ATATÜRK ÜNİVERSİTESİ YAYINLARI
ATATURK UNIVERSITY PUBLICATIONS

Research Article / Araştırma Makalesi DOI: 10.62425/crihs.1628360

Antioxidant Potential and Phenolic Content of *Plantago major* L.

Plantago major'un Antioksidan Potansiyeli ve Fenolik İçeriği

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ABSTRACT

Objective: This study aimed to evaluate the antioxidant capacity and bioactive compound content of the aerial parts of *Plantago major*, a medicinal plant with potential therapeutic applications.

Methods: The aerial parts were extracted using 70% methanol, and the solvent was evaporated. Total phenolic content (TPC) and total flavonoid content (TFC) were quantified. Antioxidant capacity was assessed using DPPH, ABTS, and FRAP assays.

Results: The DPPH radical scavenging assay showed an IC_{50} value of 127,33 ± 1,07 µg/mL, while the ABTS assay revealed an IC_{50} value of 46,74 ± 2,53 µg/mL. The FRAP assay demonstrated a reducing power equivalent to 44,62 ± 0,61 mg TE/g extract.

Conclusion: The high phenolic and flavonoid content of *Plantago major* extract contributes significantly to its strong antioxidant activity. These findings suggest its potential application as a natural antioxidant source in the pharmaceutical and nutraceutical industries.

Keywords: ABTS, Antioxidant, DPPH, FRAP, *Plantago major* L.

ÖZ

Amaç: Bu çalışma, terapötik potansiyeli sahip, tıbbi bir bitki olan *Plantago major*'un toprak üstü kısımlarının antioksidan kapasitesini ve biyoaktif bileşik miktarını değerlendirmeyi amaçlamıştır.

Yöntemler: Toprak üstü kısımlar %70 metanol kullanılarak ekstre edilmiş ve çözücü buharlaştırılmıştır. Toplam fenolik içerik (TPC) ve toplam flavonoit içerik (TFC) miktarları belirlenmiştir. Antioksidan kapasitesi DPPH, ABTS ve FRAP analizleri ile değerlendirilmiştir.

Bulgular: DPPH serbest radikal süpürme testi IC_{50} değerini 127,33 ± 1,07 µg/mL olarak gösterirken, ABTS testi IC_{50} değerini 46,74 ± 2,53 µg/mL olarak ortaya koymuştur. FRAP analizi ise indirgeme gücünün 44,62 ± 0,61 mg TE/g ekstrakt eşdeğerinde olduğunu göstermiştir.

Sonuç: *Plantago major* ekstraktının yüksek fenolik ve flavonoid içeriği, güçlü antioksidan aktivitesine önemli ölçüde katkıda bulunmaktadır. Bu bulgular, bitkinin doğal bir antioksidan kaynağı olarak farmasötik ve nutrasötik endüstrilerinde potansiyel kullanımını desteklemektedir.

Anahtar Kelimeler: ABTS, Antioksidan, DPPH, FRAP, *Plantago major* L.

Introduction

The genus *Plantago* L. (Plantaginaceae) is represented worldwide by more than 200 species and in Turkey by 27 species. *Plantago major* L., a perennial herbaceous plant, is one of the most widespread species within the genus. It is characterized by its rosette-forming leaves, which are broadly ovate with prominent parallel venation, and small, inconspicuous flowers arranged in dense spikes. The plant thrives in a wide range of habitats, including meadows, roadsides, and disturbed areas, and is well-adapted to diverse environmental conditions (Haddadian et al., 2014; Kolak et al., 2011).

Pollen research has demonstrated that *P. major* was introduced into the Nordic nations concomitant to the establishment of the first crude cultivated fields in the stone age around 4000 years ago (Samuelsen, 2000). P. major was spread all over the world by humans starting in Europe. The Indians called it 'White man's footprint' since it was found everywhere Europeans had gone. The genus name *Plantago*, which comes from the Latin planta, which means sole of the foot, has been derived from this (Samuelsen, 2000).

