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Research Article

Unlocking The Therapeutic Potential of *Silene compacta*: A Comparative Study of Antioxidant and Enzyme Inhibitory Activities Across Solvent Extracts

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ABSTRACT

There has been a growing focus on the pharmacological research of medicinal plants, particularly their physiological and pharmacological effects. This study explores the chemical composition, antioxidant, and enzyme inhibitory activities of water, methanol, and ethyl acetate extracts from *Silene compacta*. The methanol extract demonstrated the highest total phenolic (30.88 mg GAEs/g) and flavonoid (50.19 mg REs/g) contents, translating to superior antioxidant activities in the DPPH• (45.82 mg TEs/g) and ABTS•+ (57.03 mg TEs/g) assays, as well as in CUPRAC and FRAP assays. In contrast, the ethyl acetate extract, while lower in phenolics, exhibited remarkable activity in the phosphomolybdenum assay (275.10 mg TEs/g) and showed strong enzyme inhibitory activities, particularly against α-glucosidase (1470.25 mg ACEs/g) and AChE (3.11 mg GALAEs/g). The water extract, with intermediate phenolic content, displayed balanced antioxidant properties across different assays, but its enzyme inhibitory effects were weaker. Correlation analysis revealed strong positive relationships between total phenolic content and most antioxidant assays, underscoring the importance of phenolic compounds in contributing to the observed bioactivities. The findings suggest that methanol extracts are particularly promising for applications requiring potent antioxidant properties, while ethyl acetate extracts might be more suited for enzyme inhibition-related applications. Future research should consider *in vivo* studies and explore the synergistic effects among different phytochemicals to fully understand the therapeutic potential of *S. compacta*.

Araştırma Makalesi

Silene compacta'nın Terapötik Potansiyelinin Ortaya Çıkarılması: Çözücü Özütleri Arasında Antioksidan ve Enzim İnhibitör Aktivitelerin Karşılaştırmalı Bir Çalışması

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ÖZ

Son yıllarda, tıbbi bitkilerin farmakolojik araştırmalarına, özellikle fizyolojik ve farmakolojik etkilerine artan bir ilgi gösterilmiştir. Bu çalışma, *Silene compacta* bitkisinin su, metanol ve etil asetat özütlerinin kimyasal bileşimini, antioksidan ve enzim inhibitör aktivitelerini incelemektedir. Metanol özütü, toplam fenolik (30.88 mg GAEs/g) ve flavonoit (50.19 mg REs/g) içerikleri açısından en yüksek değerlere sahip olup, DPPH• (45.82 mg TEs/g) ve ABTS•+ (57.03 mg TEs/g) testlerinde, ayrıca CUPRAC ve FRAP testlerinde de üstün antioksidan aktiviteler göstermiştir. Buna karşın, etil asetat özütü, fenolik içerik açısından daha düşük olmasına rağmen, fosfomolibdenum testinde (275.10 mg TEs/g) dikkat çekici bir aktivite sergilemiş ve özellikle α-glukozidaz (1470.25 mg ACEs/g) ve AChE (3.11 mg GALAEs/g) üzerinde güçlü enzim inhibitör aktiviteleri göstermiştir. Su özütü, orta düzeyde fenolik içerik ile farklı testlerde dengeli antioksidan özellikler sergilemiş, ancak enzim inhibitör etkileri daha zayıf olmuştur. Korelasyon analizi, toplam fenolik içerik ile çoğu antioksidan test arasında güçlü pozitif ilişkiler olduğunu ortaya koymuş, bu da fenolik bileşiklerin gözlemlenen biyolojik aktiviteler üzerindeki önemini vurgulamaktadır. Bulgular, metanol özütünün güçlü antioksidan özellikler gerektiren uygulamalar için özellikle umut verici olduğunu, etil asetat özütünün ise enzim inhibisyonu ile ilgili uygulamalar için daha uygun olabileceğini önermektedir. Gelecek araştırmalar, *S. compacta*'nın terapötik potansiyelini tam olarak anlamak için *in vivo* çalışmaları ve farklı fitokimyasallar arasındaki sinerjik etkileri keşfetmeyi dikkate almalıdır.

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Yazarlar, bu makalede bildirilen çalışmayı etkiliyor gibi görünebilecek bilinen hiçbir rakip mali çıkarları veya kişisel ilişkileri olmadığını beyan ederler. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.
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1. Introduction

Medicinal and aromatic plants have played a pivotal role in improving human health, forming the foundation of traditional medicine practices globally. The World Health Organization (WHO) estimates that approximately 80% of the global population relies on herbal medicines for primary healthcare, with these plants contributing over 25% of the world's pharmaceuticals (Farnsworth, 1984; Mukherjee and Wahile, 2006; Rawat et al., 2023; Tripathi, 2002). Given their immense therapeutic potential, there has been a growing focus on the pharmacological research of medicinal plants, particularly their physiological and pharmacological effects (Rawat et al., 2023; Thakur et al., 2023; Thapa et al., 2022; Yue et al., 2021).

One noteworthy genus in this context is *Silene* L. (Caryophyllaceae), which comprises 150 taxa in Turkey, 67 of which are endemic (Boğa, 2017). Known by various local names such as "Nakıl çiçeği" and "Gıvışganotu," Silene species have been traditionally used in Anatolia for treating urinary bladder and biliary tract diseases, and Silene vulgaris is even consumed as food in regions of Anatolia and Europe (Baytop, 1984; Laghetti and Perrino, 1994). The therapeutic potential of *Silene* species is largely attributed to their rich content of triterpene saponins and ecdysteroids, with the latter found in over 120 species of Silene. These compounds exhibit immunosuppressive, anti-inflammatory, and anticancer properties, making them promising candidates for drug development (Gaidi et al., 2002; Gąsiorowski et al., 1999; Glensk et al., 1999; Zibareva et al., 2009). Additionally, research into the fatty acid and essential oil composition of various *Silene* species further underscores their medicinal value (Bajpai et al., 2008; Kucukboyaci et al., 2010; Mamadalieva et al., 2010).

The antioxidant properties of many plants also play a critical role in protecting cells from the harmful effects of reactive oxygen species (ROS), which are linked to various human diseases. Studies have shown an inverse relationship between the consumption of antioxidant-rich plants and the prevalence of certain diseases, highlighting the importance of medicinal plants in health care (Dasgupta and De, 2007; Rice-evans et al., 1995). This is particularly relevant in the current global trade environment, where oxidative stress is recognized as a major health concern (Padmaja et al., 2011).

