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Exploring *Artemisia judaica subsp. sahariensis* (L. Chevall.) Maire, from Tamanrasset: Antioxidant and Antispasmodic Properties of an Endemic Species of the Algerian Sahara

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ABSTRACT

Artemisia judaica L., a plant belonging to the Asteraceae family, is also known as *Judean Wormwood*. It is widespread in the eastern Algerian Sahara, specifically in the Tamanrasset region, where it grows in specific locations. This investigation aimed to identify its chemical composition, assess toxicity, and test its antioxidant and antispasmodic effects. Phytochemical screening demonstrated the presence of several phytochemicals, including glucosides, saponins, quinones, tannins, sterols, triterpenes, polyphenols and flavonoids. Specific metabolites such as coumarins, anthocyanins, alkaloids, and mucilages were absent. The total polyphenol and flavonoid contents were determined to be 256.95 ± 7.11 mg GAE/g DW and 19.12 ± 0.57 mg QE/g DW, respectively, indicating that the plant is particularly abundant in polyphenols compared to other *Artemisia* species. Antioxidant activity showed a higher rate of DPPH radical inhibition than ascorbic acid. The assessment of acute toxicity and LD_{50} at 1000 mg/kg and 500 mg/kg in rabbits showed no mortality or occurrence of specific clinical signs, indicating the non-toxic effect of the plant. The investigation of antispasmodic activity revealed a dose-dependent response. The aqueous extract administered at a dosage of 500 mg/kg demonstrated efficacy comparable to the reference control SPASMODYL®, with a spasms inhibition rate of 97.25%. However, the positive control results were not statistically significant ($p \leq 0.05$). Further research is needed to explore the potentially unknown biological properties of this plant.

Keywords: *Artemisia judaica* L., Antioxidant, Acute toxicity, Antispasmodic.

Introduction

Artemisia judaica L. (Asteraceae), commonly called *Judean Wormwood*, is indigenous to multiple Saharan regions across the Middle East and North Africa.[1,2] The *Artemisia* genus comprises approximately 400 species distributed across various geographical areas worldwide.[3] The species *Artemisia judaica* L. includes three subspecies: *A. judaica subsp. judaica*, *A. judaica* var. *sinaitica* Täckh., and *A. judaica subsp. sahariensis* (L. Chevall.) Maire. The latter subspecies is found in Algeria and was first described by Maire (1933). In Algeria, this species is present in the eastern Sahara and has a more widespread distribution in the central Sahara. However, it is less common in the east of the northern Sahara. It is found in the Tademaït regions, specifically in In Salah and El Goléa. Additionally, it is present in the Hoggar at elevations reaching 2050 meters and is relatively prevalent in the western Algerian Sahara, particularly in the Tindouf, Béchar, and Tamanrasset regions.[4,5] The species is also found in abundance in the deserts of Egypt's Sinai Peninsula.[6]

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Phytochemical analyses of *A. judaica* from Egypt and Saudi Arabia have demonstrated the existence of phenolic compounds, flavonoids and tannins, with variations in compound composition influenced by environmental factors. This comprehensive understanding of the taxonomy of *A. judaica* highlights its complex classification within the genus *Artemisia*.[7]

A. judaica is regarded as an aromatic plant in North Africa, the Middle East and the Mediterranean region. People use it to flavour their dishes and beverages.[8] Touaregs incorporate it into their tea due to its vermifuge properties.[9] In Turkish popular medicine, *A. judaica* is a sedative for treating kidney stones. Turks also use the plant to flavour alcoholic drinks during the winter months.[10] Research has demonstrated that *A. judaica* exhibits anti-inflammatory, analgesic, antioxidant, and antiangiogenic properties, rendering it a promising candidate for medicinal applications.[11] The plant extract and the chitosan nanoparticle-loaded extract exhibited antimicrobial and anticancer activities, with compounds such as kaempferol and apigenin demonstrating potential as prostate cancer inhibitors.[11] *A. judaica* L. essential oil has been demonstrated to possess notable antibacterial and antibiofilm properties. It affects bacterial cell membranes and walls, effectively overcoming bacterial resistance and preventing biofilm formation.[12] Due to its rich composition of oxygenated monoterpenes and cinnamic acid derivatives, the plant's essential oil has demonstrated healing effects through antioxidant and anti-inflammatory mechanisms comparable to standard treatments.[13]

The current study aims to conduct a phytochemical evaluation of *A. judaica*, an endemic species collected in the Tamanrasset region of the Algerian Sahara. The principal purposes are to elucidate its secondary metabolite composition, assess its toxicity profile and study its antioxidant and antispasmodic activities.

