



***Penicillus capitatus* as a promising marine bioresource: integrated evaluation of antioxidant, antimicrobial, and enzyme inhibitory activities**

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Abstract:

Penicillus capitatus is a green macroalgae traditionally used for medicinal purposes and has attracted increasing attention due to its potential pharmacological properties. Algae are important sources of bioactive metabolites with significant roles in nutrition and drug discovery. In this study, the total phenolic content (TPC), total flavonoid content (TFC), antioxidant capacity, antibacterial activity, and enzyme inhibitory potential of methanol, ethanol, and water extracts of *P. capitatus* were evaluated. The extracts showed TPC values ranging from 16.09 ± 1.47 to 39.75 ± 0.71 $\mu\text{g GAE/mg}$ and TFC values between 10.66 ± 0.84 and 32.71 ± 0.98 $\mu\text{g QE/mg}$. All extracts exhibited antibacterial activity against Gram-positive and Gram-negative bacteria, with minimum inhibitory concentration (MIC) values of 1.562–6.25 mg/mL. The ethanol extract demonstrated the highest antioxidant activity in the ABTS•⁺ assay (IC_{50} : 39.52 ± 0.41 $\mu\text{g/mL}$) and CUPRAC assay (A0.50 : 146.02 ± 0.69), while no significant DPPH radical scavenging activity was observed (IC_{50} : >400 $\mu\text{g/mL}$). Metal chelating activity was detected in ethanol (IC_{50} : 135.41 ± 0.38 $\mu\text{g/mL}$) and methanol extracts (IC_{50} : 215.67 ± 0.36 $\mu\text{g/mL}$). Enzyme inhibition assays revealed that the water extract exhibited the strongest α -amylase (IC_{50} : 10.84 ± 0.92 mg/mL) and α -glucosidase inhibition (IC_{50} : 5.21 ± 0.04 mg/mL), whereas all extracts showed weak acetylcholinesterase inhibition.

Overall, these findings suggest that *P. capitatus* is a promising natural source of bioactive compounds with potential applications in food and pharmaceutical industries.

1. Introduction

Unsustainable industry and the increasing demand for wealth are further damaging natural ecosystems [14,15]. For this reason, the importance of marine life has increased, and marine macroalgae with high species diversity constitute indispensable organism groups that are among the basic components of marine ecosystems [13,23]. Algae constitute one of the most diverse groups of photosynthetic organisms and represent an important natural resource with increasing relevance to biotechnology, nutrition, and pharmaceutical research. In recent years, macroalgae have gained significant attention due to their ability to produce a

wide variety of bioactive metabolites beneficial to human and animal health [4,17,21]. These organisms are rich in macronutrients such as proteins, lipids, carbohydrates, and dietary fibers, as well as micronutrients including essential minerals and vitamins. In addition to their nutritional value, macroalgae synthesize numerous secondary metabolites particularly polyphenols, carotenoids, phlorotannins, enzymes, and antimicrobial compounds—that contribute to their pharmacological potential [3,17,24].

Recent studies have reported that many marine macroalgae exhibit strong antioxidant and antibacterial properties, which are primarily attributed to their phenolic content and other

oxygen-radical-scavenging components [4,18,20, 27,31]. These biological activities have positioned macroalgae as promising raw materials for developing natural health products, functional foods, and novel therapeutic agents. The increasing interest in algae-based compounds also stems from the global trend toward safer, more sustainable, and naturally sourced bioactive molecules.

P. capitatus, a green macroalga belonging to the family Udoteaceae, is an economically and ecologically important species distributed in marine

environments. Although traditionally used for various local applications, scientific data on its biochemical composition and bioactivities remain antioxidant properties DPPH•, ABTS•⁺, CUPRAC, and metal-chelating activities of methanol, ethanol, and water extracts of *P. capitatus*. Generating comprehensive biochemical and biological activity data for this species may provide insights into its potential applications in food, pharmaceutical, and natural product research.

