroon. Available data indicate significant variations in artemisinin content between different regions and agro-ecological zones of the country, with higher values observed under certain harvesting conditions. These differences suggest that the growing environment and local conditions influence the accumulation of artemisinin in plant biomass (SHINYUY *et al*., 2025; ANYINKENG *et al*., 2023). In addition, phytochemical analyses performed on *Artemisia annua* from Cameroon reveal a profile of secondary metabolites that varies depending on geographical origin and, in some cases, the harvest season. Phytochemical research has confirmed the isolation of approximately 700 secondary metabolites from *Artemisia annua* and nearly 500 secondary metabolites from *Artemisia afra*. However, studies report that artemisinin is not present in *Artemisia afra*, but the species has two compounds that *A. annua* does not have: luteotin and rutin (SHINYUY *et al*., 2025).

Another study that analyzed the artemisinin content of various plants harvested from different areas of Cameroon showed that the percentage of artemisinin in plant material ranged from 0.18% to 0.80%. The highest artemisinin values in the leaf and flower fraction were recorded in samples from Bamenda (0.61%), while the lowest values were determined in samples from Ngaoundere (0.18%). In the stems, the maximum concentration of artemisinin was observed in samples from Ngaoundere, and the lowest in samples from Bamenda (0.34%). Artemisinin was not detected in plant samples collected from Buea. A comparative analysis of the average artemisinin values in samples from the three sites where it was identified showed statistically significant differences ($p < 0.05$). The identification of artemisinin, a sesquiterpene compound, on the total ion chromatograms (TIC) of the four extracts analyzed was based on specific retention times, namely 7.213 min for the samples from Bamenda, 7.214 min for the samples from Ngaoundere, and 7.211 min for the samples from Yaounde (ANYINKENG *et al*., 2023).

Marinaș et al. (2015) analyzed the composition of essential oil extracted by hydrodistillation from the aerial parts of *Artemisia annua* from Romania, using GC/MS techniques. The authors identified 94.64% of the total volatile constituents, with the profile dominated by camphor (17.74%), followed by α-pinene (9.66%), germacrene D (7.55%), 1,8-cineole (7.24%), trans-β-caryophyllene (7.02%), and artemisia ketone (6.26%). The profile obtained provides a clear picture of the dominant volatile compounds of the analyzed plant material (MARINAS *et al*., 2015). In addition, Segneanu et al. (2021) performed the first complete metabolic profile of *Artemisia annua* grown spontaneously in Romania, using ESI-QTOF-MS mass spectrometry in positive mode. Analysis of the plant extract diluted in methanol revealed a broad phytochemical composition, consisting of 103 metabolites belonging to 13 chemical classes, including terpenoids, sesquiterpenoids, flavonoids, amino acids, sterols, coumarins, organic acids, fatty acids, phenolic acids, carbohydrates, glycosides, alcohols, and aldehydes. The percentage distribution of the compounds was dominated by terpenoids and sesquiterpenoids (27.2%), followed by flavonoids (24.2%) and amino acids (12.6%), with the

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other categories being represented in smaller proportions (SEGNEANU *et al*. 2021). Both studies highlight the predominance of terpenic compounds, suggesting that terpenoids and sesquiterpenoids are a major component of the phytochemical profile of the Romanian *A. annua* plant material analyzed.

Significant variations in chemical composition have been reported in the literature, both between species of the genus *Artemisia* and between different parts of the same plant. In this regard, Țicolea et al. (2025) analyzed the total phenolic compound (TPC) and flavonoid (TFC) content in ethanol extracts obtained from the flowers and leaves of *A. absinthium* and *A. annua*. The authors observed that, in the case of *A. absinthium*, TPC values were higher in flower extracts compared to leaf extracts, but the difference was not statistically significant ($p > 0.05$). For *A. annua*, flower extracts also had a higher TPC content than leaf extracts, with a statistically significant difference ($p < 0.01$). Comparing the species, the ethanol extracts from *A. annua* flowers had a higher TPC content than that determined in *A. absinthium* flowers ($p < 0.01$), while the extracts from *A. absinthium* leaves had higher TPC values than those from *A. annua* leaves. HPLC-ESI-MS analysis revealed the presence of 26 phenolic compounds in flowers and leaves, most of which belonged to hydroxycinnamic acids (85.2–94.7%), followed by flavonols in smaller proportions, with the other phenolic subclasses being identified at low levels (ȚICOLEA *et al*., 2025).