Geliş Tarihi/Received 28.01.2025
Kabul Tarihi/Accepted 10.02.2025
Yayın Tarihi/Publication Date 27.02.2025

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Cite this article: Gözcü, S., & Atmaca, M. (2025). Antioxidant Potential and Phenolic Content of *Plantago major* L. *Current Research in Health Sciences*, *2*(1), 27-32.

P. major has a long history of being used traditionally to treat wounds. In the first century, Dioscorides wrote about it in "De materia medica." The leaves were used as a remedy for dog bites (Roca-Garcia, 1970). It is known that in Turkey, it is used externally in folk medicine for furuncle, mastitis, wounds, anti-inflammatory, vaginitis, conjunctivitis (Gözcü, Korkmaz, et al., 2024; Yiğit & Gözcü, 2024).

Traditional medicine has long utilized *P. major* for its anti-inflammatory and antimicrobial properties, yet the specific compounds responsible for these effects remain poorly understood. A detailed phytochemical and bioactivity analysis is therefore necessary to scientifically validate these traditional claims and identify potential therapeutic applications. In previous phytochemical analyses conducted in this direction, the presence of alkaloids (Samuelsen, 2000), caffeic acid derivatives (Skari et al., 1999), flavonoids (Skari et al., 1999), and iridoids (Taskova et al., 1999) in the herba of the plant was reported. Again, in studies conducted on the aerial parts of the plant, it has been reported that it has antiulcerogenic (Ragheb et al., 2021), anticancer (Daştan et al., 2016), antibacterial (Sousa et al., 2025), antiviral (McCutcheon et al., 1995), anti-inflammatory (Núñez Guillén et al., 1997), analgesic (Núñez Guillén et al., 1997), antioxidant and free radical scavenger (Stanisavljević et al., 2008) activities.

The aerial parts of *P. major* were subjected to methanolic extraction to evaluate their antioxidant and phytochemical properties. The study comprehensively assessed the *P. major* extract's which is traditionally used in folk medicine in Erzincan radical scavenging capacity using ABTS and DPPH assays, alongside its reducing power potential. Furthermore, the total phenolic and total flavonoid contents were quantified, providing valuable insights into the plant's bioactive compound profile. This study emphasizes *Plantago major*'s importance as a possible natural antioxidant source and its use in the functional food, pharmaceutical, and nutraceutical industries.

Methods

Plant Material and Extraction

The plant material was collected in May 2024 from Yanızbağ, Erzincan, Türkiye (39° 48' 23.94"N, 39° 22' 54.31"E), located at an altitude of 1324 m. Fresh *Plantago major* was used for extraction. The herbarium specimens were prepared by drying the collected plant material under shaded conditions with adequate ventilation to ensure preservation and prevent degradation of morphological and chemical characteristics. The authentication of voucher specimens was conducted by Prof. Dr. Ali Kandemir and deposited at the Herbarium of Erzincan Binali Yıldırım University in Erzincan, Turkiye (Akşit 13885)

In a shaded area, the plant material (Herba) was allowed to dry at room temperature. A laboratory mill was used to crush the dried aerial parts into a fine powder, and 12 g of the powdered material was macerated in 70% methanol (3 × 500 mL) at room temperature (It was used to extract both lipophilic and hydrophilic secondary metabolites). This process was performed using a mechanical mixer for 8 hours per day over 3 consecutive days to maximize extraction efficiency. After that, the methanolic extract was filtered and It was vacuum concentrated at 40 °C in a rotating evaporator. Following dry concentration, 2.4 g of methanolic extract was obtained. The obtained methanolic extract was stored at +4 °C away from light and moisture for further analysis.

DPPH·Free Radical Scavenging Ability

The free radical scavenging activity was evaluated using a modified version of the Akman et al. method (Akman et al., 2023). The experiment involved preparing a 0.26 mM DPPH· solution and stock solutions of extracts at 1 mg/mL. The stock solutions were taken in varying volumes (20-400 µL) and adjusted to a final volume of 3 mL with MeOH. After adding 1 mL of the DPPH· solution, each solution was vortexed and incubated for 30 minutes at room temperature. At the end of the incubation time, each reaction mixture's absorbance was measured at 517 nm. The method was repeated six times, and the mean and standard deviation of the findings were determined. The absorbance results were converted to a percentage of DPPH· scavenging activity, and the IC_{50} (µg/mL) for each extract was calculated.