2. Material and Methods

2.1 Collection and Extraction of Macroalgal Material

Samples of *P. capitatus* Lamarck, 1813 (Figure 2) were collected from the coastal locality of Gökliman (Finike, Antalya, Türkiye) at a depth of 15–22 m (36°53'1.14"N, 30°41'59.89"E) (Figure 1). The taxonomic identification of the collected material was performed by Dr. Emine Şükran Okudan. A voucher specimen was deposited in the Herbarium of Akdeniz University (Antalya, Türkiye) under accession number E-140. Fresh macroalgae were transferred to the laboratory in cooled, sterile containers and thoroughly washed with seawater followed by distilled water to remove epiphytes, sediments, and associated organisms. After cleaning, the samples were dried under controlled ambient conditions and subsequently pulverized using a mechanical grinder under aseptic conditions. expected to contain noteworthy levels of phenolic compounds, flavonoids, and other secondary metabolites with potential antioxidant and antibacterial effects. limited. Considering the phytochemical diversity reported in many green algae, *P. capitatus* is

In this context, the present study aimed to determine the total phenolic content, total flavonoid content, antibacterial activity, and in vitro

Figure 1. Geographic location of *P. capitatus* sampling site at Gökliman coast, Finike, Antalya, Türkiye coordinates.



Figure 2. Representative image of *P. capitatus* obtained from AlgaeBase.

For extraction, 20 g of dried and powdered *P. capitatus* biomass was separately extracted with 270 mL of methanol, ethanol, and distilled water using a Soxhlet apparatus. The extraction was carried out for 6 h under continuous reflux conditions. Following extraction, the solutions were filtered through Whatman No. 1 filter paper and concentrated under reduced pressure using a rotary evaporator according to the procedure described by [16]. The extraction yields were calculated based on the dry weight of the recovered extracts and were determined as 38.25%, 29.35%, and 24.50% for methanol, ethanol, and aqueous extracts, respectively. The concentrated extracts were subsequently homogenized using an ultrasonic bath and re-dissolved to obtain stock solutions at a final concentration of 50 mg/mL. The extracts were transferred into sterile amber vials and stored at +4 °C until further biochemical and biological activity analyses.



2.2. Total Phenolic (TPC) and Total Flavonoid Contents (TFC)

The total phenolic content (TPC) of the macroalgae extracts was determined using the Folin–Ciocalteu colorimetric method as described by [4,30], with minor modifications. Briefly, the extracts were reacted with Folin–Ciocalteu reagent and sodium carbonate solution, and the absorbance was measured spectrophotometrically at 765 nm after incubation in the dark. TPC values were quantified using a calibration curve prepared with gallic acid and expressed as µg gallic acid equivalents per mg extract (µg GAE/mg). The total flavonoid content (TFC) was measured using the aluminum nitrate colorimetric assay according to the procedure of [28]. After reaction of the extracts with aluminum nitrate and appropriate reagents, absorbance was recorded at 415 nm. TFC values were calculated from a standard curve constructed with quercetin and expressed as µg quercetin equivalents per mg extract (µg QE/mg).

2.3. Antioxidant Activity Assays (DPPH, ABTS, CUPRAC and Iron Chelating Capacity)

The radical scavenging and reducing activities of *P. capitatus* extracts were evaluated using DPPH•, ABTS•⁺, CUPRAC, and metal chelation assays. DPPH• activity was determined following the methods of [4,5,7]. Extracts at various concentrations were reacted with DPPH• solution, incubated in the dark, and absorbance was measured at 517 nm. BHT and BHA were included as reference antioxidants.

ABTS•⁺ scavenging activity was measured according to [2,29]. The ABTS•⁺ radical cation was generated using ABTS and potassium persulfate, adjusted to the desired absorbance, and reacted with the extract solutions. Absorbance was recorded at 734 nm, with BHT and BHA serving as reference standards.

