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Short Communication

The First Global Report on the Alkaloid Aspidospermidine in *Vinca herbacea*: A Potential Source of Anticancer Alkaloid Precursors

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Abstract
Vinca herbacea Waldst. & Kit., a rare perennial species of the Apocynaceae family, is distributed across temperate regions of Western Asia and Eastern Europe. However, its presence in Iran is restricted to a few recorded sites. This plant remains poorly investigated despite the extensive study of other *Vinca* species. The present research collected aerial parts of *Vinca herbacea* from Mazandaran Province, Iran, and subjected them to phytochemical analysis. The propanol extract was analyzed using GC-MS, which revealed several chemical constituents. Aspidospermidine was identified in the leaf extract at a retention time of 42.74 min, representing 2.73% of the total compounds, with a 96% quality match to the NIST library. No Aspidospermidine was detected in stems or flowers. This finding constitutes the first global report of Aspidospermidine in *Vinca herbacea*, expanding its phytochemical profile and highlighting its potential as a natural source of pharmacologically important indole monoterpenoid alkaloids (IMAs) with anticancer and antimicrobial relevance.
Keywords: Alkaloids, Asidospermidine, Iran, *Vinca herbacea*

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Introduction

Vinca herbacea Waldst. & Kit. is a perennial herbaceous species belonging to the Apocynaceae family, distributed across temperate regions of Western Asia and Eastern Europe. According to the Royal Botanic Gardens, Kew (Plants of the World Online) and World Flora Online, this species is native to countries including Iran, Turkey, Iraq, Lebanon-Syria, Palestine, Armenia, Ukraine, Russia, Hungary, Germany, Austria, and Romania (1,2). However, data from the Global Biodiversity Information Facility (GBIF) indicate that its confirmed presence in Iran is limited to only six recorded locations, mainly in the northern provinces along the slopes of the Alborz Mountain range (1,2). This restricted distribution highlights its rarity and underscores the need for detailed ecological, physiological, and phytochemical studies to support conservation and sustainable utilization. Studies have shown that *Vinca herbacea* possesses diverse physiological and morphological adaptations, enabling it to grow and survive across various environmental conditions, including temperature, light intensity, salinity, and drought. Its highest abundance and occurrence have been reported in mountainous regions with semi-arid to humid conditions (1-3). Despite extensive research on other species of the genus, *Vinca herbacea* remains relatively underexplored in terms of its phytochemical profile, antioxidant capacity, and physiological responses to stress (2-4).

Materials and Methods

Sample Collection and Environmental Conditions

Vinca herbacea specimens were collected in June 2024 from the Baleskuh Protected Area, Tonekabon County, Mazandaran Province, Iran (38°36′21.6″ N, 44°50′27.5″ E, at an elevation of 1,095 meters above sea level). Verified plant materials were obtained from the Iranian Biological Resource Center (IBRC) under code IBRC P1006834. All aerial parts of the plant (leaves, flowers, and stems) were used for phytochemical and biological analyses. The environmental conditions at the time of collection were recorded according to the Islamic Republic of Iran Meteorological Organization (2024); average seasonal temperatures ranged from 20–30°C in spring, approximately 30°C in summer, 15–17°C in autumn, and 8–17°C in winter. Relative humidity levels were generally stable throughout the year, ranging from 70% to 80%, with

considerable annual rainfall. These moderate and humid climatic conditions, particularly during the plant's peak growth period in June, are conducive to the biosynthesis of secondary metabolites in *Vinca herbacea*.

Extraction Method

For extraction, 5 g of dried, powdered leaves, 2 g of stems, and 1 g of flowers were used. 10 mL of 96% 1-propanol (Merck, Germany) was added for each gram of dried powder. The mixtures were subjected to cold maceration at 4°C for three weeks. After extraction, the samples were centrifuged at 4,000 rpm for 20 minutes using a BH-1200 centrifuge (Behdad, Iran) to remove suspended particles and settle the solids. The supernatant was collected and passed through Whatman No. 1 filter paper (Whatman, UK). The filtered solution was stored under sterile, light-protected conditions at 4°C. Finally, under reduced pressure, the solvent was removed using a rotary evaporator (Hei-VAP Expert, Heidolph, Germany). The final extracts yielded approximately 0.052 g from leaves, 0.021 g from stems, and 0.013 g from flowers (5).

