OKU Fen Bilimleri Enstitüsü Dergisi
8(4): 1768-1779, 2025

OKU Journal of The Institute of Science and Technology, 8(4): 1768-1779, 2025

Osmaniye Korkut Ata Üniversitesi Fen Bilimleri Enstitüsü Dergisi

Osmaniye Korkut Ata University Journal of The Institute of Science and Technology

# *Ceratophyllum Submersum*'un Antioksidan, Antikolinesteraz ve Antiproliferatif Aktivitelerinin Değerlendirilmesi

**Nuh KORKMAZ**[1*]

[1]Department of Biology, Faculty of Engineering and Natural Sciences, Osmaniye Korkut Ata University, Osmaniye, Türkiye

[1]https://orcid.org/ 0000-0001-8299-910X
*Corresponding author: korkmazhun@gmail.com

**Araştırma Makalesi**

***Makale Tarihçesi:***
Geliş tarihi: 06.04.2025
Kabul tarihi: 28.04.2025
Online Yayınlanma:16.09.2025

***Anahtar Kelimeler:***
*Ceratophyllum submersum*
Antioksidan aktivite
Antikolinesteraz aktivite
Antiproliferatif etki
Oksidatif stres
Biyoaktif bileşikler

**ÖZ**

Bu çalışmada *Ceratophyllum submersum* L. etanol özütünün antioksidan, antikolinesteraz ve antiproliferatif aktivitelerinin değerlendirilmesi amaçlanmıştır. Antioksidan aktivite, toplam antioksidan seviyesi (TAS), toplam oksidan seviyesi (TOS) ve oksidatif stres indeksi (OSI) parametreleri ile belirlenmiştir. *C. submersum*'un TAS değeri 4.271±0,126 mmol/L, TOS değeri 10.505±0.147 µmol/L ve OSI değeri 0.246±0.004 olarak belirlenmiştir. Düşük OSI değeri bitkinin güçlü bir antioksidan savunma sistemine sahip olduğunu göstermektedir. Antikolinesteraz aktivitesi açısından, *C. submersum* özütü asetilkolinesteraz (AChE) ve bütirilkolinesteraz (BChE) enzimlerine karşı sırasıyla 139.68±2.40 µg/mL ve 171.99±1.81 µg/mL seviyelerinde inhibisyon göstermiştir. Bu değerler standart inhibitör galantamin ile karşılaştırıldığında düşük olsa da özütün potansiyel biyoaktif bileşikler içerdiğini göstermektedir. A549 akciğer kanseri hücre hattında antiproliferatif aktivite değerlendirmesi yapılmıştır. Sonuçlar *C. submersum* etanol özütünün artan konsantrasyonlarda hücre canlılığını önemli ölçüde azalttığını ve antiproliferatif etki gösterdiğini göstermiştir. Elde edilen bulgular *C. submersum*'un biyolojik olarak aktif bileşikler içerdiğini ve oksidatif stresle mücadelede etkili bir bitki türü olduğunu göstermektedir. Ancak bu bitkinin biyoyararlanımı, moleküler mekanizmaları ve terapötik potansiyelini daha iyi anlamak için daha fazla çalışmaya ihtiyaç vardır.

# Evaluation of Antioxidant, Anticholinesterase and Antiproliferative Activities of *Ceratophyllum Submersum*

**Research Article**

***Article History:***
Received: 06.04.2025
Accepted: 28.04.2025
Published online:16.09.2025

***Keywords:***
*Ceratophyllum submersum*
Antioxidant activity
Anticholinesterase activity
Antiproliferative effect
Oxidative stress
Bioactive compounds

**ABSTRACT**

This study aimed to evaluate the antioxidant, anticholinesterase and antiproliferative activities of *Ceratophyllum submersum* L. ethanol extract. Antioxidant activity was determined by the parameters of total antioxidant level (TAS), total oxidant level (TOS) and oxidative stress index (OSI). TAS value of *C. submersum* was determined as 4.271±0.126 mmol/L, TOS value as 10.505±0.147 µmol/L and OSI value as 0.246±0.004. Low OSI value indicates that the plant has a strong antioxidant defense system. In terms of anticholinesterase activity, *C. submersum* extract showed inhibition against acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) enzymes at 139.68±2.40 µg/mL and 171.99±1.81 µg/mL levels, respectively. Although these values are low compared to the standard inhibitor galantamine, they indicate that the extract contains potential bioactive compounds. Antiproliferative activity assessment was performed on A549 lung cancer cell line. The results showed that *C. submersum* ethanol extract significantly reduced cell viability at increasing concentrations and showed antiproliferative effect. The findings obtained show that *C. submersum* contains biologically active compounds and is an effective plant species in combating oxidative stress. However, further studies are needed to better understand the bioavailability, molecular mechanisms and therapeutic potential of this plant.