Alzheimer's disease (AD), first identified by Alois Alzheimer in 1907, is a progressive neurodegenerative disorder affecting over 20 million people worldwide. The disease's prevalence increases with age, significantly impacting the elderly population (Bachurin, 2003; Colombres et al., 2004). The cholinergic hypothesis links AD to reduced acetylcholine (ACh) levels, resulting from its rapid degradation by acetylcholinesterase (AChE) in key brain regions involved in memory and learning, such as the hippocampus and neocortex (Ladner and Lee, 1998). Meanwhile, the amyloid hypothesis suggests that AChE also promotes beta-amyloid (Aβ) deposition, leading to the formation of senile plaques and neurofibrillary tangles, which are characteristic of AD (Castro and Martinez, 2001; Selkoe, 2002). Butyrylcholinesterase (BuChE), another enzyme involved in ACh hydrolysis, shows increased activity in AD-affected brain areas and contributes to Aβ aggregation during plaque formation (Anand and Singh, 2013). Given these findings, inhibiting both AChE and BuChE has become a key therapeutic strategy for managing AD, though current AChE inhibitors like donepezil and rivastigmine offer limited effectiveness and come with potential side effects (Anand and Singh, 2012). Consequently, there is an ongoing search for more potent, selective cholinesterase inhibitors, with plant-based compounds showing particular promise (Anand and Singh, 2013).

Similarly, in the context of type 2 diabetes (T2D), where hyperglycemia results from inadequate insulin secretion or increased insulin resistance, controlling postprandial glucose levels is crucial. This can be achieved through the inhibition of enzymes like α-glucosidase and α-amylase, which reduce glucose absorption, and by using agents like metformin to enhance glucose uptake in peripheral tissues (Hirshman and Horton, 1990; Shulman, 2000; Yao et al., 2010). Plant polyphenols have emerged as valuable tools in this approach, as they not only inhibit carbohydrate-hydrolyzing enzymes but also promote glucose disposal, offering a comprehensive strategy for managing T2D (de Sousa et al., 2004; Hanamura et al., 2005). Many traditionally used plants for diabetes treatment contain bioactive compounds, including anthraquinones and flavonol glycosides, although scientific validation of their efficacy remains limited (Rai et al., 1997; Thilagam et al., 2013).

Another area of interest in plant-based therapies is the inhibition of tyrosinase, a copper-containing enzyme involved in melanin production. Tyrosinase catalyzes the hydroxylation of monophenols and the oxidation of diphenols, leading to the formation of melanin pigments (Ochiai et al., 2016). Overactivation of tyrosinase can result in hyperpigmentation disorders, such as lentigo, melasma, and age spots, as well as contributing to neurodegenerative diseases like Parkinson's (Chen et al., 2014; D'Mello et al., 2016; Slominski et al., 2004). Although some tyrosinase inhibitors, such as kojic acid and hydroquinone, are used clinically, they have limitations, including cytotoxicity and mutagenicity, necessitating the development of new, safer inhibitors (Fujimoto et al., 1999; Ubeid et al., 2012). This has driven research towards discovering novel compounds with better safety profiles and effectiveness in inhibiting tyrosinase (Joompang et al., 2020; Nie et al., 2017).

The present study aims to explore the chemical composition and evaluate the antioxidant and enzyme inhibitory activities of water, methanol, and ethyl acetate extracts of *Silene compacta*. Given the limited existing research on the biological activities of this species, as evidenced by the sole reference to Boğa (2017), the findings from this study are anticipated to provide novel insights and make a significant contribution to the literature, especially in areas not previously investigated, thereby enriching the understanding of *Silene compacta*'s potential medicinal properties.

2. Material and Methods

2.1. Plant material

The aerial parts of *Silene compacta* Fisch. ex Hornem were collected in 2022 at an altitude of 800 meters from Menteşe village, Kavaklıdere district, Muğla-Türkiye (37° 24' 86" N, 28° 26' 34.20" E). The specimen was identified by Dr. Olcay CEYLAN from the Department of Biology at Muğla Sıtkı Koçman University, and the type specimens are deposited in the herbarium of the same department (Herbarium numbers: O.1836).

2.2. Preparation of extracts

The aerial parts of the plant were dried in an environment with no direct sunlight and good air circulation for several weeks. Subsequently, they were ground into

small pieces using a laboratory blender and then subjected to the extraction process. Ethyl acetate and methanol extracts were prepared by macerating 5 grams of the plant material in each solvent for 24 hours with continuous stirring at 150 rpm. This process was repeated twice more. The solvents were then removed by concentrating under vacuum. The aqueous extract was prepared by treating a 5-gram sample of the plant with 100 mL of boiling distilled water for 15 minutes. After freezing the aqueous extract at -18 °C, it was lyophilized. The extracts were stored at +4 °C until use (Sarikurkcu et al., 2020b).

2.3. Determination of phenolic compositions of the extracts

The total phenolic and flavonoid contents of the extracts were quantified using spectroscopic methods (Zengin et al., 2017). The detailed phytochemical profile was assessed using a previously validated analytical procedure (Cittan and Çelik, 2018), with the analytical parameters detailed in Tables 1 and 2 of the supplementary material.

2.4. Biological activity

Information regarding the antioxidant assays (Apak et al., 2006; Kocak et al., 2016; Sarikurkcu et al., 2020a) and enzyme inhibition activity tests (Sarikurkcu et al., 2018; Sarikurkcu et al., 2020c) is provided in the supplementary file.

2.5. Statistical analysis

Detailed information on the Relative Antioxidant Capacity Index (RACI) (Sun and Tanumihardjo, 2007) and the statistical analyses performed is available in the supplementary file.

3. Results and Discussion

3.1. Chemical composition of S. compacta extracts

The total phenolic content of *S. compacta* extracts demonstrated significant variability across different solvents (Figure 1). The methanol extract exhibited the highest phenolic content at 30.88 mg GAEs/g, which was statistically distinct ($p < 0.05$) from the water and ethyl acetate extracts, measuring 24.58 mg GAEs/g and 19.04 mg GAEs/g, respectively. Similarly, the total flavonoid content varied significantly among the extracts, with the methanol extract again showing the highest concentration at 50.19 mg REs/g. This was significantly higher than the water and ethyl acetate extracts, which contained 12.31 mg REs/g and 1.58 mg REs/g, respectively.