Gas Chromatography–Mass Spectrometry (GC-MS)

The chemical constituents of the propanol extract of *Vinca herbacea* aerial parts were analyzed using GC-MS. A gas chromatograph**,** Agilent 6890, and a mass selective detector**,** Agilent 5973 (Agilent, USA), were used. A 2 µL aliquot of the concentrated extract was injected in split mode (1:5) onto an HP-5MS capillary column (30 m × 0.25 mm, 1 µm film thickness; Agilent, USA). Helium (99.999% purity) was used as the carrier gas at a constant flow rate of 1.0 mL/min. The oven temperature was programmed from 60°C (held for 2 min) to 280°C at a rate of 5°C/min, with a final hold time of 20 min. Mass spectrometry was conducted using electron impact ionization at 70 eV, scanning the mass range m/z 40–500. Compound identification was achieved by comparing retention times and mass spectra to the NIST spectral library. This analysis identified major bioactive compounds in the propanol extract of *Vinca herbacea* aerial parts and provided its phytochemical profile (5).

Results

GC-MS analysis of the propanol extract of *Vinca herbacea* aerial parts revealed several chemical constituents. Notably, in the leaf extract, a compound identified as Aspidospermidine (CAS No. 32975-46-5) was detected at peak number 18, with a retention time of 42.74 minutes (Figure 1).

Aspidospermidine accounted for 2.73% of the total compounds identified by GC-MS, and its identification was confirmed with a quality match of 96% according to the NIST library (Figures 2A, B).

The chromatogram shows multiple peaks corresponding to the chemical constituents of the aerial parts. Peak 18, at a retention time of 42.74 min, corresponds to Aspidospermidine, as identified by GC-MS library matching with the NIST database with a 96% match confidence, confirming its presence in the leaf extract. The mass spectrum displays the characteristic fragmentation pattern of Aspidospermidine, an IMA. The horizontal axis represents m/z (mass-to-charge ratio), and the vertical axis shows abundance (relative intensity of ions).

No Aspidospermidine was detected in the stem or flower extracts. This finding represents the first global report of Aspidospermidine in *Vinca herbacea*, expanding the species' phytochemical profile and highlighting its potential as a natural source of pharmacologically important monoterpenoid indole alkaloids (3).

Discussion

The identification of Aspidospermidine in the leaf extracts of *Vinca herbacea* represents an important addition to the phytochemical profile of this species, and this study is the first global report of the presence of this compound in *Vinca herbacea*. Aspidospermidine is an IMA and a precursor of many important indole alkaloids, the most notable of which is tabersonine. Tabersonine is a precursor of vindoline, which subsequently leads to the production of clinically important anticancer drugs such as vincristine and vinblastine. The detection of this compound only in the leaves—not in the stems or flowers—indicates tissue-specific accumulation, which may be associated with metabolic activity and enzyme localization in the aerial parts of the plant (3,4,6,7).

Previous studies on other Vinca species have shown a high diversity of indole alkaloids, often in varying concentrations across different plant organs. The amount of Aspidospermidine (2.73% of the total compounds identified by GC-MS) in the leaves of *Vinca herbacea* is consistent with similar observations in other wild Vinca species, where secondary metabolite content is influenced by environmental factors such as altitude, temperature, and light intensity (3,8). With its mild and humid climate, the collection site in Mazandaran Province likely contributed to the synthesis and accumulation of this alkaloid in the leaves.

Aspidospermidine and its derivatives possess significant biological activities, including antimicrobial and anticancer properties. These alkaloids can inhibit the growth of cancer cells and exhibit antitumor effects, and act against certain bacteria and fungi (2,3, 9-13).