**To Cite**: Korkmaz N. Evaluation of Antioxidant, Anticholinesterase and Antiproliferative Activities of *Ceratophyllum submersum*. Osmaniye Korkut Ata Üniversitesi Fen Bilimleri Enstitüsü Dergisi 2025; 8(4): 1768-1779.

## 1. Introduction

Seaweed has important medicinal properties thanks to the bioactive compounds it contains. It is increasingly gaining attention in the field of health because it is rich in polysaccharides, proteins and phenolic compounds that have antioxidant, antimicrobial, anti-inflammatory and anticancer effects (Ganesan et al., 2019; Rengasamy et al., 2020; El-Beltagi et al., 2022; Matos et al., 2024; Sadeghi et al., 2024; Sevindik et al., 2025). Phenolic compounds can prevent cellular damage, especially by neutralizing free radicals (Akgul et al., 2020). These components are also widely found in medicinal plants and are known for their oxidative stress-reducing effects (Pehlivan et al., 2021; Uysal et al., 2023). Phenolic substances obtained from seaweed may have a synergistic effect when used together with herbal compounds. Therefore, algae and medicinal plants are important in health support products developed using natural compounds (Sevindik et al., 2023; El-Gammal et al., 2024).

*Ceratophyllum submersum* L. is an aquatic plant species, usually found in freshwater environments such as lakes and ponds. *C. submersum* is an aquatic plant with branched stems that are usually free-floating. Its leaves have a thin and branched structure arranged in rings of 6-12. Its fruits can be hard, wingless, and have spiny edges. Male and female flowers are usually found in different nodes. Male flowers contain many stamens, while female flowers contain a single ovary (Lowden, 1978; Wilmot-Dear, 1985). *C. submersum* is common in habitats with low light transmittance, chlorophyll, and coloured waters (Martínez-Taberner and Moya, 1993; Nagengast and Gąbka, 2017). It has low salt tolerance and is more common in nitrate-rich waters (Nagengast and Gąbka, 2017). Recent studies have further emphasized the biomedical potential of aquatic plants such as *C. submersum* L. due to their content of sulfated polysaccharides. In a pioneering study, Hoang et al. (2022) isolated and characterized fucoidan from *C. submersum* for the first time, reporting significant antioxidant, antimicrobial, anti-inflammatory, anticoagulant, and anticancer activities, particularly against MCF-7 breast cancer cells. This fucoidan showed strong radical scavenging activity and exhibited structural features similar to those of bioactive marine-derived fucoidans. In another comparative study, Jebamalar and Sumathy (2016) evaluated the antioxidant capacity of *C. submersum* and *Chaetomorpha antennina*, supporting the view that freshwater plants like *C. submersum* can serve as alternative sources of antioxidant compounds. In a similar study by Jebamalar and Sumathy (2018), polysaccharides extracted from *C. submersum* and *C. antennina* were compared in terms of yield and structural characteristics. Although the study did not assess biological activity, previous literature indicates that sulphated polysaccharides from various aquatic sources may possess pharmacological properties such as anticoagulant, antioxidant, anti-inflammatory, and antiviral effects. Therefore, the polysaccharide content of *C. submersum* makes it a promising candidate for further biomedical investigation.

Therefore, the present study aimed to investigate the antioxidant, anticholinesterase, and antiproliferative activities of *C. submersum* L. in order to evaluate its potential for future applications in pharmaceutical and functional food industries.

## 2. Material and Methods

*C. submersum* plant samples used in this study were obtained from Osmaniye, Turkey. Collected samples were dried in a laboratory environment and prepared following analysis. Within the scope of the extraction process, 10 grams of dried plant material was processed using the Soxhlet extraction method. During this process, 250 mL of ethanol was preferred as the solvent, and the extraction process was continued at 50 °C for approximately 6 hours. The obtained crude extracts were concentrated and completely freed from the solvent using a Buchi R100 Rotary Evaporator at 40 °C. Finally, the extracts were stored at 4 °C until experimental analyses were performed.