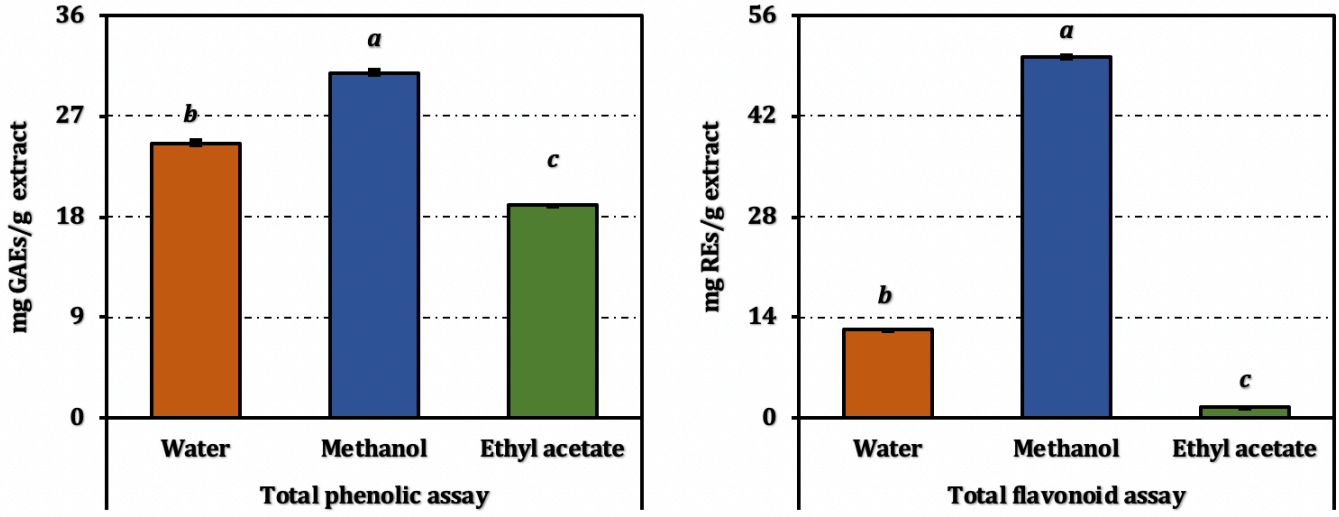

Figure 1. Total phenolic and flavonoid contents of *Silene compacta* extracts. REs and GAEs: Rutin and gallic acid equivalents, respectively. Values indicated by the same superscripts are not different from the honestly significant difference after Tukey's hoc test at 5% significance level.

Comparing the two groups, it is evident that methanol is a superior solvent for extracting both phenolic and flavonoid compounds from *S. compacta*. The water extract, although significantly lower in flavonoid content, still retained a relatively high phenolic content, indicating a more balanced extraction profile compared to the ethyl acetate extract, which showed the lowest levels of both phenolic and flavonoid compounds. This suggests that methanol might be more effective in extracting bioactive compounds with potential antioxidant properties, while water may offer a more moderate yield, and ethyl acetate appears to be less efficient for this purpose.

The chemical composition of *S. compacta* extracts varied significantly depending on the solvent used (Table 1). Methanol extract demonstrated the highest concentrations for several phytochemicals, notably ferulic acid (974 µg/g), *p*-coumaric acid (355 µg/g), 4-hydroxybenzoic acid (181 µg/g), vanillic acid (155 µg/g), and protocatechuic acid (151 µg/g), indicating methanol's effectiveness in extracting polyphenolic compounds. In contrast, water extract showed the highest concentration of *p*-coumaric acid (900 µg/g) and ferulic acid (2235 µg/g), while the ethyl acetate extract had the lowest concentrations for most compounds, such as hesperidin (0.6 µg/g) and hyperoside (2.0 µg/g).

The differences in the phytochemical content among the extracts can be attributed to the polarity of the solvents. Methanol, a highly polar solvent, efficiently extracted polyphenolic compounds, which are generally polar. The water extract, while also polar, favored the extraction of acids like *p*-coumaric and ferulic acid, which are highly abundant in this extract. Ethyl acetate, a less polar solvent, was less effective in extracting polar compounds, resulting in lower concentrations of most phytochemicals.

Table 1.

Table 1. Concentration (µg/g extract) of selected phenolic compounds in *Silene compacta* extracts.

Compound	Water	Methanol	Ethyl acetate
Gallic acid	4.4±0.1^{b}	9.4±0.1^{a}	3.8±0.1^{c}
Protocatechuic acid	60.4±0.5^{b}	151±1^{a}	13.3±0.9^{c}
3,4-Dihydroxyphenylacetic acid	13.5±0.1^{b}	15.1±0.4^{a}	13.6±0.5^{ab}
Pyrocatechol	33.1±2.2^{a}	33.7±0.6^{a}	35.6±0.2^{a}
(+)-Catechin	nd	149±6^{a}	nd
Chlorogenic acid	4.2±0.1^{a}	5.5±0.1^{a}	4.5±0.1^{b}
(-)-Epicatechin	2.5±0.2^{b}	4.5±0.2^{a}	2.3±0.1^{b}
2,5-Dihydroxybenzoic acid	11.7±0.3^{b}	11.9±0.1^{b}	14.2±0.6^{a}
4-Hydroxybenzoic acid	146±3^{b}	181±5^{a}	28.9±0.1^{c}
Vanillic acid	190±9^{a}	155±1^{a}	170±12^{a}
Caffeic acid	31.5±0.5^{a}	29.2±0.3^{b}	16.4±0.4^{c}
Syringic acid	6.6±0.4^{b}	10.5±1.2^{a}	4.0±0.1^{b}
3-Hydroxybenzoic acid	12.6±1.2^{b}	17.9±1.1^{a}	14.7±1.0^{ab}
Vanillin	35.4±2.3^{c}	79.8±1.9a	52.1±0.4^{b}
Verbascoside	5.6±0.1^{c}	11.0±0.1^{a}	6.1±0.1^{b}
Taxifolin	7.2±0.1^{b}	10.7±0.3^{a}	7.5±0.1^{b}
p-Coumaric acid	900±6^{a}	355±3^{b}	30.3±1.3^{c}
Sinapic acid	5.2±0.2^{b}	37.8±2.3^{a}	5.1±0.4^{b}
Ferulic acid	2235±12^{a}	974±6^{b}	50.2±0.5^{c}
Luteolin 7-glucoside	nd	122.2±3.6^{a}	nd
Hyperoside	26.9±1.0^{b}	86.4±0.8^{a}	2.0±0.1^{c}
Hesperidin	1.4±0.2^{b}	113±1a	0.6±0.1^{b}
Rosmarinic acid	7.6±0.1^{b}	8.0±0.3^{b}	8.8±0.1^{a}
Apigenin 7-glucoside	4.7±0.1^{a}	4.0±0.1^{b}	nd
2-Hydroxycinnamic acid	8.8±0.2^{a}	2.0±0.1^{b}	2.1±0.4^{b}
Eriodictyol	16.2±1.0^{a}	15.4±0.1^{a}	10.2±0.3^{b}
Pinoresinol	90.0±2.5^{a}	nd	nd
Quercetin	1.4±0.1^{b}	18.7±0.6^{a}	2.2±0.2^{b}
Kaempferol	nd	nd	nd
Luteolin	7.0±0.1^{a}	nd	nd
Apigenin	8.0±0.2^{a}	nd	nd

The values indicated by the same superscripts within the same row are not different according to the Tukey's honestly significant difference post hoc test at 5% significance level. nd: Not detected

This variation in extraction efficiency highlights the importance of solvent selection in phytochemical studies, particularly when targeting specific bioactive compounds. The high levels of compounds such as ferulic acid and *p*-coumaric acid in the water extract suggest potential antioxidant activities, while the methanol extract's rich content of flavonoids and other phenolics indicates its possible utility in pharmacological applications.