A separate study conducted by Trifan et al. (2022) investigated extracts from several *Artemisia* species, determining the total phenolic compound (TPC) and flavonoid (TFC) content using colorimetric methods and highlighting significant variations generated by both the solvent and the plant organ analyzed. Methanolic extracts consistently showed higher TPC and TFC values than those obtained with chloroform, and the aerial parts accumulated higher amounts of phenolic compounds than the roots in most of the species investigated. The highest levels of phenols were reported in the methanolic extract of the aerial parts of *A. vulgaris* (106.34 mg GAE/g), followed by *A. pontica* and *A. annua*, while for flavonoids, the maximum values were identified in the methanolic extract of the aerial parts of *A. annua* (47.74 mg RE/g) (TRIFAN et al., 2022). The data reported by Țicolea et al. (2025) and Trifan et al. (2022), indicate that the aerial organs of *Artemisia* species have higher phenolic concentrations, a finding that converges towards highlighting a well-defined phytochemical profile of the plant.
Studies on the essential oil of *Artemisia annua* from Serbia indicate a profile dominated by artemisia ketone and trans-β-caryophyllene, together with 1,8-cineole, camphor, and germacrene D, similar to that reported for plant material from Romania (MARINAS *et al*., 2015; SEGNEANU *et al*. 2021; AĆIMOVIĆ *et al*. 2022). The differences between the two regions are mainly quantitative, with camphor being the dominant compound in Romanian samples, whereas artemisia ketone showed the highest proportion in Serbian samples, and β-selinene was identified exclusively in the Serbian profile. Data obtained for *A. annua* from Bulgaria confirm the presence of a common set of major volatile compounds, particularly sesquiterpenes, artemisia ketone, and camphor, suggesting a relatively stable phytochemical profile across the Balkan–Carpathian region, with variations dependent on local environmental conditions (TZENKOVA *et al*. 2014).

In Cameroon, *Artemisia annua* is cultivated in several distinct agro-ecological zones, including the high Guinean savannah, western mountainous areas, and humid forest regions with monomodal and bimodal rainfall patterns. The seeds used come from local community networks ("Artemisia Houses"), coordinated by organizations promoting the cultivation of the plant, and are initially intended for the production of planting material in nurseries. Sowing is done by scattering seeds in plastic containers (40×20 cm) filled with a substrate of fine sifted soil and sand, kept in semi-shade conditions. About 30 days after germination, when the seedlings reach the 4–5 true leaf stage, they are individually transplanted into polyethylene bags (10×12 cm) and grown until they are eight weeks old, during which time they undergo acclimatization. Field cultivation is established on land prepared by fine loosening, with prior soil analysis, and planting is carried out on raised beds (4×2.5 m), at distances of 60×50 cm between plants, ensuring a density of approximately 35 plants per bed. Plant development is monitored until the onset of flowering, which occurs approximately 120 days after transplanting, at which point harvesting is carried out, targeting mainly the leaves and flowers, which are considered the organs of interest for artemisinin accumulation (ANYINKENG *et al*., 2023).

The cultivation of *Artemisia annua* in Romania was initiated for its therapeutic potential, being tested in Transylvania using standard seedling production and field transplanting technologies. The cultivation technology tested in Transylvania used two varieties of *Artemisia annua* (one German – ANAMED A3, and one Romanian), obtained by sowing in a greenhouse on peat, followed by transplanting and acclimatization. Transplanting in the field was carried out on alluvial soil, moderately fertile and slightly alkaline, after plowing, discing, and herbicide application. The plants were placed at distances of 30, 60, and 90 cm, with 70 cm between rows, and fertilization was applied with 40–80 kg NPK/ha, according to the experiment. In the study year, marked by drought, the crop required regular watering in June–August, and weed control was carried out mechanically. Harvests, carried out at three distinct times, showed that density and variety significantly influence vegetative development and the proportion of dry leaves, an essential indicator for the pharmaceutical use of the plant. The data quantified by Pop et al. (2017) indicate that *Artemisia annua* can be successfully cultivated in Transylvania, but the yield depends heavily on climatic conditions, especially rainfall, requiring frequent watering in years of prolonged drought. Crop density also directly influenced yield per unit area, with the Romanian variety producing a higher yield of dried leaves than the German variety (POP *et al*., 2017).