### 2.1. Antioxidant Activity Test

Rel Assay determined the total antioxidant capacity (TAS) and total oxidant level (TOS) of the ethanolic extract used in the study using commercial kits. Analyses were performed by the protocols recommended by the kit manufacturer. Trolox was used to calibrate TAS measurements, and hydrogen peroxide was used as a calibrator in TOS analyses. The TAS and TOS values were expressed in mmol/L and μmol/L units, respectively (Erel, 2004; Erel, 2005). Oxidative Stress Index (OSI) was calculated by converting TOS and TAS values to the same units and then dividing TOS by TAS, and the results were reported as percentages (Sevindik, 2019).

### 2.2. Anticholinesterase Activity Test

In this study, the anticholinesterase activity of the ethanolic extract was analysed based on the Ellman method (Ellman et al., 1961). Inhibitory effects against acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) enzymes were evaluated, and galantamine was used as a reference inhibitor for comparative analysis. Before the experiment, extracts were diluted to 200 to 3.125 μg/mL concentrations, and stock solutions were prepared. During the analysis process, 130 μL of 0.1 M phosphate buffer (pH 8.0), 10 μL of extract solution, and 20 μL of the enzyme (AChE or BChE) were added to the microplate wells, respectively, and incubated at 25 °C in the dark for 10 min. After incubation, 20 μL of DTNB [5.5'-dithiobis-(2-nitrobenzoic acid)] solution and 20 μL of substrate (acetylcholine iodide or butyrylcholine iodide) were added to the wells, respectively, to initiate the enzymatic reaction. Spectrophotometric measurements determined enzyme activity at 412 nm wavelength. The enzyme inhibition potential of the extracts was evaluated by calculating IC50 values (μg/mL), and each analysis was performed with three independent replicates.

### 2.3. Antiproliferative Activity Test

In this study, the cytotoxic effects of ethanolic extract on the A549 lung cancer cell line were investigated using the MTT (Cell Viability Test) method. Before the experiment, stock solutions were prepared at 25, 50, 100, and 200 µg/mL concentrations. After the cells were 70-80% confluent, the cells were detached from the surface with 3.0 mL of Trypsin-EDTA solution (Sigma-Aldrich, MO, USA). The detached cells were added to culture plates and incubated for 24 hours. After the incubation period, plant extracts at different concentrations were applied to the cells, and the cells were incubated for another 24 hours. After the process, the supernatant medium was removed, 1 mg/mL MTT solution was added, and the cells were incubated at 37 °C. After the purple formazan crystals formed with the MTT solution were observed, dimethyl sulfoxide (DMSO) (Sigma-Aldrich, MO, USA) was added to dissolve the precipitate. The viability of the cells was measured at a wavelength of 570 nm using an Epoch spectrophotometer (BioTek Instruments, Winooski, VT, USA) (Ünal et al., 2025).

## 3. Results and Discussion

### 3.1. Antioxidant Activity

Aquatic plants contain various bioactive components that are important in combating oxidative stress. Phenolic compounds, flavonoids, and carotenoids can reduce cellular damage by neutralizing reactive oxygen species (ROS) (El-Chaghaby et al., 2024). Oxidative stress occurs when free radical formation in cells increases due to environmental pollution, ultraviolet rays, and other stress factors (Gürgen & Sevindik, 2022; Bal et al., 2023). Antioxidant compounds can delay cellular aging and protect the health of biological systems by neutralizing these free radicals (Islek et al., 2021; Saridogan et al., 2021). In addition, using extracts from these plants in medical and pharmaceutical fields offers a promising approach to prevent oxidative stress-induced diseases (Pradhan et al., 2020). In this study, the antioxidant potentials of *C. submersum* were evaluated. The obtained data are presented in Table 1.

**Table 1.** TAS, TOS and OSI values of *Ceratophyllum submersum*

| Sample | TAS mmol/L | TOS µmol/L | OSI |
|---|---|---|---|
| *C. submersum* | 4.271±0.126 | 10.505±0.147 | 0.246±0.004 |