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Materials and Methods

Plant collection and identification

Artemisia judaica subsp. sahariensis (L. Chevall.) was collected from the Tamanrasset region (Figure 1) in the southeastern Sahara of Algeria in February 2024. The taxonomic identification of the plant was validated by the herbarium of the Botany Department of the National High School of Agronomy (ENSA). A voucher specimen (AJSTA224) was deposited at the University of Blida 1 laboratory.

Figure 1: Geographical location of the Tamanrasset area of southern Algeria.

Animals

Male New Zealand rabbits (6 months old) were supplied by the ITLEV (Institut Technique de l'Elevage, Baba Ali, Algeria). The animals, weighing 3.6 ± 0.1 kg were transported to the Blida University experimental station. The rabbits were housed in individual cages under controlled conditions (22 ± 2°C) and a constant photoperiod (8h light/16h dark cycle). Animals had access to a standard diet (rabbit food manufactured by SIM Sandres Algeria, Spa) and water ad libitum. All experimental procedures were conducted following ethical guidelines established by the local Scientific Institutional Review Committee and the European Union Directive (2010/63/EU) on protecting animals for scientific purposes.

Phytochemical Screening

Phytochemical screening was performed to identify the primary secondary metabolites, including glycosides, saponins, flavonoids, tannins, anthocyanins, sterols and terpenes, alkaloids, polyphenols, quinones, and mucilage, using an established protocol.[14]

Antioxidant activity

Antioxidant activity was carried out according to the methodology proposed by Okafor *et al.* (2024),[15] with slight modifications. First, the DPPH test solution was obtained by dissolving 2.4 mg of 2,2-diphenyl-1-picrylhydrazyl (DPPH) in 100 mL of methanol. Then, 25 µL of the methanol plant extract was mixed with 975 µL of the DPPH solution. The plant extracts and ascorbic acid, which served as the standard, were evaluated at different concentrations (100, 200, 400, 600, 800, and 1,000 µg/mL). The assay was conducted in triplicate for each concentration. Samples were incubated in the dark for 30 minutes, after which the degree of discolouration relative to the negative control (containing only DPPH solution), was quantified at 517 nm using a spectrophotometer (Shimadzu UV-1800 UV/Visible, Japan). The radical scavenging activity was calculated using the following equation 1:

$$AA\% = \left[\frac{(Abs\ control - Abs)}{Abs\ control}\right] \times 100 \qquad (1)$$

Where; AA: antioxidant activity, Abs: absorbance at 517 nm.

IC_{50} (50% free radical neutralising concentration) was computed using GraphPad Prism software, version 8.0 (GraphPad Software, San Diego, CA, USA).

Determination of total polyphenols

Total polyphenol content was determined using the Folin Ciocalteu reagent method reported by Singleton *et al.* (1965), [16] and Ainsworth & Gillespie (2007).[17] The sample was prepared with 1 g dried plant powder diluted in 10 mL with 80% methanol, mixing for 2 hours, then centrifuging at 4,000 rpm for 10 minutes. The supernatant was collected and made up to 10 mL with 80% methanol. For the assay, 1 mL of plant extract was added to 1 mL of Folin Ciocalteu reagent. After 3 min, 1 mL of 25% sodium carbonate was added. The mixture was incubated for 2 hours and centrifuged at 4,000 rpm for 4 minutes. Absorbance was measured using a spectrophotometer (Shimadzu UV-1800 15 UV/Visible, Japan) at 670 nm. Three replicates were performed for each concentration. A calibration curve was constructed using gallic acid dilutions (25, 35, 45, 55, 75, 17 100, 125 µg/mL). Values were reported as milligrams of gallic acid equivalent per gram of dry matter (mg GAE/g).