The CUPRAC assay was performed based on [1]. The extracts' reducing potential was assessed by monitoring the reduction of the Cu(II)–neocuproine complex at 450 nm. The $A_{0.5}$ values were calculated from the linear absorbance–concentration relationship. Metal chelating activity was evaluated using the method of [9]. Extracts were mixed with Fe²⁺ and ferrozine, and the formation of the ferrous–ferrozine complex was monitored at 562 nm. EDTA was employed as a reference chelator.

For all antioxidant assays, the inhibition percentage was calculated as (1):

$$\text{Inhibition (\%)} = \frac{A_{\text{control}} - A_{\text{sample}}}{A_{\text{control}}} \times 100 \quad (1)$$

IC₅₀ values (or A_{0.50} for CUPRAC) were obtained from concentration response curves generated for each assay.

2.4. Antibacterial Activity Assay (Broth Microdilution Method, MIC)

The antibacterial potential of the extracts was assessed using the broth microdilution method as described by [10,19]. Mueller–Hinton Broth (MHB) served as the assay medium, while Brain Heart Infusion Broth (BHIB) was used to cultivate fresh overnight bacterial cultures. The activity was tested against the following standard strains: *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Klebsiella pneumoniae* ATCC 70603, methicillin-resistant *Staphylococcus aureus* (MRSA) ATCC 43300, *Salmonella enteritidis* ATCC 13076, *Sarcina lutea* ATCC 9341, and *Bacillus cereus* ATCC 11778, all obtained from Selçuk University's culture collection. Extract stock solutions (25 mg/mL) were prepared in DMSO and subjected to two-fold serial dilutions in sterile 96-well microplates. After the addition of bacterial inoculum and culture medium, the final extract concentrations ranged from 6.25 to 0.0061 mg/mL, and the microbial density was adjusted to 5×10^5 CFU/mL. Gentamicin (0.02–0.78 mg/mL) was used as the positive control, while DMSO-containing wells without extract served as solvent controls. Following incubation at 37 °C for 24 h, microbial growth was assessed using 2,3,5-triphenyltetrazolium chloride (TTC) as a growth indicator. Wells showing no color development after TTC addition were considered growth-inhibited. The minimum inhibitory concentration (MIC) was defined as the lowest extract concentration completely preventing visible microbial growth. DMSO were used as positive and negative controls, respectively. Plates were incubated at 37 °C, and microbial growth was visualized by adding 2,3,5-triphenyltetrazolium chloride (TTC). Wells without color change after TTC addition were considered growth-inhibited, and the minimum inhibitory concentration (MIC) was defined as the lowest extract concentration completely preventing visible microbial growth [10].

2.5. Enzyme Inhibitory Assays (α-Amylase, α-Glucosidase, and AChE)

The enzyme inhibitory activities of *P. capitatus* extracts were evaluated against α -amylase, α -glucosidase, and acetylcholinesterase (AChE) using spectrophotometric methods with minor modifications from previously reported protocols. Porcine pancreatic α -amylase, α -glucosidase from *Saccharomyces cerevisiae*, and AChE from electric eel were purchased from Sigma-Aldrich. Extracts were tested at concentrations ranging from 0.1 to 10 mg/mL, and all measurements were performed in triplicate. Appropriate sample blanks were included to correct for possible extract-related absorbance interference. The α -amylase inhibitory activity was determined according to the method described by [5,26]. The reaction mixture consisted of extract solution and α -amylase enzyme prepared in phosphate buffer (pH 6.9). After pre-incubation at 37 °C, soluble starch solution was added as the substrate. The reaction was stopped using dinitrosalicylic acid (DNS) reagent, followed by heating in a boiling water bath. Absorbance was measured at 540 nm. Acarbose was used as the reference inhibitor. The α -glucosidase inhibitory activity was measured based on the method of [22]. The enzyme solution was prepared in phosphate buffer (pH 6.8) and incubated with extract samples. The reaction was initiated by adding p-nitrophenyl- α -D-glucopyranoside (pNPG) as the substrate. After incubation at 37 °C, the reaction was terminated by adding sodium carbonate solution. Absorbance was recorded at 405 nm. Acarbose served as the positive control. AChE inhibitory activity was determined using Ellman's method [11]. The reaction mixture contained extract, AChE enzyme, and phosphate buffer (pH 8.0). After incubation, acetylthiocholine iodide was added as the substrate together with 5,5'-dithiobis-(2-nitrobenzoic acid) (DTNB). The formation of the yellow-colored product was measured at 412 nm. Galantamine was used as the standard inhibitor. Enzyme inhibition was calculated by comparing the absorbance of the sample with that of the control, after blank correction. IC_{50} values were calculated from concentration–response curves and expressed as μ g/mL.