- Values are presented as mean±SD

In this study, total antioxidant level (TAS), total oxidant level (TOS), and oxidative stress index (OSI) values of *C. submersum* species were determined. According to the obtained data, TAS value was determined as 4.271±0.126 mmol/L in *C. submersum* sample. This result reveals the presence of natural components such as phenolic compounds, flavonoids, and ascorbic acid that show antioxidant properties in plant tissue and the capacity of these components to neutralize free radicals effectively. Indeed, various studies conducted on aquatic plants with high antioxidant capacity have reported that these species develop protective biochemical mechanisms against environmental stress conditions (Silvestre, 2020; Mishra et al., 2023). TOS value was determined as 10.505±0.147 µmol/L. This value indicates the level of potentially pro-oxidant compounds and reactive oxygen species (ROS) in the plant. High TOS values indicate oxidative processes occurring under biotic and abiotic stress conditions (Krupodorova and Sevindik, 2020). However, the OSI value determined in this study is 0.246±0.004, which is relatively low. OSI is a parameter obtained by dividing TOS by TAS and quantitatively expressing the level of oxidative stress in the system. The low OSI value shows that the antioxidant defense system of *C. submersum* effectively suppresses the existing oxidant compounds and can maintain the oxidative balance. The findings are also remarkable when compared with the values of some land-based plant species reported in the literature. For example, TAS values for *Mentha longifolia*, *Echium italicum*, *Centaurea rigida*, *Alcea kurdica*, and *Sinapis arvensis* species were reported as 6.094, 6.056, 3.522, 3.298, and 5.232 mmol/L, respectively. In the same studies, TOS values were reported as 14.050, 19.107, 15.424, 8.312, and 7.564 µmol/L, respectively; OSI values were reported as 0.231, 0.316, 0.440, 0.252, and 0.146 (Kına et al., 2021; Uysal et al., 2021; Mohammed et al., 2022; Mohammed et al., 2023; Sevindik et al., 2024). In this context, the TAS value of *C. submersum* is higher than *C. rigida* and *A. kurdica* but lower than *M. longifolia*, *E. italicum*, and *S. arvensis*. The TOS value is lower than *M. longifolia*, *E. italicum*, and *C. rigida* and higher than *A. kurdica* and *S. arvensis*. When evaluated regarding OSI value, *C. submersum* exhibits a higher oxidative stress level than *M. longifolia* and *S. arvensis* but lower than *E. italicum*, *C. rigida*, and *A. kurdica*. In conclusion, *C. submersum* can be considered an aquatic plant species that can cope with oxidative stress. Its strong antioxidant defence system has developed resistance to environmental stress conditions. These properties may constitute an important reference point in future biological activity and environmental adaptation studies.

### 3.2. Anticholinesterase Activity

Aquatic plants attract attention with their antioxidant properties and their bioactive components that exhibit anticholinesterase activity. Alkaloids, phenolic compounds, and flavonoids found in these plants can slow down the destruction of acetylcholine, which plays a role in neurotransmission, by inhibiting the activity of acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) enzymes (Olasehinde et al., 2021). While excessive activity of cholinesterase enzymes is associated with Alzheimer's and other neurodegenerative diseases, natural compounds that inhibit these enzymes are evaluated as potential therapeutic agents (Sabik et al., 2024). Extracts obtained from aquatic plants are of interest in pharmaceutical research, mainly due to their neuroprotective effects, and are among the promising natural resources for treating cognitive dysfunctions (Grina et al., 2020). In this study, the anticholinesterase activity of *C. submersum* was investigated, and the results are presented in Table 2.

**Table 2.** Anti-AChE and anti-BChE values of *Ceratophyllum submersum*

| **Sample** | **AChE µg/mL** | **BChE µg/mL** |
|---|---|---|
| *C. submersum* | 139.68±2.40 | 171.99±1.81 |
| Galantamine | 9.49±0.29 | 15.36±0.33 |

* The values were studied with 3 repetitions and the std values are given.

This study evaluated the inhibitory effects of *C. submersum* against acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) enzymes. AChE and BChE enzymes play a role in the regulation of acetylcholine levels, and excessive activity of these enzymes plays a role in the pathophysiology of various neurodegenerative diseases, especially Alzheimer's disease (Gürgen & Sevindik, 2025). Therefore, inhibitors of these enzymes are important pharmacological agents used in treating Alzheimer's disease today. In the study, the AChE inhibition value of *C. submersum* was determined as 139.68±2.40 µg/mL and the BChE inhibition value as 171.99±1.81 µg/mL. These values indicate that they are quite low compared to the activity of galantamine (AChE: 9.49±0.29 µg/mL; BChE: 15.36±0.33 µg/mL) used as the positive control. This situation shows that the enzyme inhibition activity of *C. submersum* is weak. However, it should be considered that crude plant extracts have lower bioavailability compared to purified pharmaceutical agents. Therefore, isolating specific active compounds found in plant extracts and evaluating the biological activities of pure fractions separately is important for a more accurate understanding of the inhibitory activity. Compared with similar studies, it is reported that AChE inhibition values of different extracts of *Ulva lactuca*, an aquatic macroalgae, ranged between 37.66–43.82 µg/mL, and BChE inhibition values ranged between 48.04–58.14 µg/mL (Korkmaz, 2025). These results reveal that *U. lactuca* has a more substantial inhibitory effect on cholinesterase enzymes than *C. submersum*. However, the fact that *C. submersum* showed a particular inhibitory activity, albeit at higher concentrations, suggests that the extract contains potentially active compounds.