When these findings are compared with the literature, they show a degree of congruence with previously reported data on other *Silene* species, yet also contribute novel insights. For instance, Boğa (2017) reported the presence of similar phenolic acids in *S. compacta*, confirming that these compounds are indeed characteristic of this species. Additionally, Ouzounidou (1994) highlighted the importance of phenolic compounds in the root and pigment composition of *S. compacta* under stress conditions, further validating the significance of these compounds as identified in the present study. However, the current research also identifies certain phytochemicals that have not been previously reported in the literature, such as the high levels of ferulic acid in the water extract. This finding is particularly noteworthy, as it represents a novel contribution to the phytochemical profile of *S. compacta* and provides new data for future reference in the scientific literature.

Overall, the differences in phytochemical content among the extracts underline the importance of solvent choice in phytochemical studies, particularly when targeting specific bioactive compounds. The identification of previously unreported phytochemicals emphasizes the need for further exploration of *S. compacta* and related species to fully understand their chemical diversity and potential applications.

3.2. Antioxidant activity of S. compacta extracts

The antioxidant activities of the water, methanol, and ethyl acetate extracts from *S. compacta* were evaluated using multiple assays, revealing distinct differences based on the solvent used (Figure 2). In the phosphomolybdenum assay, ethyl acetate extract exhibited the highest activity (275.10 mg TEs/g), significantly surpassing methanol (189.30 mg TEs/g) and water extracts (143.40 mg TEs/g). Conversely, in the DPPH$^{\bullet}$ and ABTS$^{\bullet+}$ assays, methanol extract showed superior radical scavenging ability, with values of 45.82 and 57.03 mg TEs/g, respectively. Notably, ethyl acetate extract demonstrated lower scavenging activity in these assays.

The CUPRAC and FRAP assays also highlighted the stronger reducing power of the methanol extract, recording 73.40 and 48.68 mg TEs/g, respectively, compared to water and ethyl acetate extracts. However, in the ferrous ion chelating assay, the methanol extract again showed the highest chelating activity (19.12 mg EDTAEs/g).

The varying antioxidant activities across the assays can be linked to the phytochemical composition of the extracts. The methanol extract, rich in phenolic acids like ferulic, *p*-coumaric, 4-hydroxybenzoic, vanillic, and protocatechuic acids, correlates with its higher radical scavenging and reducing activities. In contrast, the ethyl acetate extract, while exhibiting strong phosphomolybdenum activity, contains lower amounts of these phenolics, explaining its reduced performance in other assays. The water extract's intermediate performance reflects its balanced composition, with notable levels of ferulic acid and *p*-coumaric acid contributing to its antioxidant activity. The findings suggest that the methanol extract may be particularly effective in applications requiring potent radical scavenging and reducing capacities, while the ethyl acetate extract's strengths lie in its total antioxidant capacity as measured by the phosphomolybdenum assay.

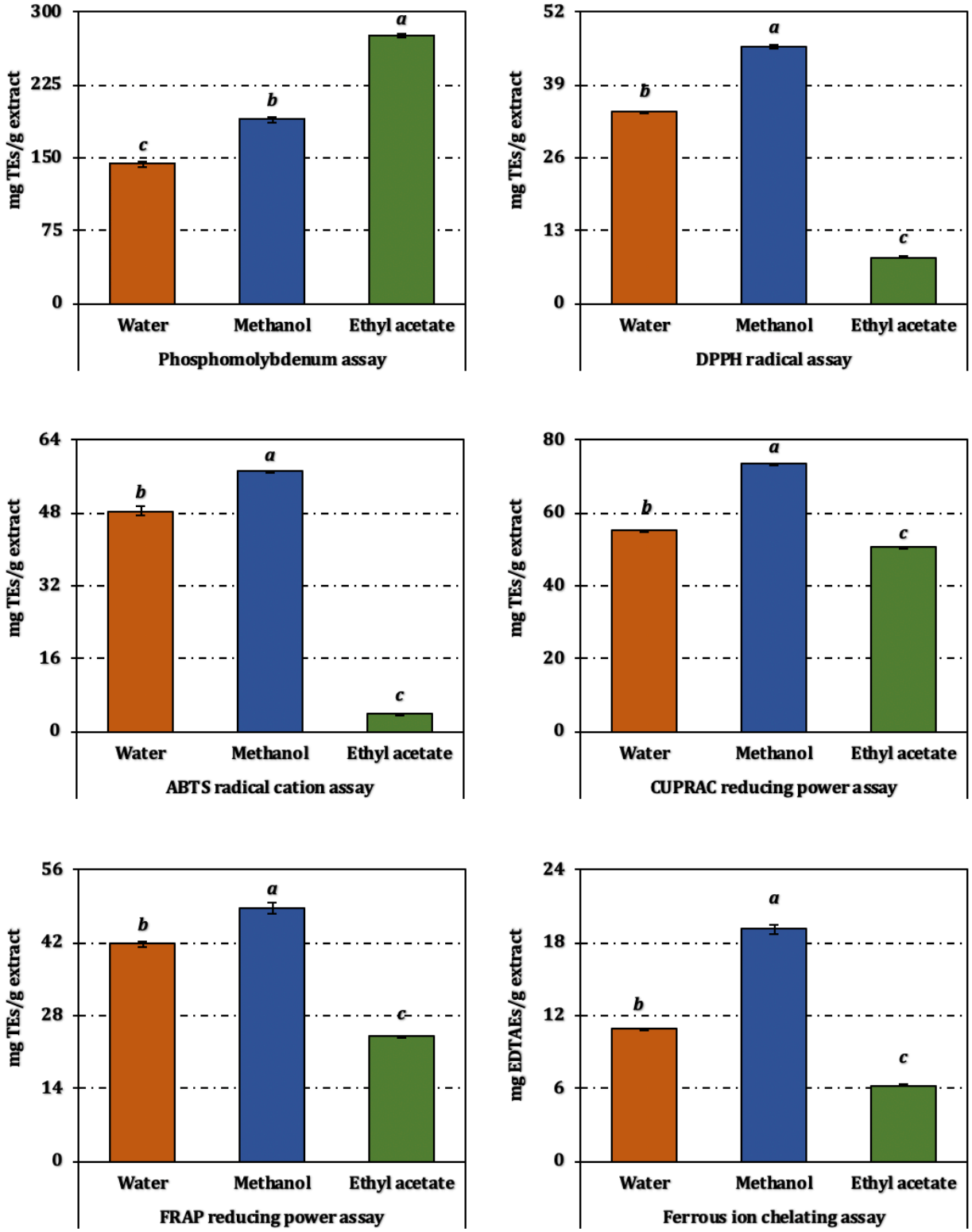

Figure 2. Antioxidant activity of *Silene compacta* extracts [TEs and EDTAEs mean trolox and ethylenediaminetetraacetic acid (disodium salt) equivalents, respectively]. Values indicated by the same superscripts are not different from the honestly significant difference after Tukey's hoc test at 5% significance level.