Determination of total flavonoid

The total flavonoid content was determined using the method described by Chang et *al.* (2002),[18] with minor modifications. One gram of plant sample was finely ground and mixed with 10 mL of 80% (v/v) methanol for 2 hours at ambient temperature with continuous stirring. The extract was filtered through Whatman N°1 filter paper, and the volume was adjusted to 25 mL with 80% methanol. A calibration curve was prepared using quercetin as standard. A quercetin stock solution (1 mg/mL in methanol) was diluted to obtain concentrations (0, 10, 15, 20, 25, 35, 45, 50 µg/mL). For the assay, 1 mL of sample extract or standard solution was mixed with 1 mL of 2% (w/v) aluminium chloride ($AlCl_3$) solution and 1 mL of 80% methanol. Mixtures were homogenised by vortexing and incubated for 10 minutes at room temperature in the dark. Absorbance was measured at 438 nm using a spectrophotometer (Shimadzu UV-1800 UV/Visible, Japan) against a methanol blank. Values were expressed as quercetin equivalents (QE) in mg per gram of extract [19]

Acute plant toxicity study

The acute oral toxicity test followed the OECD Guideline 423 (OECD, 2001).[20] Two doses were tested: 500 mg/kg and 1000 mg/kg in rabbits weighing an average of 3.5 kg. For the study, 6 male rabbits were randomly assigned to 2 groups of 3 animals each. The rabbits were placed in individual cages. After a 24-hour fast and gavage administration of *A. judaica* aqueous extract, the animals were observed for 14 days to record specific symptoms such as agitation, lack of appetite, motor difficulties, dyspnea and other symptoms. Mortality was also recorded to determine the LD_{50}, which was calculated using equation 2.[21]

$$DL_{50} = DL_{100} - \sum \frac{a \times b}{n} \qquad (2)$$

LD_{50}: 50% lethal dose; LD_{100}: 100% lethal dose; a: average of deaths between two successive doses; b: difference between two consecutive doses; n: average number of animals used per group.

Antispamodic activity :

The antispasmodic effect of *A. Judaica* on rabbits was performed using the Rahman *et al.* (2005),[22] method. Abdominal twitches were induced by intraperitoneal injection of 1% acetic acid (10 mL/kg) into rabbits. The animals were separated into 5 groups (n=5). The 1st group received 9 mL physiological solution (negative control); the 2nd received 200 mg/kg SPASMODYL® 80 mg (Phloroglucinol) as positive control; and The 3rd, 4th, and 5th groups received an oral aqueous plant extract at 125 mg/kg, 250 mg/kg, 500 mg/kg, respectively. The number of writhes was recorded for 10 minutes, starting 5 minutes after acetic acid administration, by visually monitoring abdominal spasms. The protection percentage was calculated using Equation 3 :

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$$\% \, Protection = \left[\frac{(Control - Treated)}{Control}\right] \times 100 \qquad (3)$$

Where : Control: represents the number or intensity of spasms by visual observations in the control group; Treated: represents the number or intensity of spasms in the group treated with the antispasmodic substance.

Statistical analysis

The data were presented as mean ± standard deviation (mean ± SD). A Student's t-test was employed to compare the experimental and control groups using GraphPad Prism software version 8.0 (GraphPad Software, San Diego, CA, USA). $p \leq 0.05$ was considered statistically significant.

Results and Discussion

The phytochemical screening of the aerial part of *Artemisia judaica* L. revealed the presence of several chemical compounds, including flavonoids, tannins, glucosides, saponins, quinones, sterols, triterpenes and polyphenols (Table 1). The abundance of phenolic compounds and flavonoids such as kaempferol and apigenin confers potential anticancer activities on *A. judaica*.[11] Moreover, the terpenoids present in *A. judaica* extracts, which include monoterpenes, sesquiterpenes, and triterpenes (including sterols), contain compounds such as piperitone, santonin, and linalool. These compounds contribute to the plant's antimicrobial and anticancer properties.[23] However, some chemical compounds such as coumarins, anthocyanins, alkaloids and mucilages were absent.

Table 1: Secondary metabolites in several plant preparations (powder, aqueous extract, methanolic extract).

Secondary metabolites	Presence
Plant powder	
Glycosides	+
Saponin	+
Coumarins	-
Quinones	+
Sterols triterpenes	+
Aqueous extract	
Tannins	+
Anthocyanins	-
Mucilage	-
Methanol extract	
Polyphenols	+
Alkaloids	-
Flavonoids	+

-: not present, +: present

The DPPH radical scavenging test revealed significant antioxidant potential in the plant's methanol extract. This antioxidant activity increased gradually with the concentration of the plant extract. Furthermore, the plant extract showed a notable percentage inhibition of the DPPH radical, with activity higher than ascorbic acid, which was used as a positive control. Specifically, at a concentration of 1000 µg/mL, the plant extract showed 89.55% inhibition, while ascorbic acid at the same concentration showed 65.95% inhibition (Figure 2).