In conclusion, it was observed in our study that *C. submersum* exhibited a specific inhibitory effect against AChE and BChE enzymes. However, this effect was limited compared to standard inhibitors such as galantamine. However, considering the plant extract's complex structure and metabolite diversity, the possibility of obtaining more potent inhibitors by examining isolated compounds should not be ignored.

### 3.3. Antiproliferative Activity

Aquatic plants are among the natural resources that attract attention in cancer research by exhibiting antiproliferative activity thanks to the bioactive compounds they contain. Phenolic compounds, flavonoids, alkaloids, and terpenoids found in these plants can prevent excessive proliferation of cancer cells and trigger apoptotic mechanisms (Martínez et al., 2022). Thanks to their antiproliferative effects, extracts obtained from aquatic plants are evaluated as potential chemopreventive agents by suppressing cell division in various types of cancer, especially breast, lung, and colon cancer. In addition, the roles of these plants in combating oxidative stress can reduce the risk of tumor formation by preventing DNA damage. Therefore, studies on the biological activities of aquatic plants provide important findings that can contribute to developing new-generation anticancer drugs (Mridha et al., 2020). In this study, the effects of *C. submersum* on A549 lung cancer cells were examined, and the results obtained are presented in Figure 1 as µg/mL.

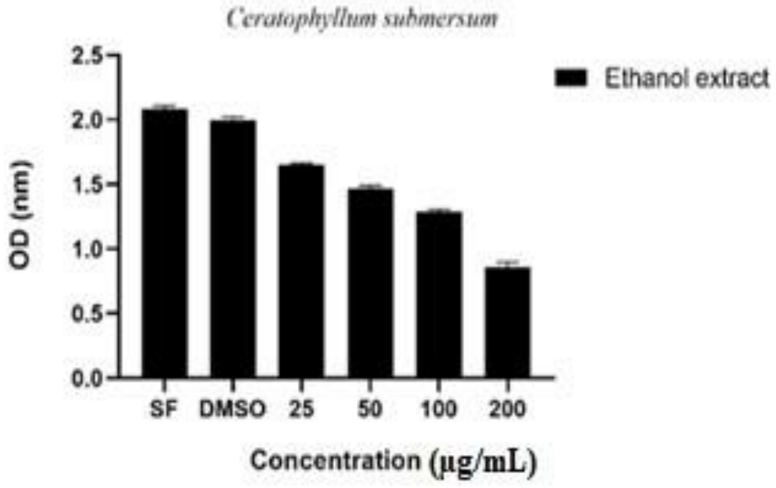


**Figure 1.** Antiproliferative activity of *Ceratophyllum submersum*

In this study, the antiproliferative activity of *C. submersum* ethanol extract was evaluated via optical density (OD) values reflecting cell viability. The results show that increasing extract concentrations caused a significant decrease in cell viability. The highest OD values were observed in the serum-free medium (SF) group, which was used as the negative control group, and in the DMSO group, which was used as the solvent control. This confirms that the cells proliferated healthily in both conditions. On the other hand, it was found that OD values decreased gradually in the ethanol extract-applied groups. This decrease reveals the antiproliferative effect of the extract. Mainly, a significant decrease in OD values was observed at concentrations of 100 and 200 µg/mL. This finding shows that *C. submersum* ethanol extract significantly inhibited cell proliferation at high doses.