The relative antioxidant capacity index (RACI) values for the water, methanol, and ethyl acetate extracts of *S. compacta* indicate varying levels of antioxidant activity (Figure 3). The methanol extract, with a RACI value of 0.92, demonstrated the highest antioxidant activity, aligning well with its strong performance in assays such as DPPH$^{\bullet}$, ABTS$^{\bullet+}$, CUPRAC, and FRAP, where it consistently showed superior radical scavenging and reducing power. Conversely, the ethyl acetate extract, with a RACI of −0.79, showed the lowest antioxidant activity, which is consistent with its lower performance in the DPPH$^{\bullet}$ and ABTS$^{\bullet+}$ assays despite its higher phosphomolybdenum activity. The water extract, with a RACI of −0.12, exhibited moderate antioxidant activity, correlating with its intermediate performance across the various assays.

These RACI values provide a comprehensive comparison of the extracts' antioxidant capacities, confirming that the methanol extract's higher antioxidant activity is well-

supported by the assay results, while the ethyl acetate extract's lower activity is also consistent with its overall assay performance. The differences in RACI values and assay results are likely attributable to the distinct phytochemical compositions of the extracts, with the methanol extract's richness in phenolic acids like ferulic, *p*-coumaric, 4-hydroxybenzoic, vanillic, and protocatechuic acids contributing significantly to its superior antioxidant capacity.

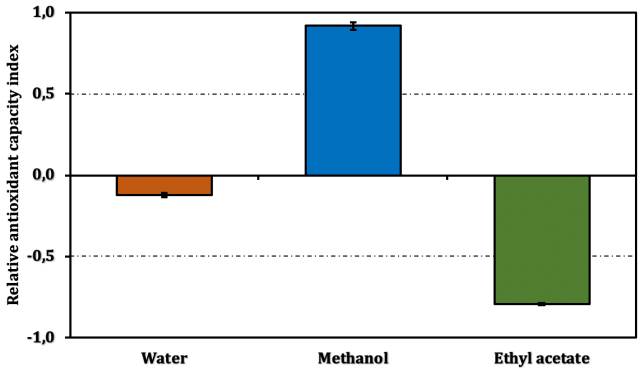

Figure 3. Relative antioxidant capacity index of *Silene compacta* extracts.

In the study by Ouzounidou (1994), *S. compacta* demonstrated copper-induced oxidative stress, leading to altered root growth and pigment composition, particularly affecting chlorophyll and carotenoid levels. This stress response is associated with the plant's antioxidant defense mechanisms, including enzymatic and non-enzymatic pathways.

Comparatively, the current study's findings on the antioxidant activities of different *S. compacta* extracts align with Ouzounidou (1994)'s observations, particularly in the context of the methanol extract's superior radical scavenging abilities, which could be related to its rich phenolic content. These phenolics may play a crucial role in mitigating oxidative damage, similar to the plant's response to copper stress. The consistency between the methanol extract's antioxidant capacity and the stress-induced responses observed by Ouzounidou (1994) suggests that *S. compacta*'s phytochemical composition is integral to its ability to counteract oxidative stress, regardless of the stressor's nature.

3.3. Enzyme inhibitory activity of S. compacta extracts

The enzyme inhibitory activities of *S. compacta* extracts were assessed against various enzymes, revealing distinct patterns (Figure 4). The ethyl acetate extract demonstrated the strongest inhibitory activity across most assays, including AChE (3.11 mg GALAEs/g), BChE (2.29 mg GALAEs/g), α-amylase (442.55 mg ACEs/g), and α-glucosidase (1470.25 mg ACEs/g). The methanol extract showed moderate activity, while the water extract exhibited the weakest inhibition.

The pronounced activity of the ethyl acetate extract can be attributed to its higher content of specific phenolic compounds such as ferulic acid, which is known for its enzyme inhibitory potential. The methanol extract's moderate inhibition is likely related to its balanced phytochemical composition, including quercetin and catechin, which contribute to both antioxidant and enzyme inhibitory activities. Conversely, the water extract, with its lower concentration of these bioactive compounds, correlates with its reduced enzyme inhibition.

These findings align with the chemical composition data, where the presence of particular phenolic acids and flavonoids, especially in the ethyl acetate and methanol extracts, supports their significant enzyme inhibitory activities. The variation in inhibition among the extracts may be linked to the differential extraction of these bioactive compounds based on the solvent's polarity.

This study provides the first investigation into the enzyme inhibitory activities of *S. compacta* extracts, contributing novel data to the literature. The ethyl acetate extract showed the most potent inhibition against several enzymes, which is consistent with its high content of bioactive phenolic compounds like ferulic acid.

Comparatively, other *Silene* species have demonstrated significant enzyme inhibitory activities, further supporting the findings of this study. For example, *S. salsuginea* exhibited strong inhibition in cholinesterase and α-glucosidase assays, primarily due to its rich phenolic profile, as reported by Zengin et al. (2018). Similarly, *S. viridiflora* was found to contain a new triterpene glycoside, silviridoside, which showed promising inhibitory effects, as highlighted by Makhmudova et al. (2022). These observations suggest that the enzyme inhibitory potential may be a common characteristic within the *Silene* genus, driven by the presence of bioactive compounds such as flavonoids and triterpene glycosides.

Further supporting this hypothesis, Aygun et al. (2022) identified distinct phytochemical compositions in different parts of *Silene* species, which correlated with their enzyme inhibitory activities. Additionally, the study by Boğa (2017) on *S. compacta* emphasized its cytotoxic and cholinesterase inhibitory activities, highlighting its potential therapeutic relevance. This is echoed by Almasi and Zarei (2021), who reported strong α-glucosidase inhibition in *S. ampullata*, further illustrating the genus's bioactive potential.

The results of the current study align with these findings, suggesting that *S. compacta* and other *Silene* species may serve as valuable sources of natural enzyme inhibitors. These compounds could be particularly relevant in developing treatments for conditions such as neurodegenerative diseases and diabetes, where enzyme inhibition plays a critical role.

3.4. Correlations among phenolic compounds and assays

The correlation analysis between the chemical composition of *S. compacta* extracts and their antioxidant activities reveals several significant relationships (Table 2). Total phenolic content exhibits a strong positive correlation with the DPPH$^{\bullet}$ radical scavenging (r = 0.966), ABTS$^{\bullet+}$ radical scavenging (r = 0.917), CUPRAC reducing power (r = 0.955), FRAP reducing power (r = 0.957), and ferrous ion chelating activity (r = 0.992). Similarly, total flavonoid content shows a positive correlation with most assays, particularly with CUPRAC (r = 0.999) and ferrous ion chelating activity (r = 0.987). This suggests that phenolic and flavonoid compounds are major contributors to the antioxidant activities observed. Conversely, vanillic acid, *p*-coumaric acid, and ferulic acid demonstrate weak or negative correlations with these activities, indicating that their presence may not directly enhance antioxidant capacity or may even inversely affect certain activities.

These results suggest that while phenolic and flavonoid contents are generally reliable predictors of antioxidant activity, individual compounds like vanillic acid, *p*-coumaric acid, and ferulic acid may interact with the radical scavenging and reducing assays in complex ways that do not

straightforwardly enhance activity. The strong correlations of phenolic and flavonoid contents with most antioxidant assays further reinforce their importance as key contributors to the observed antioxidant activities in *S. compacta* extracts.