Traditional use and antimalarial role in Cameroon, *Artemisia annua* is widely used in the form of infusions or decoctions to treat fevers and symptoms associated with malaria. Several ethnobotanical studies confirm this traditional use, as well as the existence of useful levels of artemisinin in locally grown plants (SHINYUY *et al*., 2025; SUH NCHANG *et al*., 2024). Medically, the active component is artemisinin, the basis of ACT combination therapies recommended in Cameroon. The use of teas as monotherapy is discouraged due to the risk of resistance developing Role in generic drugs/modern treatments Artemisinin and its derivatives (artesunate, artemether) are integrated into ACTs, the first-line therapy in national policy. Various official reports and public health studies describe the implementation and improvement of access to ACTs in Cameroon (EBOUMBOU MOUKOKO *et al*., 2024; ONGOLO-ZOGO & BONONO, 2010). Use during the COVID-19 pandemic Between 2020 and 2021, the use of *Artemisia annua* spread widely in Cameroon, becoming one of the most commonly used remedies for the perceived prevention or treatment of COVID-19. Local initiatives, political support, and institutional openness to traditional medicine contributed to its popularity (FEDOUNG *et al*., 2023). The Ministry of Health has supported the monitored integration of traditional remedies into the national response, which has reinforced the perception of a partial official endorsement. However, the WHO has emphasized that the efficacy of *Artemisia annua*-based preparations against COVID-19 must be demonstrated through rigorous clinical trials (WHO-AFRO, 2020). Researchers have warned that uncontrolled use cannot replace validated treatments and may create a false sense of security (KAPEPUȚLA *et al*., 2020).

Experimental reports and *in vitro* studies indicate that extracts of *Artemisia annua* exhibit insecticidal and repellent properties against mosquitoes, particularly *Anopheles*, suggesting potential for the development of local biopesticides. However, toxicological and ecological validations are required before any large-scale application. In traditional medicine, *Artemisia annua* is used to treat diarrhea, abdominal pain, and intestinal parasites. Pharmacological studies suggest anti-inflammatory, antimicrobial, and antiparasitic effects; however, clinical evidence in humans remains limited (FEDOUNG *et al*., 2023; KAPEPUȘA *et al*., 2020).

Bordean et al. evaluated the antibacterial activity of ethanolic extracts obtained from the leaves and stems of *Artemisia annua* L. collected from the spontaneous flora of Romania, demonstrating efficacy against several standard bacterial strains, with higher sensitivity observed in Gram-positive bacteria. The lowest minimum inhibitory concentration (MIC) value was recorded for *Staphylococcus aureus* (<2.00 mg/mL), whereas the high MIC values obtained for *Escherichia coli* and *Salmonella enteritidis* (375.00 mg/mL) indicate reduced effectiveness against Gram-negative bacteria (BORDEAN *et al*., 2023). Complementary results highlighted significant antibacterial activity against problematic strains such as ESBL-producing *Klebsiella* and CRE *Klebsiella*, as well as against *E. coli*. In this context, silver nanoparticles synthesized from *A. annua* plant material demonstrated notable antibacterial efficacy, particularly against *Escherichia coli*, confirming the plant's potential for nanotechnological applications with antimicrobial relevance (RÎMBU *et al*., 2025). In addition, the essential oil obtained from Romanian *A. annua* plants exhibited significant antimicrobial and antibiofilm activity, with MIC values ranging from 0.51 to 16.33 mg/mL, as well as the ability to inhibit biofilm formation and the expression of several microbial virulence factors (MARINAS *et al*., 2015).