Although it is not yet fully known how the bioactive compounds contained in the plant suppress cellular growth, it is thought that this effect may be due to phenolic compounds, flavonoids, or other secondary metabolites (Efenberger-Szmechtyk et al., 2021; Esmeeta et al., 2022). There are studies in the literature supporting the antiproliferative effects of *Ceratophyllum* species. For example, it has been reported that *C. demersum* exhibited antiproliferative activity against the HT-29 human colon cancer cell line (Awati et al., 2021). This suggests that the *Ceratophyllum* genus may generally have inhibitory properties against cancer cell proliferation. Similarly, it has been reported that the macroalgae *Ulva lactuca* is effective against the A549 lung cancer cell line (Korkmaz, 2025). These data indicate that aquatic plants and algae may contain potential bioactive compounds for cancer treatment. In this context, the antiproliferative activity observed in our study is thought to be due to the biologically active components of *C. submersum*. However, further research is needed to determine the molecular mechanisms of this effect. In the future, investigating the effects on cell cycle regulation, apoptotic markers, and signalling pathways may clarify this plant's potential use areas. In conclusion, the antiproliferative effect of *C. submersum* ethanol extract is consistent with similar studies in the literature, indicating that this plant may be a potential source of natural compounds that can be evaluated in cancer research. However, further in vitro and in vivo studies should confirm its efficacy and safety.

## 4. Conclusion

This study evaluated the antioxidant, anticholinesterase, and antiproliferative activities of *C. submersum* species using ethanol extract. The results revealed that this aquatic plant contains biologically active compounds that may have various pharmacological potentials. High antioxidant capacity, low oxidative stress index, and certain levels of cholinesterase enzyme inhibition indicate that the plant is remarkable regarding neuroprotective and anti-aging effects. In addition, the antiproliferative effect observed on the A549 lung cancer cell line suggests that *C. submersum* may have anticancer potential. However, the obtained data are at a basic level, and advanced studies are required to provide a more detailed understanding of the molecular mechanisms of biological activity. In future studies, the isolation and characterization of secondary metabolites such as phenolic compounds, flavonoids, and alkaloids found in this plant should be a priority. In addition, supporting in vitro findings with in vivo models, performing toxicological evaluations, and determining pharmacokinetic profiles will clarify the potential use of this species in medical or pharmaceutical fields. In conclusion, *C. submersum* is a valuable aquatic plant species that should be considered in natural product research and new-generation therapeutic agent development studies of its resistant structure to environmental stress factors and versatile biological activities.

## Conflict of Interest

The author declares that there is no conflict of interest.

## Author's Contributions

The author declares that he has contributed 100% to the article.

## References

Akgul H., Korkmaz N., Dayangaç A., Sevindik M. Antioxidant potential of endemic *Salvia absconditiflora*. Turkish Journal of Agriculture-Food Science and Technology 2020; 8(10): 2222–2224.

Awati SS., Singh SK., Wadkar KA. In vitro antioxidant potential and anticancer activity of *Ceratophyllum demersum* Linn. extracts on HT-29 human colon cancer cell line. Research Journal of Pharmacy and Technology 2021; 14(1): 28-36.

Bal C., Eraslan EC., Sevindik M. Antioxidant, antimicrobial activities, total phenolic and element contents of wild edible mushroom *Bovista nigrescens*. Prospects in Pharmaceutical Sciences 2023; 21(2): 37–41.

Efenberger-Szmechtyk M., Nowak A., Czyzowska A. Plant extracts rich in polyphenols: Antibacterial agents and natural preservatives for meat and meat products. Critical Reviews in Food Science and Nutrition 2021; 61(1): 149–178.

El-Beltagi HS., Mohamed AA., Mohamed HI., Ramadan KM., Barqawi AA., Mansour AT. Phytochemical and potential properties of seaweeds and their recent applications: A review. Marine Drugs 2022; 20(6): 342.

El-Chaghaby GA., Mohammed FS., Rashad S., Uysal I., Koçer O., Lekesiz Ö., Doğan M., Şabik AE., Sevindik M. Genus *Hypericum*: General properties, chemical contents and biological activities. Egyptian Journal of Botany 2024; 64(1): 1–26.

El-Gammal MI., Abou-Dobara MI., Ibrahim HA., Abdulhafith SA., Okbah MA. Polyphenols in selected marine algae and aromatic herbs with antimicrobial properties: A comparative study. Egyptian Journal of Aquatic Research 2024; 50(1): 71–77.

Ellman GL., Courtney KD., Andres JrV., Featherstone, RM. A new and rapid colorimetric determination of acetylcholinesterase activity. Biochemical Pharmacology 1961; 7(2): 88–95.

Erel O. A novel automated direct measurement method for total antioxidant capacity using a new generation, more stable ABTS radical cation. Clinical Biochemistry 2004; 37(4): 277–285.

Erel O. A new automated colorimetric method for measuring total oxidant status. Clinical Biochemistry 2005; 38(12): 1103–1111.