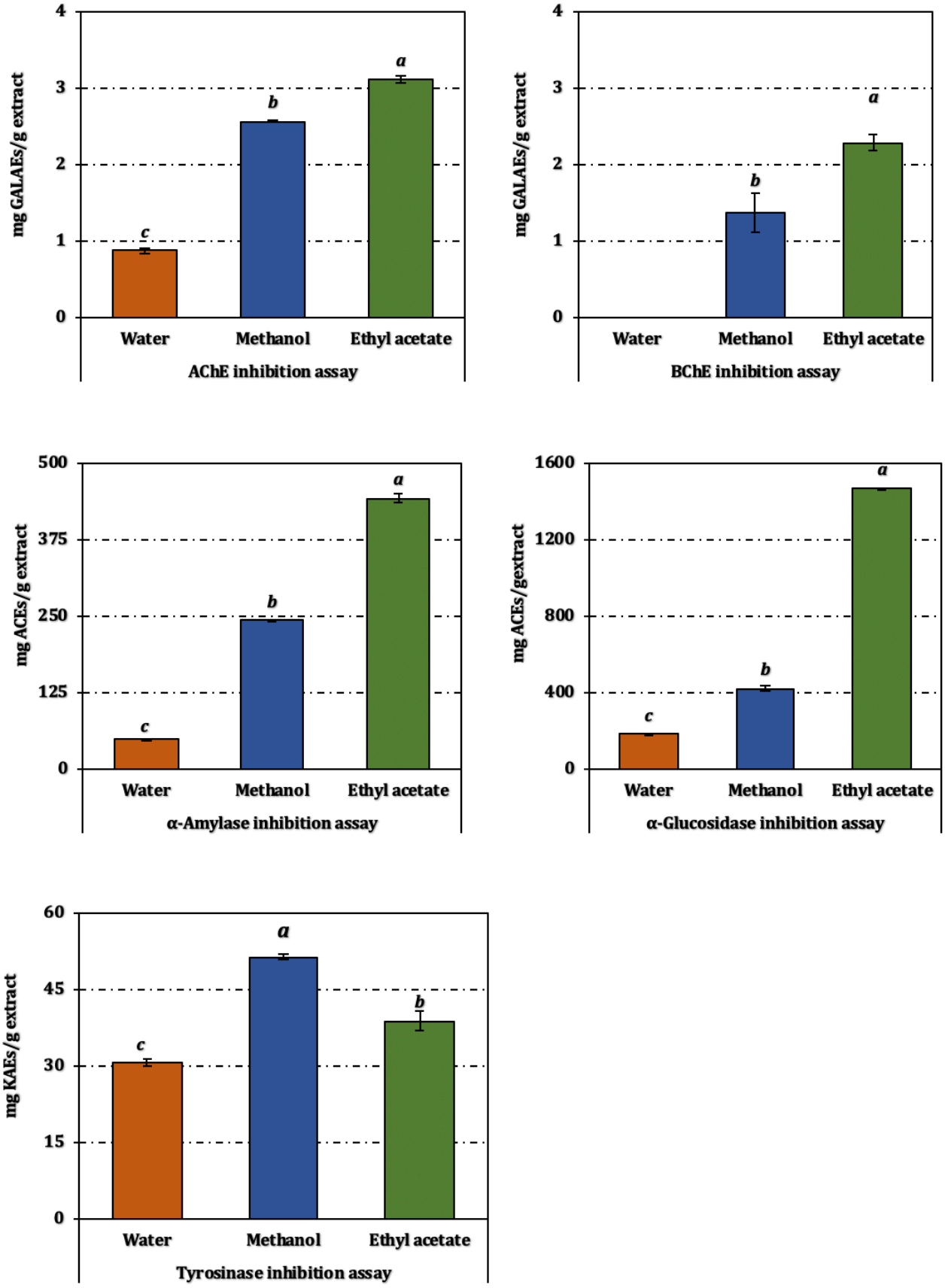

Figure 4. Enzyme inhibition activity of *Acanthus spinosus* extracts. ACEs, GALAEs and KAEs mean acarbose, galanthamine and kojic acid equivalents, respectively. Values indicated by the same superscripts are not different from the honestly significant difference after Tukey's hoc test at 5% significance level.

Table 2. Correlations among phenolic compounds and assays.

	Phosphomolybdenum	DPPH· radical	ABTS·+ radical	CUPRAC reducing	FRAP reducing	Ferrous ion chelating activity
ABTS·+ radical	-0.795					
ABTS·+ radical	-0.875	0.989				
CUPRAC reducing	-0.354	0.849	0.762			
FRAP reducing	-0.807	0.998	0.992	0.835		
Ferrous ion chelating activity	-0.515	0.930	0.866	0.983	0.921	
Total phenolic	-0.613	0.966	0.917	0.955	0.957	0.992
Total flavonoid	-0.375	0.861	0.776	0.999	0.847	0.987
Vanillic acid	-0.387	-0.188	-0.051	-0.638	-0.162	-0.506
p-Coumaric acid	-0.949	0.565	0.680	0.043	0.584	0.222
Ferulic acid	-0.965	0.610	0.720	0.100	0.629	0.277

4. Conclusions

The study highlights the significant influence of solvent choice on the extraction efficiency of phenolic and flavonoid compounds from *S. compacta*, which in turn affects both antioxidant and enzyme inhibitory activities. Methanol proved to be the most effective solvent, yielding extracts rich in bioactive compounds with strong radical scavenging and reducing capacities, as well as moderate enzyme inhibition. Ethyl acetate, although less efficient in extracting phenolics, exhibited remarkable enzyme inhibitory activities, possibly due to its ability to concentrate specific bioactives like ferulic acid.

The correlations observed between phenolic content and antioxidant assays underscore the critical role of these compounds in the plant's bioactivity. However, the negative or weak correlations associated with certain individual phenolics suggest a complex interaction that warrants further investigation. The study's findings suggest potential applications for *S. compacta* extracts in pharmaceutical and nutraceutical fields, particularly as antioxidants and enzyme inhibitors.

Despite these promising results, several limitations should be addressed in future research. The study's reliance on *in vitro* assays, while informative, may not fully capture the bioactivity *in vivo*, where metabolic processes could alter the effectiveness of the extracts. Additionally, the negative correlations observed with certain phenolic acids suggest that further studies are needed to elucidate the underlying mechanisms. Expanding the scope of solvents and exploring synergistic effects among phytochemicals could also provide a more comprehensive understanding of *S. compacta*'s therapeutic potential.

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References

Almasi, H., Zarei, M.A., (2021), α-glucosidase inhibition activity and antioxidant properties of aerial parts methanol extract from *Silene ampullata* Bioss and *Campanula involucrate* Auch. ex DC, *Journal of Plant Research (Iranian Journal of Biology),* 34, 1-20.