ABTS·+ Radical Scavenging Ability

The extract's ABTS·+ radical scavenging activity was established by refining the Re et al. Method (Re et al., 1999). In short, 2.45 mM $K_2S_2O_8$ (potassium persulfate) solution and 2 mM ABTS (2,2-Azinobis(3-ethylbenzothiazoline-6-sulfonic acid)) solution were produced in 0.1 mM pH: 7.4 phosphate buffer. The ABTS·+ radical was produced by mixing these two solutions at a ratio of 1:2. It was subsequently kept at room temperature for 12 hours in the dark. Following that, stock solutions containing 1 mg/mL of the test samples were prepared. After adding 3 mL of phosphate buffer to extract solution (20–400 µL), 1 mL of the ABTS·+ solution was added to each solution. After 60 minutes of incubation at room temperature in the dark, the absorbance was measured at 734 nm. The method was repeated six times. The extract's IC_{50} (µg/mL) is calculated by converting the read absorbance measurements to % activity. The findings were compared to BHT, BHA, and trolox, which are common antioxidants.

Ferric Reducing Power

Akyüz's method was adjusted for the sample's reducing power. 250 µL of extract was diluted with 1.25 mL of $K_3Fe(CN)_6$ solution after preparing up to 1.25 mL with 0.2 M phosphate buffer (pH 6.6). Following a 20-minute incubation period at 50°C in a water bath, the mixture was allowed to cool to room temperature. The cooled liquid was combined with 1.25 mL of TCA (10 %) and 0.25 mL of $FeCl_3$ (0.1 %), and the absorbance of the mixture at 700 nm was then measured. The calibration curve was used to convert the absorbance of the samples to mmol TE activity/g. Trolox concentrations ranging from 10 to 100 µmol/L made up the calibration curve. Absorbances were measured

three times in order to calculate mean values and standard deviations (Akyüz, 2019).

Total Phenolic Content

The extract's total phenol content (TPC) was determined, and the findings were expressed in milligrams of gallic acid equivalents per gram of extract (mg GAE/g extract), according to Gözcü et al. stock solutions containing 1 mg/mL of extract and gallic acid were made. 4.5 milliliters of distilled water were used to dilute 0.1 milliliters of the extract stock solution. It was prepared up to 5 mL using 0.1 mL of Folin-Ciocalteu reagent and 0.3 mL of Na_2CO_3 (2%) in total. It was vortexed and incubated for 120 minutes in the dark after 10 minutes at room temperature. At 760 nm, the solution's absorbance was measured in triplicate (Gözcü, Akşit, et al., 2024).

Total Flavonoid Content

The total flavonoid content (TFC) in the extract was measured using spectrophotometric technique with aluminum chloride. The standard utilized was quercetin. Methanol was used to create stock solutions of the extract and quercetin (1 mg/mL). A cuvette was filled with 0.1 mL of extract stock solution, 4.7 mL of methanol, 0.1 mL of 10% $AlCl_3$, and 0.1 mL of 1 M ammonium acetate solution. The cuvette was then vortexed. At room temperature, the mixture was incubated for 45 min. A spectrophotometer was used to measure the absorbance at 415 nm following incubation. Different concentrations of quercetin (1-800 µg/mL) were used to create a calibration curve. The extract's total flavonoid content (TFC) was determined using a calibration curve and represented as mg of quercetin equivalent (QE) per gram. The mean and standard deviation of the TFC were calculated (Chang et al., 2002).