Given the role of Aspidospermidine as a precursor for producing tabersonine, vindoline, and important anticancer drugs, further studies on this species are strongly recommended. Expanded research in this field will help complete its phytochemical profile, enhance species conservation, and draw more attention to this valuable plant. Considering the limited distribution of *Vinca herbacea* in Iran, conservation efforts combined with detailed chemical and pharmacological studies are crucial to ensure both the protection of the species and the utilization of its medicinal potential (7,8).

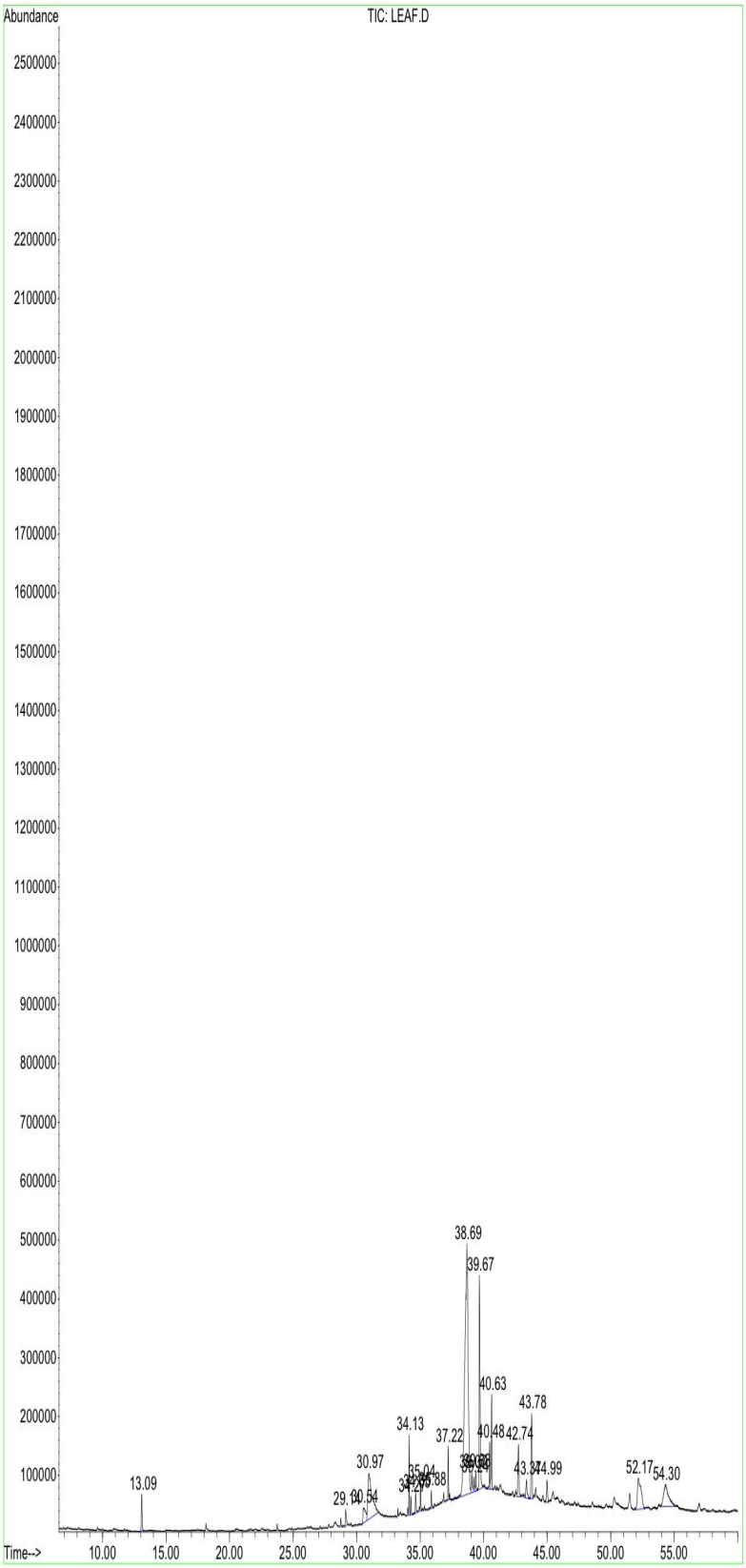

Figure 1. Total Ion Chromatogram (TIC) of the propanol extract of Vinca herbacea leaves