Anand, P., Singh, B., (2012), Synthesis and evaluation of novel 4-[(3H, 3aH, 6aH)-3-phenyl)-4, 6-dioxo-2-phenyldihydro-2H-pyrrolo [3, 4-d] isoxazol-5 (3H, 6H, 6aH)-yl] benzoic acid derivatives as potent acetylcholinesterase inhibitors and anti-amnestic agents, *Bioorganic & Medicinal Chemistry,* 20, 521-530.

Anand, P., Singh, B., (2013), A review on cholinesterase inhibitors for Alzheimer's disease, *Archives of Pharmacal Research,* 36, 375-399.

Apak, R., Güçlü, K., Özyürek, M., Esin Karademir, S., Erçağ, E., (2006), The cupric ion reducing antioxidant capacity and polyphenolic content of some herbal teas, *International Journal of Food Sciences and Nutrition,* 57, 292-304.

Aygun, R.B., Zengin, G., Yıldıztugay, E., Jugreet, S., Yılmaz, M.A., Mahomoodally, F.M., (2022), Chemical characterization, anti-oxidant and anti-enzymatic properties of extracts from two *Silene* species: A focus on different plant parts and extraction methods, *Process Biochemistry,* 116, 206-213.

Bachurin, S.O., (2003), Medicinal chemistry approaches for the treatment and prevention of Alzheimer's disease, *Medicinal Research Reviews,* 23, 48-88.

Bajpai, V.K., Shukla, S., Kang, S.C., (2008), Chemical composition and antifungal activity of essential oil and various extract of *Silene armeria* L, *Bioresource Technology,* 99, 8903-8908.

Baytop, T., (1984), Therapy with plants in Turkey, *İstanbul University Publ., İstanbul*, 226-227.

Boğa, M., (2017), Chemical constituents, cytotoxic, antioxidant and cholinesterases inhibitory activities of *Silene compacta* (Fischer) extracts, *Marmara Pharmaceutical Journal,* 21, 445-454.

Castro, A., Martinez, A., (2001), Peripheral and dual binding site acetylcholinesterase inhibitors: implications in treatment of Alzheimer's disease, *Mini Reviews in Medicinal Chemistry,* 1, 267-272.

Chen, X.-X., Shi, Y., Chai, W.-M., Feng, H.-L., Zhuang, J.-X., Chen, Q.-X., (2014), Condensed tannins from *Ficus virens* as tyrosinase inhibitors: structure, inhibitory activity and molecular mechanism, *PLoS One,* 9, e91809.

Cittan, M., Çelik, A., (2018), Development and validation of an analytical methodology based on Liquid Chromatography–Electrospray Tandem Mass Spectrometry for the simultaneous determination of phenolic compounds in olive leaf extract, *Journal of Chromatographic Science,* 56, 336-343.

Colombres, M., Sagal, J.P., Inestrosa, N.C., (2004), An overview of the current and novel drugs for Alzheimer's disease with particular reference to anti-cholinesterase compounds, *Current Pharmaceutical Design,* 10, 3121-3130.

D'Mello, S.A., Finlay, G.J., Baguley, B.C., Askarian-Amiri, M.E., (2016), Signaling pathways in melanogenesis, *International Journal of Molecular Sciences,* 17, 1144.

Dasgupta, N., De, B., (2007), Antioxidant activity of some leafy vegetables of India: A comparative study, *Food Chemistry,* 101, 471-474.

de Sousa, E., Zanatta, L., Seifriz, I., Creczynski-Pasa, T.B., Pizzolatti, M.G., Szpoganicz, B., Silva, F.R.M.B., (2004), Hypoglycemic Effect and Antioxidant Potential of

Kaempferol-3, 7-O-(α)-dirhamnoside from *Bauhinia forficata* Leaves, *Journal of Natural Products,* 67, 829-832.

Farnsworth, N.R., (1984), The role of medicinal plants in drug development, *Natural Products and Drug Development,* 17, 30-34.

Fujimoto, N., Onodera, H., Mitsumori, K., Tamura, T., Maruyama, S., Ito, A., (1999), Changes in thyroid function during development of thyroid hyperplasia induced by kojic acid in F344 rats, *Carcinogenesis,* 20, 1567-1572.

Gaidi, G., Miyamoto, T., Laurens, V., Lacaille-Dubois, M.-A., (2002), New Acylated Triterpene Saponins from *Silene fortunei* that Modulate Lymphocyte Proliferation, *Journal of Natural Products,* 65, 1568-1572.

Gąsiorowski, K., Brokos, B., Gleńsk, M., Schöpke, T., (1999), Immunomodulatory activity of the saponin-rich fraction from roots of *Silene vulgaris* Garcke: initial study, *Pharmazie,* 54, 864-866.

Glensk, M., Wray, V., Nimtz, M., Schöpke, T., (1999), Silenosides A− C, triterpenoid saponins from *Silene vulgaris*, *Journal of Natural Products,* 62, 717-721.

Hanamura, T., Hagiwara, T., Kawagishi, H., (2005), Structural and functional characterization of polyphenols isolated from acerola (*Malpighia emarginata* DC.) fruit, *Bioscience, Biotechnology, and Biochemistry,* 69, 280-286.

Hirshman, M.F., Horton, E.S., (1990), Glyburide increases insulin sensitivity and responsiveness in peripheral tissues of the rat as determined by the glucose clamp technique, *Endocrinology,* 126, 2407-2412.

Joompang, A., Jangpromma, N., Choowongkomon, K., Payoungkiattikun, W., Tankrathok, A., Viyoch, J., Luangpraditkun, K., Klaynongsruang, S., (2020), Evaluation of tyrosinase inhibitory activity and mechanism of Leucrocin I and its modified peptides, *Journal of Bioscience and Bioengineering,* 130, 239-246.

Kocak, M.S., Sarikurkcu, C., Cengiz, M., Kocak, S., Uren, M.C., Tepe, B., (2016), *Salvia cadmica*: Phenolic composition and biological activity, *Industrial Crops and Products,* 85, 204-212.

Kucukboyaci, N., Ozcelik, B., Adiguzel, N., Goren, A.C., (2010), Fatty-acid compositions of *Silene vulgaris* and *S. cserei* subsp. *aeoniopsis* seeds and their antimicrobial activities, *Chemistry of Natural Compounds,* 46, 88-91.

Ladner, C.J., Lee, J.M., (1998), Pharmacological drug treatment of Alzheimer disease: the cholinergi hypothesis revisited, *Journal of Neuropathology and Experimental Neurology,* 57, 719.

Laghetti, G., Perrino, P., (1994), Utilization of *Silene vulgaris* (Moench) Garcke in Italy, *Economic Botany,* 48, 337-339

Makhmudova, M.M., Bacher, M., Zengin, G., Rosenau, T., Youssef, F.S., Almasri, D.M., Elhady, S.S., Mamadalieva, N.Z., (2022), Silviridoside: A New Triterpene Glycoside from *Silene viridiflora* with Promising Antioxidant and Enzyme Inhibitory Potential, *Molecules,* 27, 8781.