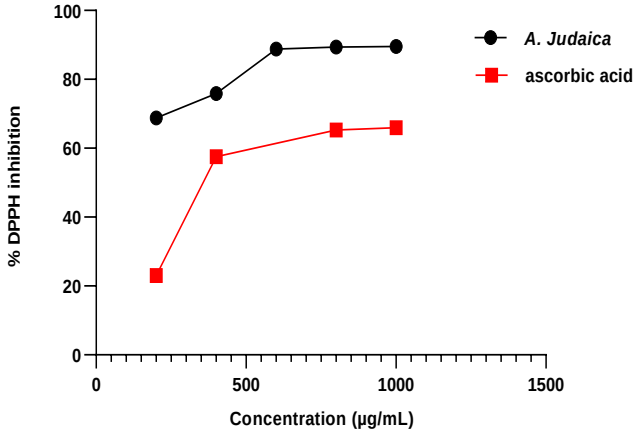

Figure 2: % DPPH inhibition by *A. judaica* methanol extract and ascorbic acid (positive control).

A. judaica recorded an IC_{50} = 90.67 µg/mL, considerably lower than ascorbic acid IC_{50} =440.3 µg/mL. The same result was demonstrated by Salih et *al*. (2023),[24] who showed that *Artemisia* species (*A. judaica*, *A. monosperma*, and *A. sieberi*) exhibited high antioxidant activity at a concentration of 500 µg/mL, which was the most effective concentration for significant scavenging of H_2O_2 compared to other concentrations. Moreover, other studies have shown that the free radical scavenging activity of *A. judaica* essential oil is superior to that of BHT, a highly effective synthetic antioxidant widely used in the food industry.[25]

This high antioxidant power of *A. judaica* is likely due to phenolic compounds such as phenolic acids, flavonoids and tannins, which are considered the main contributors to the antioxidant capacity of plants.[26] Hence, the antioxidant effects of *A. Judaica* extracts provide the plant with numerous therapeutic possibilities, particularly for disorders induced by free radical generation.[27] The methanol extract of *A. judaica* L. contained 256.95 mg GAE/g DW of total polyphenols and 19.12 mg QE/g DW of flavonoids (Table 2). Our results showed a higher polyphenol content than that reported by Salih *et al*. (2023),[24] who recorded 175.25 mg GAE/g DW of polyphenols in *A. judaica* collected in Saudi Arabia. In contrast, they recorded a slightly higher flavonoid content of 24.67 mg QE/g DW. In comparison with other species of the genus *Artemisia*, our investigation revealed higher total polyphenol than that reported by Zahnit *et al.*(2022),[28] who recorded a content of 135.35 mg GAE/g DW in *A. campestris*, harvested in the Tamanrasset region in Algeria. Similarly, Salih *et al*. (2023) [24] reported lower contents in two Saudi Arabian species: *A. monosperma* (120.33 mg GAE/g DW) and *A. sieberi* (194.30 mg GAE/g DW). However, the total flavonoid content determined in our study was lower than that reported by Zahnit *et al.* (2022),[28] who reported a content of 61.59 mg EQ/g DW in *A. campestris*, and Salih *et al.* (2023),[24] who recorded a content of 20.39 mg EQ/g DW in *A. monosperma*. The variation in phenolic and flavonoid compounds among *Artemisia* species can be

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attributed to several factors, including geographical and climatic factors, genetics, and plant ripening, which all affect plant chemistry.[29,30]

Aqueous extracts of *A. Judaïca* at 500 mg/kg and 1000 mg/kg showed no acute toxicity, mortality or severe clinical signs. The LD_{50} could not be determined within the tested dose range, indicating very low acute toxicity. Similar results were observed by Moharram et *al.* (2021),[31] who reported that the hydro-methanolic extract of *A. Judaïca* at doses (250 and 500 mg/kg) was safe in mice. According to Semler (1992),[32] if no deaths are observed at a dose of 5000 mg/kg, the plant is not considered toxic, and there is no need to calculate an LD_{50}.

Table 2: Total phenolic content (TPC) and total flavonoid content (TFC).