Statistical analysis

The Kruskal–Wallis test was utilized to assess statistical signifcance. Data analysis was carried out using SPSS software (IBM SPSS Statistics 20, IBM Corporation, Armonk, NY, USA), with a signifcance level established at p=0.05. The IC_{50} values for the extracts are reported as mean±standard deviation

Results

The antioxidant capacity and phenolic composition of the methanolic extract of *Plantago major* were evaluated using various spectrophotometric methods. The findings, presented in Table 1, revealed significant antioxidant activity and bioactive compound content, highlighting the potential of *P. major* as a natural antioxidant source. The free radical scavenging activities of the extract were assessed using DPPH and ABTS assays. The DPPH assay showed an IC_{50} value of 127.33 ± 1.07 µg/mL, indicating moderate radical scavenging capacity compared to standard antioxidants such as BHA (8.04 ± 0.69 µg/mL), BHT (10.70 ± 0.0.73 µg/mL), and trolox (8.50 ± 0.77 µg/mL). Similarly, the ABTS assay demonstrated stronger activity, with an IC50 value of 46.74 ± 2.53 µg/mL, suggesting that *P. major* contains compounds capable of neutralizing ABTS radicals effectively. However, its activity was lower compared to standard antioxidants such as BHA (6.33 ± 0.19 µg/mL), BHT (9.42 ± 0.63 µg/mL), and trolox (7.07 ± 0.15 µg/mL), indicating that *P. major* exhibits promising antioxidant potential.

Table 1. Total phenolic (TPC), flavonoid (TFC), DPPH, ABTS, and FRAP values of methanolic extract of *P. major*

Sample and standards	DPPH IC_{50} (µg mL^{-1})	ABTS IC_{50} (µg mL^{-1})	Total phenolics mg GAE g^{-1} Extract	Total flavonoids mg QE g^{-1} Extract	Reducing power mg TE g^{-1} Extract
Plantago major	127.33±1.07	46.74±2.53	46.02±0.48	12.86±1.27	44.62±0.61
Trolox	8.50±0.77	7.07±0.15	-	-	-
BHA	8.04±0.69	6.33± 0.19	-	-	338.57± 0.31
BHT	10.70±0.73	9.42±0.63	-	-	257.80± 1.24
Ascorbic acid	9.91±0.87	8.25±0.41	-	-	394.17±0.98

The reducing power of the extract, evaluated using the FRAP assay, was 44.62 ± 0.61 mg TE/g-1 extract. While the reduced capacity was lower than that of synthetic antioxidants such as ascorbic acid (394.17 ± 0.98 mg TE/g-1), BHA (338.57 ± 0.31 mg TE/g-1), and BHT (257.80 ± 1.24 mg TE/g-1), it still indicates a notable potential for electron donation, contributing to the overall antioxidant activity of the extract.

The total phenolic content (TPC) of the extract was measured as 46.02 ± 0.48 mg GAE/g -1 extract, and the total flavonoid content (TFC) was 12.86 ± 1.27 mg QE/g -1 extract. These findings confirm the rich phenolic and flavonoid profile of *P. major*, which aligns with previous studies reporting the plant's high content of bioactive compounds with antioxidant properties.

Discussion

Antioxidants are molecules able to inhibit the oxidation of other molecules by eliminating free radicals or decreasing their formation. In biological systems the effectiveness of an antioxidant system is fundamental because of the constant generation of free radicals inside the organism at several sites, which potentially may cause oxidative damage and consequent loss of function of proteins, lipids and nucleic acids. The effectiveness of antioxidants against oxidative damage in biological environments is directly related to their chemical structure. The ability to chelate transition metals or to interact

with membranes is affected by several factors, such as type, reactivity, and stability of the free radical formed (Dorta et al., 2008; Halliwell et al., 1995; Rice-Evans et al., 1997).

The antioxidant and phenolic composition of *Plantago major* observed in the present study is supported by previous phytochemical investigations of this plant. Numerous bioactive compounds have been isolated and identified from the leaves and aerial parts of *P. major*, demonstrating a wide array of biological activities. Among the compounds isolated and identified in earlier studies are acteoside (verbascoside) (Eldesoky et al., 2018), plantamajoside (Mazzutti et al., 2017), aucubin (Mazzutti et al., 2017), catalpol (Rahamouz-Haghighi et al., 2023), luteolin (Beara et al., 2009), luteolin-7-O-glucoside (Beara et al., 2009), apigenin (Rahamouz-Haghighi et al., 2023), and ferulic acid (Bourne et al., 1999). These compounds have been linked to significant antioxidant, anti-inflammatory, and antimicrobial properties.