2.6. Statistical Analysis

All antioxidant (DPPH, ABTS, CUPRAC and metal Chelating), enzyme inhibition, and antimicrobial assays were performed in triplicate, and the results are presented as mean $\pm$ standard deviation (SD). The reported replicate values represent parallel analytical measurements obtained from the same extract preparation. Statistical analyses were carried out using Microsoft Excel software. Since a single extraction was performed

for each solvent, the replicates correspond to analytical replicates rather than independent biological extractions.

3. Results and Discussions

The total phenolic content (TPC) and total flavonoid content (TFC) of *P. capitatus* extracts are presented in Figure 3. Among the tested extracts, the ethanol extract (PCE) exhibited the highest TPC (39.75 ± 0.71 μ g GAE/mg extract) and TFC (32.71 ± 0.98 μ g QE/mg extract), followed by the methanol extract (PCM), while the water extract (PCW) showed the lowest values. These findings indicate that organic solvents, particularly ethanol, are more efficient in extracting phenolic and flavonoid compounds from *P. capitatus*. Similar observations have been reported for marine macroalgae, where organic solvents provide higher extraction yields of polyphenols due to their greater solubility in moderately polar media [3,6,8,31].

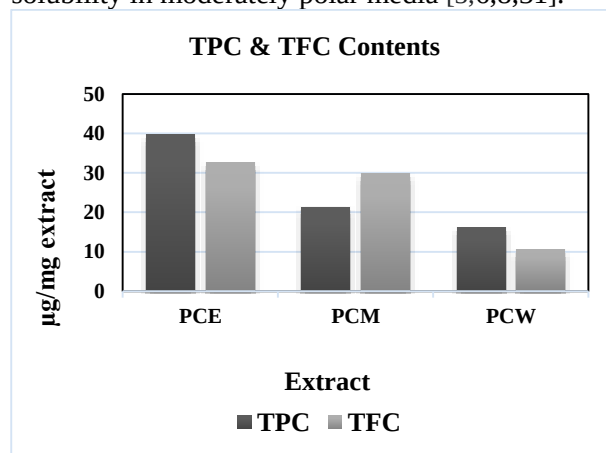


Figure 3. Total phenolic (TPC) and flavonoid (TFC) contents of *P. capitatus* extracts, expressed in μ g/mg.

The antioxidant activities of the extracts were evaluated using DPPH, ABTS, CUPRAC, and metal chelation assays (Table 1). DPPH radical scavenging activity was not detected at the tested concentration (400 μ g/mL), as all extracts exhibited IC_{50} values greater than 400 μ g/mL. In contrast, all extracts demonstrated ABTS radical scavenging activity, with inhibition values ranging from $61.90 \pm 0.29\%$ to $89.59 \pm 0.11\%$. The ethanol extract exhibited the strongest ABTS activity ($IC_{50} = 39.52 \pm 0.41$ μ g/mL), followed by the methanol extract ($IC_{50} = 112.20 \pm 0.43$ μ g/mL) and the water extract ($IC_{50} = 301.16 \pm 0.74$ μ g/mL). The ethanol extract also showed the highest CUPRAC reducing capacity ($A_{0.50} = 146.02 \pm 0.69$ μ g/mL) and metal chelating activity ($75.06 \pm 0.49\%$; $IC_{50} = 135.41 \pm 0.38$ μ g/mL). The methanol extract exhibited moderate antioxidant activity, whereas the water extract showed comparatively weaker antioxidant effects. The