Esmeeta A., Adhikary S., Dharshnaa V., Swarnamughi P., Maqsummiya ZU., Banerjee A., Pathak S., Duttaroy AK. Plant-derived bioactive compounds in colon cancer treatment: An updated review. Biomedicine & Pharmacotherapy 2022; 153: 113384.

Ganesan AR., Tiwari U., Rajauria G. Seaweed nutraceuticals and their therapeutic role in disease prevention. Food Science and Human Wellness 2019; 8(3): 252–263.

Grina F., Ullah Z., Kaplaner E., Moujahid A., Eddoha R., Nasser B., Terzioğlu P., Yılmaz MA., Ertaş A., Öztürk M., Essamadi A. In vitro enzyme inhibitory properties, antioxidant activities, and phytochemical fingerprints of five Moroccan seaweeds. South African Journal of Botany 2020; 128: 152-160.

Gürgen A., Sevindik M. Application of artificial neural network coupling multiobjective particle swarm optimization algorithm to optimize *Pleurotus ostreatus* extraction parameters. Journal of Food Processing and Preservation 2022; 46(11): e16949.

Gürgen A., Sevindik M. Single and multi-objective optimization of the red pine mushroom *Lactarius deliciosus* (Agaricomycetes) Extraction conditions using artificial intelligence methods and biological activities of optimized extracts. International Journal of Medicinal Mushrooms 2025; 27(2): 59–73.

Hoang NN., Nguyen TK., Vo TH., Nguyen NH., Nguyen DH., Tran DL. Isolation, characterization, and biological activities of fucoidan derived from *Ceratophyllum Submersum* L. Macromolecular Research 2022; 30(2): 136-145.

Islek C., Saridogan BGO., Sevindik M., Akata I. Biological activities and heavy metal contents of some *Pholiota* species. Fresenius Environmental Bulletin 2021; 30(6): 6109–6114.

Jebamalar J., Sumathy VJH. A Comparative analysis of the antioxidant potential of *Chaetomorpha antennina* and *Ceratophyllum submersum*. International Journal of Current Research in Multidisciplinary 2016; 5(2): 06-11.

Jebamalar J., Sumathy VJH. A comparative analysis of the anticoagulant property of *Chaetomorpha Antennina* and *Ceratophyllum Submersum*. Journal of Biotechnology and Biochemistry 2018; 4(5): 06-14.

Kına E., Uysal İ., Mohammed FS., Doğan M., Sevindik M. In-vitro antioxidant and oxidant properties of *Centaurea rigida*. Turkish Journal of Agriculture-Food Science and Technology 2021; 9(10): 1905-1907.

Korkmaz N. Extract optimization of *Ulva lactuca* L. and biological activities of optimized extracts. BMC Biotechnology 2025; 25(1): 21.

Krupodorova T., Sevindik M. Antioxidant potential and some mineral contents of wild edible mushroom *Ramaria stricta*. AgroLife Scientific Journal 2020; 9(1): 186–191.

Lowden RM. Studies on the submerged genus *Ceratophyllum* L. in the neotropics. Aquatic Botany 1978; 4: 127–142.

Martínez KA., Saide A., Crespo G., Martín J., Romano G., Reyes F., Lauritano C., Ianora A. Promising antiproliferative compound from the green microalga *Dunaliella tertiolecta* against human cancer cells. Frontiers in Marine Science 2022; 9: 778108.

Martínez-Taberner A., Moya G. Submerged vascular plants and water chemistry in the coastal marsh Albufera de Mallorca (Balearic Islands). Hydrobiologia 1993; 271: 129-139.

Matos J., Cardoso C., Serralheiro ML., Bandarra NM., Afonso C. Seaweed bioactives potential as nutraceuticals and functional ingredients: A review. Journal of Food Composition and Analysis 2024; 106453.

Mishra N., Jiang C., Chen L., Paul A., Chatterjee A., Shen G. Achieving abiotic stress tolerance in plants through antioxidative defense mechanisms. Frontiers in Plant Science 2023; 14: 1110622.

Mohammed FS., Sevindik M., Uysal I. Total phenolic, flavonoid, protein contents and biological activities of wild mustard. Acta Alimentaria 2023; 52(3): 449-457.

Mohammed FS., Sevindik M., Uysal I., Sevindik E., Akgül H. A natural material for suppressing the effects of oxidative stress: biological activities of *Alcea kurdica*. Biology Bulletin 2022; 49: S59-S66.