Mamadalieva, N.Z., Ul'chenko, N., Yuldasheva, N., Egamberdieva, D., Zhanibekov, A., Dzhukharova, M.K., Glushenkova, A., (2010), Fatty-acid composition and antibacterial activity of $CHCl_3$ extracts of three plants of the genus Silene, *Chemistry of Natural Compounds,* 46, 95-96.

Mukherjee, P.K., Wahile, A., (2006), Integrated approaches towards drug development from Ayurveda and other Indian system of medicines, *Journal of Ethnopharmacology,* 103, 25-35.

Nie, H., Liu, L., Yang, H., Guo, H., Liu, X., Tan, Y., Wang, W., Quan, J., Zhu, L., (2017), A novel heptapeptide with tyrosinase inhibitory activity identified from a phage display library, *Applied Biochemistry and Biotechnology,* 181, 219-232.

Ochiai, A., Tanaka, S., Imai, Y., Yoshida, H., Kanaoka, T., Tanaka, T., Taniguchi, M., (2016), New tyrosinase inhibitory decapeptide: Molecular insights into the role of tyrosine residues, *Journal of Bioscience and Bioengineering,* 121, 607-613.

Ouzounidou, G., (1994), Root growth and pigment composition in relationship to element uptake in *Silene compacta* plants treated with copper, *Journal of Plant Nutrition,* 17, 933-943.

Padmaja, M., Sravanthi, M., Hemalatha, K.P.J., (2011), Evaluation of antioxidant activity of two Indian medicinal plants, *Journal of Phytology,* 3, 86-91

Rai, K.N., Kaushalendra, K., Singh, J., (1997), Chemical Constituent from the Pods of *Cassia glauca*, Lam, *Asian Journal of Chemistry,* 9, 558-560.

Rawat, J.M., Pandey, S., Rawat, B., Rai, N., Preeti, P., Thakur, A., Butola, J.S., Bachheti, R.K., (2023), Traditional uses, active ingredients, and biological activities of *Paris polyphylla* Smith: a comprehensive review of an important Himalayan medicinal plant, *Journal of Chemistry,* 2023, 7947224.

Rice-evans, C.A., Miller, N.J., Bolwell, P.G., Bramley, P.M., Pridham, J.B., (1995), The relative antioxidant activities of plant-derived polyphenolic flavonoids, *Free Radical Research,* 22, 375-383.

Sarikurkcu, C., Andrade, J.C., Ozer, M.S., de Lima Silva, J.M.F., Ceylan, O., de Sousa, E.O., Coutinho, H.D.M., (2020), LC-MS/MS profiles and interrelationships between the enzyme inhibition activity, total phenolic content and antioxidant potential of *Micromeria nervosa* extracts, *Food Chemistry,* 328, 126930.

Sarikurkcu, C., Kirkan, B., Ozer, M.S., Ceylan, O., Atilgan, N., Cengiz, M., Tepe, B., (2018), Chemical characterization and biological activity of *Onosma gigantea* extracts, *Industrial Crops and Products,* 115, 323-329.

Sarikurkcu, C., Sahinler, S.S., Ceylan, O., Tepe, B., (2020), *Onosma pulchra*: Phytochemical composition, antioxidant, skin-whitening and anti-diabetic activity, *Industrial Crops and Products,* 154, 112632.

Sarikurkcu, C., Sahinler, S.S., Ceylan, O., Tepe, B., (2020), *Onosma pulchra*: Phytochemical composition, antioxidant, skin-whitening and anti-diabetic activity, *Ind. Crops Prod.,* 154.

Selkoe, D.J., (2002), Deciphering the genesis and fate of amyloid β-protein yields novel therapies for Alzheimer disease, *The Journal of Clinical Investigation,* 110, 1375-1381.

Shulman, G.I., (2000), Cellular mechanisms of insulin resistance, *The Journal of Clinical Investigation,* 106, 171-176.

Slominski, A., Tobin, D.J., Shibahara, S., Wortsman, J., (2004), Melanin pigmentation in mammalian skin and its hormonal regulation, *Physiological Reviews,* 84, 1155-1228.

Sun, T., Tanumihardjo, S.A., (2007), An integrated approach to evaluate food antioxidant capacity, *Journal of Food Science,* 72, R159-R165.

Thakur, U., Shashni, S., Thakur, N., Rana, S.K., Singh, A., (2023), A review on *Paris polyphylla* Smith: A vulnerable medicinal plant species of a global significance, *Journal of Applied Research on Medicinal and Aromatic Plants,* 33, 100447.

Thapa, C.B., Paudel, M.R., Bhattarai, H.D., Pant, K.K., Devkota, H.P., Adhikari, Y.P., Pant, B., (2022), Bioactive secondary

metabolites in *Paris polyphylla* Sm. and their biological activities: A review, *Heliyon,* 8.

Thilagam, E., Parimaladevi, B., Kumarappan, C., Mandal, S.C., (2013), α-Glucosidase and α-amylase inhibitory activity of *Senna surattensis*, *Journal of Acupuncture and Meridian Studies,* 6, 24-30.

Tripathi, G., (2002), Indigenous knowledge and traditional practices of some Himalayan medicinal plants, *Himalayan Medicinal Plants Potential and Prospects, gyanodaya Prakashan, Nainital*, 151-156.

Ubeid, A.A., Do, S., Nye, C., Hantash, B.M., (2012), Potent low toxicity inhibition of human melanogenesis by novel indole-containing octapeptides, *Biochimica et Biophysica Acta (BBA)-General Subjects,* 1820, 1481-1489.

Yao, Y., Sang, W., Zhou, M., Ren, G., (2010), Antioxidant and α-glucosidase inhibitory activity of colored grains in China, *Journal of Agricultural and Food Chemistry,* 58, 770-774.

Yue, J., Li, W., Wang, Y., (2021), Superiority verification of deep learning in the identification of medicinal plants: Taking *Paris polyphylla* var. *yunnanensis* as an example, *Frontiers in Plant Science,* 12, 752863.

Zengin, G., Rodrigues, M.J., Abdallah, H.H., Custodio, L., Stefanucci, A., Aumeeruddy, M.Z., Mollica, A., Rengasamy, K.R., Mahomoodally, M.F., (2018), Combination of phenolic profiles, pharmacological properties and in silico studies to provide new insights on *Silene salsuginea* from Turkey, *Computational Biology and Chemistry,* 77, 178-186.

Zengin, G., Uren, M.C., Kocak, M.S., Gungor, H., Locatelli, M., Aktumsek, A., Sarikurkcu, C., (2017), Antioxidant and Enzyme Inhibitory Activities of Extracts from Wild Mushroom Species from Turkey, *International Journal of Medicinal Mushrooms,* 19, 327-336.

Zibareva, L., Yeriomina, V.I., Munkhjargal, N., Girault, J.P., Dinan, L., Lafont, R., (2009), The phytoecdysteroid profiles of 7 species of *Silene* (Caryophyllaceae), *Archives of Insect Biochemistry and Physiology: Published in Collaboration with the Entomological Society of America,* 72, 234-248.