higher antioxidant performance of the ethanol extract coincided with its elevated phenolic and flavonoid contents. This observation is in agreement with previous studies reporting that phenolic constituents may contribute to the antioxidant properties of marine macroalgae [6,8,31]. The antibacterial activities of the extracts are summarized in Table 2. Among the tested samples,

Table 2. Antibacterial activity results of *P. capitatus* extracts

Test Microorganism	MIC (mg/ml)			
	PCE	PCM	PCW	Gentamicin (0.1 mg/ml)
<i>Escherichia coli</i>	6.25	3.125	3.125	<0.02
<i>Pseudomonas aeruginosa</i>	NA*	1.562	NA*	<0.02
<i>Klebsiella pneumoniae</i>	6.25	NA*	NA*	0.78
<i>Staphylococcus aureus</i>	NA*	3.125	3.125	<0.02
<i>Salmonella enteritidis</i>	NA*	3.125	3.125	0.04
<i>Sarcina lutea</i>	NA*	1.562	1.562	<0.02
<i>Bacillus cereus</i>	NA*	NA*	NA*	<0.02

PCE: *P. capitatus* Ethanol Extract, PCM: *P. capitatus* Methanol Extract, PCW: *P. capitatus* Water Extract.

DMSO was used solely as a solvent for extract preparation and was included as a solvent control during antimicrobial assays

* NA: not active.

the methanol extract displayed the broadest antibacterial spectrum, with MIC values ranging from 1.562 to 3.125 mg/mL against *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella enteritidis*, and *Sarcina lutea*. The ethanol extract exhibited moderate antibacterial activity, whereas the water extract showed limited effectiveness against most tested microorganisms. The antimicrobial properties observed in the methanol extract may be associated with phenolic compounds and other secondary metabolites previously identified in *P. capitatus* by chromatographic analyses. The antimicrobial activity observed in the methanol extract may be associated with phenolic compounds and other secondary metabolites previously reported in marine macroalgae. However, the specific mechanisms responsible for the observed antibacterial effects were not investigated in the present study [31]. Similar antimicrobial activities have also been reported for other marine macroalgae extracts [6,25]. The

enzyme inhibitory activities of the extracts are presented in Table 3. All extracts inhibited α -amylase and α -glucosidase enzymes; however, the strongest activity was observed in the water extract, with IC_{50} values of 10.84 ± 0.92 μ g/mL and 5.21 ± 0.04 μ g/mL, respectively. These findings suggest that highly polar constituents extracted into water may contribute to carbohydrate-hydrolyzing enzyme inhibition. Previous studies have demonstrated that marine macroalgae contain bioactive compounds capable of modulating α -amylase and α -glucosidase activities [24]. The observed inhibitory effects indicate that *P. capitatus* may represent a source of bioactive metabolites warranting further phytochemical and biological investigation.

Table 3. Enzyme inhibition results of *P. capitatus* extracts (IC_{50} values, μ g/mL)

Extract	α -amylase (μ g/mL)	α -glucosidase (μ g/mL)	AChE (μ g/mL)
PCE	13.92 ± 0.21	6.74 ± 0.05	382.15 ± 1.72
PCM	12.47 ± 0.33	6.02 ± 0.02	361.48 ± 2.36
PCW	10.84 ± 0.92	5.21 ± 0.04	205.38 ± 2.11

PCE: *P. capitatus* Ethanol Extract, PCM: *P. capitatus* Methanol Extract, PCW: *P. capitatus* Water Extract.