Acteoside (verbascoside) and plantamajoside, two phenylethanoid glycosides abundantly found in *P. major*, have been extensively reported to possess potent antioxidant activity due to their capacity to scavenge free radicals and chelate metal ions. For instance, Lin et al. demonstrated the strong radical scavenging and lipid peroxidation inhibition potential of acteoside (Li et al., 2018). Similarly, plantamajoside was reported to exhibit both antioxidant and UV-protective properties (Samuelsen, 2000).

The iridoid glycosides aucubin and catalpol are also prominent phytoconstituents of *P. major*. Aucubin has shown hepatoprotective and anti-inflammatory effects, as highlighted by Huang et al. (Huang et al., 2022), while catalpol has been recognized for its neuroprotective and antioxidant activities (Jiang et al., 2015). These compounds likely contribute to the moderate DPPH and ABTS radical scavenging activities observed in the current study.

Luteolin and its derivative, luteolin-7-*O*-glucoside, are flavonoids commonly detected in *P. major*. Both have been demonstrated to have strong antioxidant and anti-inflammatory properties (Ahmadi et al., 2020; De Stefano et al., 2021). demonstrated that luteolin effectively inhibits oxidative stress and inflammatory mediators, aligning with the high phenolic content reported in this study. Additionally, apigenin, a less abundant flavonoid in *P. major*, has been documented for its antioxidant and anticancer properties (Imran et al., 2020; Tian et al., 2021).

Ferulic acid, a hydroxycinnamic acid found in the aerial parts of *P. major*, is another compound with significant antioxidant potential. Kikuzaki et al. (Kikuzaki et al., 2002) reported its ability to protect against oxidative stress by scavenging free radicals and inhibiting lipid peroxidation.

These data suggest that the antioxidant activities seen in the methanolic extract of *P. major* are due to the synergistic actions of its phenolic components, glycosides, and flavonoids. Although the extract performed less well than standard synthetic antioxidants such as BHA, BHT, and trolox in some tests, the presence of naturally occurring bioactive compounds with multifunctional properties makes *P. major* a promising source of natural antioxidants for pharmaceutical and nutraceutical applications.

Conclusion

This study shows that *Plantago major*'s methanolic extract has a high antioxidant capacity and phenolic content. In the DPPH and ABTS evaluations, the extract demonstrated moderate free radical scavenging activity as well as detectable reducing power, which was supported by its high phenolic and flavonoid content. These effects are most likely attributed to bioactive substances such as acteoside, plantamajoside, aucubin, catalpol, luteolin, and ferulic acid, which contribute to the plant's antioxidant, antiinflammatory, and antibacterial capabilities. The extract's natural composition and multifunctionality emphasizes its potential for pharmaceutical and nutraceutical uses, even if its activity was lower than that of synthetic antioxidants such as BHA, BHT, and trolox. According to these results, *P. major* is a potential natural antioxidant source that deserves more research into its bioactive components and potential medical applications.

Ethics Committee Approval: Ethics committee approval is not required.
Peer-review: Externally peer-reviewed.
Author Contributions: Concept – M.A., S.G.; Design – S.G.; Supervision – S.G.; Resources – M.A., S.G.; Data Collection and/or Processing – M.A., S.G.; Analysis and/or Interpretation - M.A., S.G.; Literature Search - M.A., S.G.; Critical Review – M.A., S.G.
Conflict of Interest: The authors have no conflicts of interest to declare.
Financial Disclosure: The authors declared that this study has received no financial support.

Etik Komite Onayı: Etik kurul onayına ihtiyaç yoktur.
Hakem Değerlendirmesi: Dış bağımsız.
Yazar Katkıları: Fikir – M.A., S.G.; Tasarım – S.G.; Denetleme – S.G.; Kaynaklar – M.A., S.G.; Veri Toplanması ve/veya İşlemesi – M.A., S.G.; Analiz ve/ veya Yorum- M.A., S.G.; Literatür Taraması - M.A., S.G.; Eleştirel İnceleme – M.A., S.G.
Çıkar Çatışması: Yazarlar, çıkar çatışması olmadığını beyan etmiştir.
Finansal Destek: Yazarlar, bu çalışma için finansal destek almadığını beyan etmiştir.

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