Recommended next steps for future studies include

1. LC-MS/MS analysis: To obtain fragmentation spectra of the compounds and compare them with available data in reference sources and validated standards for definitive identification.
2. Isolation and purification: Preparative HPLC separates compounds and determines their precise structures using NMR spectroscopy.
3. Bioactivity assays: Evaluation of the purified compounds for anticancer, antimicrobial, and

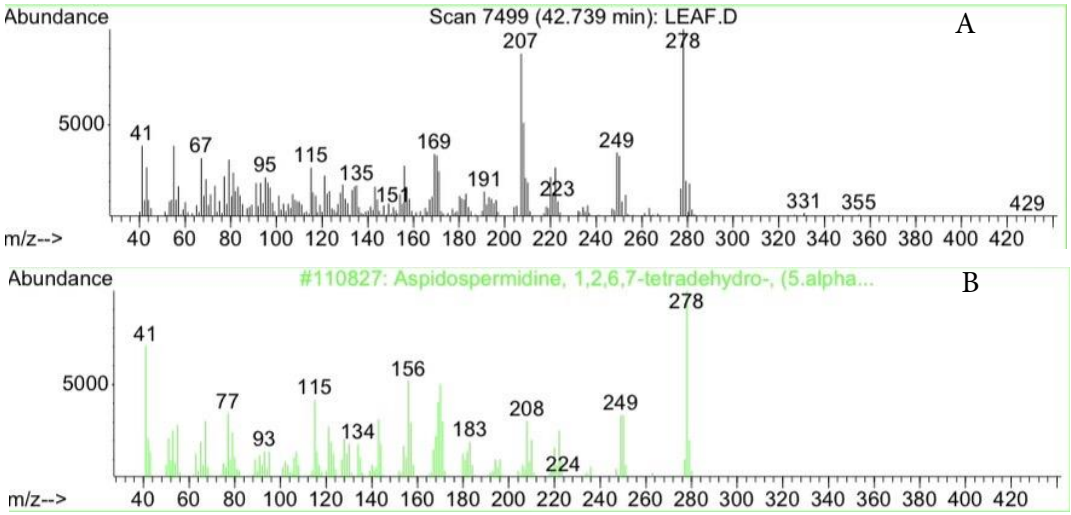

Figure 2. The related compound to Aspidospermidine in *Vinca herbacea* leaf extract was identified using GC-MS analysis. The mass spectrum of Aspidospermidine in the extract (Figure 2A) matches the reference spectrum in the NIST library (Figure 2B) with 96% confidence

antioxidant activities under laboratory conditions.

4. Population study: Examine samples collected from other geographic populations of Vinca herbacea to assess chemical variations and the influence of environmental factors on alkaloid production.

Conclusion

This study reports, for the first time globally, the presence of Aspidospermidine in the leaves of *Vinca herbacea*, thereby enriching the phytochemical profile of this species by identifying a key indole alkaloid precursor. The tissue-specific accumulation of this compound in the leaves indicates potential enzyme localization and metabolic activity in the aerial parts of the plant. The significant amount of Aspidospermidine and its role as a precursor of tabersonine and vindoline—which ultimately lead to the production of important anticancer drugs such as vincristine and vinblastine—highlight the medicinal value of this species. These findings underscore the importance of further chemical and biological studies on *Vinca herbacea* and emphasize the need to conserve this species with limited distribution in Iran. Future studies could include LC-MS/MS analysis, isolation and purification of compounds, bioactivity assays, and examination of different populations to evaluate chemical variations and environmental influences.

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Authors' Contribution

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Resources: Mohammad Kordkatouli, Aryan Sateei.
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Visualization: Mohammad Kordkatouli, Aryan Sateei.
Writing – original draft: Mohammad Kordkatouli.
Writing – review & editing: Mohammad Kordkatouli, Aryan Sateei.

Competing Interests

The authors declare that there is no conflict of interest.

Ethical Approval

Not applicable.

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