In contrast, all extracts exhibited relatively weak acetylcholinesterase (AChE) inhibitory activity, with IC_{50} values ranging from 205.38 ± 2.11 to 382.15 ± 1.72 μ g/mL. Although the water extract showed the strongest AChE inhibition among the tested samples, its activity remained considerably lower than that of standard inhibitors reported in the literature. These findings indicate limited AChE inhibitory activity under the tested experimental conditions and suggest that further studies are required before drawing conclusions regarding possible neuroprotective applications. The differences observed among the extracts indicate the influence of solvent polarity on the extraction of bioactive compounds and their associated biological activities. Ethanol extraction favored the recovery of antioxidant compounds, methanol extraction yielded extracts with stronger antibacterial properties, and water extraction produced the most effective enzyme inhibitory activity. Such variations indicate that different classes of secondary metabolites are selectively extracted depending on solvent polarity. Overall, the present study demonstrates that *P. capitatus* possesses considerable biological potential as a marine source of bioactive compounds. The ethanol and methanol extracts were rich in phenolic and flavonoid constituents and exhibited notable antioxidant and antibacterial activities, whereas the water extract showed the strongest enzyme

inhibitory effects. These findings highlight the potential application of *P. capitatus* extracts in pharmaceutical and nutraceutical formulations. Further studies focusing on the isolation and

characterization of active constituents, elucidation of their mechanisms of action, and evaluation through in vivo models are required to fully establish their therapeutic potential.

Table 4. Antioxidant activity results of *P. capitatus* extracts

		Antioxidant Activity							
		DPPH [•]		ABTS ^{•+}		CUPRAC		Metal Chelating	
		Inhibition (%) ^a	IC ₅₀ (µg/mL) ^b	Inhibition (%) ^a	IC ₅₀ (µg/mL) ^b	Absorbance ^c	A _{0.50} (µg/mL) ^d	Inhibition (%) ^a	IC ₅₀ (µg/mL) ^b
Extracts	PCE	-	>400	89,59±0,11	39,52±0,41	1,06±0,01	146,02±0,69	75,06±0,49	135,41±0,38
	PCM	-	>400	87,42±0,15	112,2±0,43	0,38±0,04	602,83±0,06	58,60±1,10	215,67±0,36
	PCW	-	>400	61,90±0,29	301,16±0,74	-	>400	-	>400
Standards	BHT	86,64±0,19	23,90±0,14	85,62±0,32	12,75±0,63	2,98±0,03	28,21±0,01		
	BHA	88,18±0,10	22,80±0,59	87,54±0,74	12,05±0,97	3,22±0,01	26,54±0,02		
	EDTA							90,21±0,24	4,29±0,06

PCE: *P. capitatus* Ethanol Extract, PCM: *P. capitatus* Methanol Extract, PCW: *P. capitatus* Water Extract.

All values are expressed as mean ± SD of three parallel analytical measurements performed on the same extract preparation.

^a: Inhibition % of 400 µg/mL concentration of the extracts.

^b: IC₅₀ values are given as a mean ±SD of three parallel measurements.

^c: Absorbance of 400 µg/mL concentration of the extracts.

^d: A_{0.50} values are given as a mean ±SD of three parallel measurements.

4. Conclusions

This study demonstrated that the biological activities of *P. capitatus* extracts vary according to the extraction solvent. The ethanol extract exhibited the highest total phenolic and flavonoid contents and showed the strongest antioxidant activity, whereas the methanol extract displayed the broadest antibacterial spectrum. The water extract exhibited the most pronounced α-amylase and α-glucosidase inhibitory activities among the tested samples.

The observed differences among the extracts highlight the influence of solvent polarity on the recovery of bioactive constituents and their associated biological properties. Overall, the results indicate that *P. capitatus* contains compounds with measurable antioxidant, antibacterial, and enzyme inhibitory activities under in vitro conditions. However, the present findings should be considered preliminary, and further studies involving bioassay-guided fractionation, identification of active compounds, toxicity assessment, mechanism-of-action studies, and in vivo validation are necessary to confirm their biological relevance and potential applications.

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