Țicolea et al. evaluated the antiproliferative activity of ethanolic extracts from the leaves and flowers of *Artemisia annua* and *Artemisia absinthium* on ovarian tumor cell lines A2780cis, OVCAR-3, and OAW-42. All extracts exhibited relevant antiproliferative activity, with IC_{50} values below 60 μg/mL. Cytotoxicity toward normal HaCaT cells was lower compared to tumor cell lines, suggesting a certain degree of biological selectivity. Mechanistic analyses revealed a reduction in MDR expression and activation of the cleaved form of PARP-1, with responses dependent on the extract type and cell line, OVCAR-3 showing the most pronounced response (ȚICOLEA *et al*., 2025). In a separate study, Stan et al. (2020) investigated the antitumor potential of *Artemisia annua* extracts originating from Romania, confirming by LC-MS the presence of artemisinin, quercetin, and gallic acid. *In vitro* assays on the WM35 melanoma cell line demonstrated selective inhibition of cell proliferation, with IC_{50} values approximately three times lower than those observed in normal fibroblasts, while *in vivo* evaluation using the Ehrlich ascites carcinoma model showed potentiation of the cytostatic effect of doxorubicin. The antitumor effects were associated with alterations in antioxidant enzyme activity and the induction of oxidative stress at the cellular level. Overall, these data indicate that *Artemisia annua* exhibits demonstrated antitumor activity both *in vitro* and *in vivo*, with selective effects on tumor cells and mechanisms dependent on extract composition and the biological model investigated (STAN *et al*., 2020).

Trifan et al. (2022) evaluated the antioxidant capacity of extracts from several species of the genus *Artemisia* using the DPPH and ABTS assays, highlighting significantly higher activities for methanolic extracts compared to chloroformic ones. The highest free radical scavenging capacity was recorded for the methanolic root extract of *Artemisia annua* (DPPH: 237.03 mg TE/g; ABTS: 240.78 mg TE/g), followed by *A. pontica* and *A. vulgaris*, while the lowest values were reported for chloroformic extracts of *A. absinthium*. The results indicate marked differences depending on species, plant organ, and extraction solvent, with *A. annua* exhibiting the highest values in both assays (TRIFAN *et al*., 2022). In a recent study Țicolea et al. (2025), reported moderate antioxidant activity for *Artemisia alba* extract, lower than that of the antioxidant standards Trolox and quercetin, but positively correlated with total phenolic content (ȚICOLEA *et al*., 2025).

In Romania, *Artemisia annua* has demonstrated relevant antiparasitic activity in the veterinary field, particularly in the prophylaxis of coccidiosis. Studies conducted on plants cultivated in Sângeorgiu de Mureș, obtained from the ANAMED A-3 cultivar, showed a reduction in fecal oocyst shedding in chicks fed with *A. annua*, indicating a promising protective effect (COROIAN *et al*., 2022). Complementary results were reported by Drăgan et al. (2014), who highlighted a significant decrease in oocyst counts (95.6%) and lesion scores (56.3%) in *Eimeria tenella* infection, as well as improvements in zootechnical performance, with *A. annua* extract administered as a powder (1.5%) showing efficacy comparable to or superior to lasalocid (DRĂGAN *et al*., 2014). The literature also presents other interesting effects of *Artemisia annua* harvested in Romania: increased viability of human keratinocytes, in vitro wound healing effect on human keratinocytes, potential pro-angiogenic effects at the tested concentration, sweet wormwood extracts may be particularly beneficial in the vascular phase of wound healing (MINDA *et al*., 2022).

CONCLUSIONS

The comparative analysis of the approaches, chemical composition, cultivation, uses, and therapeutic effects of *Artemisia annua* in Cameroon and Romania reveals both similarities and notable differences. In Cameroon, *A. annua* has been cultivated for decades, playing an important role in malaria control and exhibiting a phytochemical profile consistently characterized by significant artemisinin concentrations. The plant is widely used to treat fever and other malaria-associated symptoms and represents a key component of ACT combination therapy recommended by health authorities. Consequently, research in Cameroon is primarily focused on the antimalarial potential of the plant, as well as on emerging applications in COVID-19 treatments, supported by initiatives promoting traditional medicine. By contrast, in Romania, *Artemisia annua* occurs as a spontaneous species, and interest in its cultivation, although still limited, is driven by the plant's promising pharmacological properties. Although artemisinin is also present in Romanian *A. annua*, concentrations in the temperate zone are lower than those reported in Cameroon and other tropical regions. Moreover, Romania does not face the same pressure to combat malaria; therefore, studies focus on broader biological and pharmacological properties of the plant. This reflects a different approach compared to Cameroon, where *A. annua* is cultivated primarily for malaria control.

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