Sample	TPC. Mg GAE/g DW	TFC. Mg QE/g DW
Methanolic extract	256.95 ± 7.11	19.12 ± 0.57

Furthermore, the Antispasmodic activity revealed a significant ($p \leq 0.001$) reduction in the number of spasms in rabbits treated with plant extracts at the respective doses (125, 250, 500 mg/kg) compared to the control group receiving physiological water, which showed a high number of spasms (Table 3). The effect of the aqueous extract at 500 mg/kg proved dose-dependent, showing similar effects to the positive control, SPASMODYL. However, the results were not statistically significant (Figure 3). Moharram et *al*. (2021)[31] demonstrated the efficacy of *A. judaica* at the same doses (250 mg/kg and 500 mg/kg) with a hydromethanolic extract in mice. The antispasmodic effect of *A. Judaica* can be attributed, at least in part, to its phytoconstituents, particularly its flavonoid components.[31] Abdalla and Zarga (1987),[33] showed that cirsimaritin, a flavone isolated from *A. judaïca*, exhibited antispasmodic properties on isolated guinea pig ileum. This finding suggests that cirsimaritin's potential therapeutic application. Additionally, Aziz *et al.* (2012),[34] reported that the spasmolytic activity of *Artemisia* species could be attributed to compounds such as camphor, terpinene, 1,8-cineole and α- and *β*-pinene, which are known smooth muscle relaxants.

Table 3: Percentage reduction in the number of spasms with different doses.

Groups	Dose (mg/kg)	Mean (number of spasms)	% reduction
Control (-) Physiological water	-	36. 40 ± 3.05	_
Control (+) SPASMODYL®	2.66	0.40 ± 0.49.08***	98.90
AE	125	6.40 ± 1.14***	82.41
AE	250	3. 00 ± 0.70***	91.75
AE	500	1.00±0.70***	97.25

AE: Aqueous extract of plant
Data are represented as mean value ± SD (n = 5).
* Significant difference when compared to control (-) at *$p \leq 0.05$ **$p \leq 0.01$. ***$p \leq 0.001$.

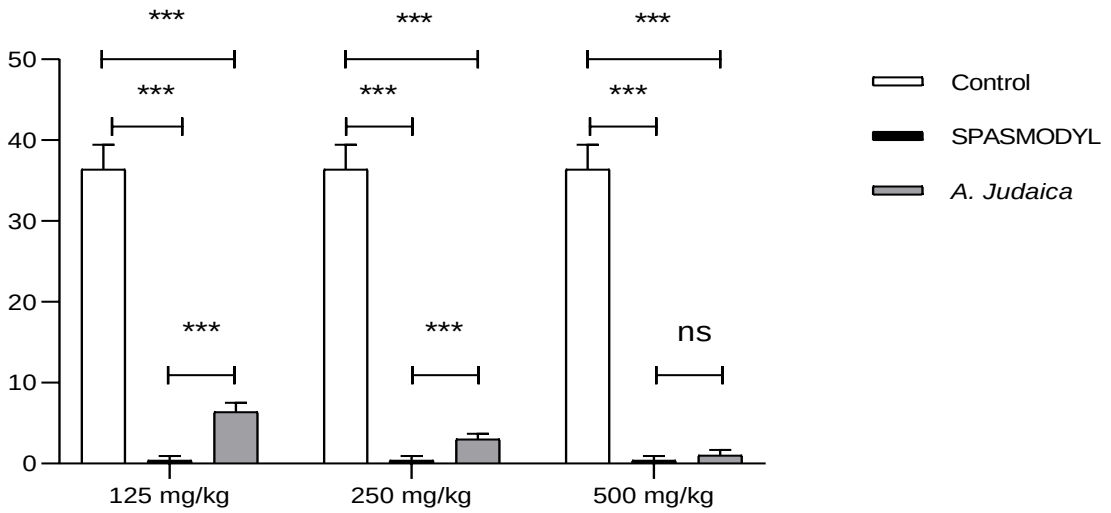

Figure 3: Number of spasms as a function of dose (aqueous plant extract) compared to negative control (physiological water) and positive control (SPASMODYL®).
* Significant difference when compared to controls at *$p \leq 0.05$ **$p \leq 0.01$. ***$p \leq 0.001$. n s= no significant.

Conclusion

The results of this study underline the therapeutic potential of *Artemisia judaica* L., particularly concerning its phytochemical content, antioxidant, oral toxicity and antispasmodic properties. The plant's high content of secondary metabolites, notably polyphenols and flavonoids, makes it a powerful antioxidant. Hence, this plant could be a potent source of antioxidants that could replace certain synthetic drugs to reduce tissue damage induced by free radicals. This study demonstrated the low toxicity of this plant, encouraging further investigations to test other biological activities. However, more research is required to ascertain the mechanisms of action, evaluate long-term toxicity, and determine the optimal doses for the safe and effective therapeutic. This research could pave the way for future investigations into developing

new phytopharmaceutical products derived from this unique desert species.

Conflict of interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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