Mridha A., Gopal PK., Paul S. Screening data reveals that *Spirogyra triplicata*, a fresh water alga induces robust anti-proliferative activity against A549 cells. Pharmacognosy Journal 2020; 12(3): 569–577.

Nagengast B., Gąbka M. Apparent niche partitioning of two congeneric submerged macrophytes in small water bodies: The case of *Ceratophyllum demersum* L. and *C. submersum* L. Aquatic Botany 2017; 137: 1–8.

Olasehinde TA., Olaniran AO., Okoh AI. Cholinesterase inhibitory activity, antioxidant properties, and phytochemical composition of *Chlorococcum* sp. extracts. Journal of Food Biochemistry 2021; 45(3): e13395.

Pehlivan M., Mohammed FS., Şabik AE., Kına E., Dogan M., Yumrutaş Ö., Sevindik M. Some Biological activities of ethanol extract of *Marrubium globosum*. Turkish Journal of Agriculture-Food Science and Technology 2021; 9(6): 1129–1132.

Pradhan B., Nayak R., Patra S., Jit BP., Ragusa A., Jena M. Bioactive metabolites from marine algae as potent pharmacophores against oxidative stress-associated human diseases: A comprehensive review. Molecules 2020; 26(1): 37.

Rengasamy KR., Mahomoodally MF., Aumeeruddy MZ., Zengin G., Xiao J., Kim DH. Bioactive compounds in seaweeds: An overview of their biological properties and safety. Food and Chemical Toxicology 2020; 135: 111013.

Sabik AE., Sevindik M., Mohammed FS., Dogan M. A new natural source against a549 lung cancer cells *anthemis cotula* and its Biological Activities and Phenolic Contents. Pharmaceutical Chemistry Journal 2024; 1–7.

Sadeghi A., Rajabiyan A., Nabizade N., Nezhad NM., Zarei-Ahmady A. Seaweed-derived phenolic compounds as diverse bioactive molecules: A review on identification, application, extraction and purification strategies. International Journal of Biological Macromolecules 2024; 266: 131147.

Saridogan BGO., Islek C., Baba H., Akata I., Sevindik M. Antioxidant antimicrobial oxidant and elements contents of *Xylaria polymorpha* and *X. hypoxylon* (Xylariaceae). Fresenius Environmental Bulletin 2021; 30(5): 5400–5404.

Sevindik M. The novel biological tests on various extracts of Cerioporus varius. Fresenius Environmental Bulletin 2019; 28(5): 3713–3717.

Sevindik M., Gürgen A., Krupodorova T., Uysal İ., Koçer O. A hybrid artificial neural network and multi-objective genetic algorithm approach to optimize extraction conditions of *Mentha longifolia* and biological activities. Scientific Reports 2024; 14(1): 31403.

Sevindik M., Mohammed FS., Uysal I. Autism: plants with neuro-psychopharmacotherapeutic potential. Prospects in Pharmaceutical Sciences 2023; 21(3): 38–48.

Sevindik M., Krupodorova T., Sevindik E., Koçer O., Uysal I., Ünal O. *Elaeagnus angustifolia* L.: A comprehensive review of its biological activities, phenolic and chemical constituents, and applications. Applied Fruit Science 2025; 67(2): 70.

Silvestre F. Signaling pathways of oxidative stress in aquatic organisms exposed to xenobiotics. Journal of Experimental Zoology Part A: Ecological and Integrative Physiology 2020; 333(6): 436–448.

Uysal İ., Mohammed FS., Şabik AE., Kına E., Sevindik M. Antioxidant and oxidant status of medicinal plant *Echium italicum* collected from different regions. Turkish Journal of Agriculture-Food Science and Technology 2021; 9(10): 1902-1904.

Uysal I., Koçer O., Mohammed FS., Lekesiz Ö., Doğan M., Şabik AE., Sevindik E., Özbas-Gerçeker F., Sevindik M. Pharmacological and nutritional properties: Genus *Salvia*. Advances in Pharmacology and Pharmacy 2023; 11(2): 140–155.

Ünal O., Gürgen A., Krupodorova T., Sevindik M., Kabaktepe Ş., Akata I. Optimization of *Phellinus hartigii* extracts: Biological activities, and phenolic content analysis. BMC Complementary Medicine and Therapies 2025; 25: 113.

Wilmot-Dear M. *Ceratophyllum* revised: a study in fruit and leaf variation. Kew Bulletin 1985; 243–271.