Biotechnological Potential of *Sargassum ilicifolium* Seaweed: A Proximate Composition of Antibacterial, Antioxidant, and Hypoglycemic Bioactive Compounds

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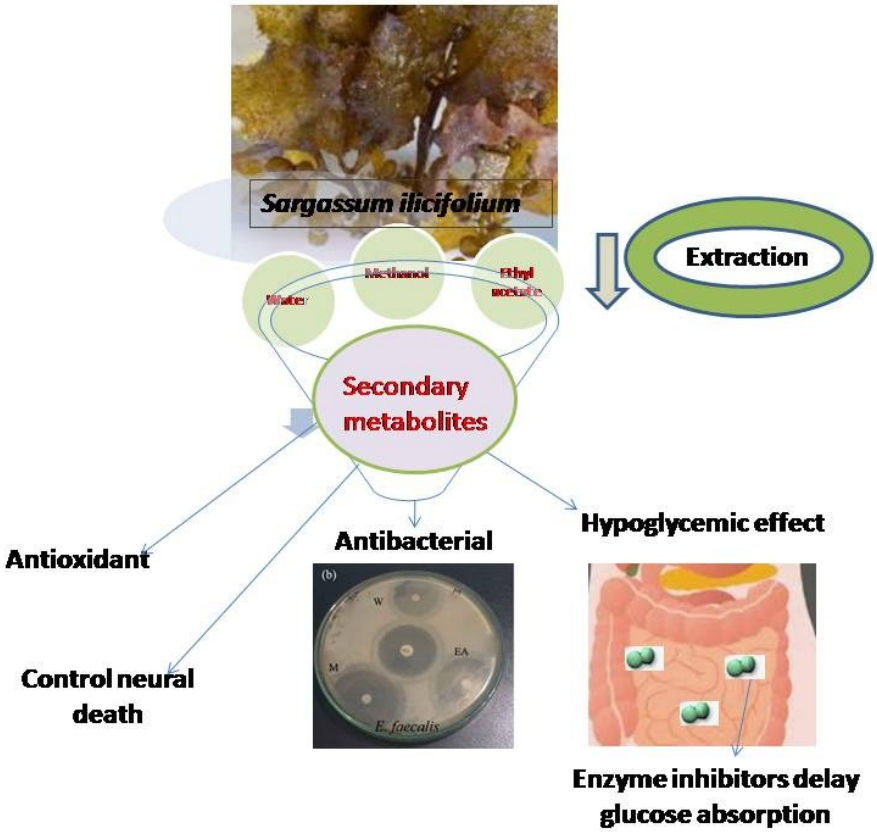
GRAPHICAL ABSTRACT



Biotechnological Potential of *Sargassum ilicifolium* Seaweed: A Proximate Composition of Antibacterial, Antioxidant, and Hypoglycemic Bioactive Compounds

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Seaweed has gained significant attention due to its extensive use in nutraceuticals and pharmaceuticals. Therefore, this study was conducted to perform proximate analysis, screen and quantify phytochemicals, and analyze the pharmacological potential of *Sargassum ilicifolium* (S. *ilicifolium*) extract *via* antimicrobial, hypoglycemic, and antioxidant activities. The results of the proximate composition revealed 38.2±1.1% ash, 9.3±0.9% moisture, 23.4±1.1% protein, and 3.1±0.2% fat. The methanol extract increased the levels of alkaloids (26.3±0.9 g PE/g), phenols (145±3.1 mg GAE/g), and flavonoids (97.5±3.1 mg QE/g). The methanol extract exhibited strong activity, with a zone of inhibition of 27±2 mm against *E. faecalis* and a 22±0 mm zone of inhibition against *S. aureus*. The phytochemicals in the methanolic extract had a greater total antioxidant capacity (58.2±0.8%) than did the ethyl acetate extract (49.4±0.4%) and the water extract (44.6±0.3%) at 2.5 mg/mL The *S. ilicifolium* extract also exhibited α-glucosidase and α-amylase inhibitory activities. The seaweed inhibited tyrosinase activity in the ethyl acetate extract but not in the methanol or water extracts. The seaweed *S. ilicifolium* exhibited bioactivity and biotechnological potential, as evidenced by its antimicrobial, antioxidant, and hypoglycemic properties.

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Keywords: Seaweeds; Solvent extract; Antibacterial; Antioxidant; Antifungal; Enzyme inhibitors; Blood glucose; Hypoglycemic

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INTRODUCTION

Marine seaweed is considered the major source of several bioactive secondary metabolites because of its unique bioactive properties and diversity. A diverse array of bioactive compounds, such as fucosterol, phlorotannins, polysaccharides, fucoxanthin (Hakim and Patel 2020), and bromophenols (Jacobtorweihen and Spiegler 2023), are present in seaweed, which constitutes one of the major types of biomasses in marine ecosystems. Seaweed generates several bioactive compounds in response to the surrounding environment that exhibit antimicrofouling, antifungal, antimicrobial, and other bioactive properties (El-Sheekh *et al*. 2014; Araújo *et al*. 2021; Lomartire *et al*. 2021). They are generally consumed as food in various countries, especially in Asian countries. Several products are derived from marine algae, including algin, agar, and carrageenan (Güven *et al*. 2020). Seaweeds are prevalent in shallow coastal water, rocky areas, especially those exposed during low tide. Coastal people throughout the world

harvest and consume these seaweeds (Akhoundian and Safaei 2022). Diverse aquatic organisms utilize seaweed-rich environments as habitats, sources of shelter, and vegetation. They are broadly classified as green seaweed (*e.g.*, phylum Chlorophyta), brown seaweed (phylum Rhodophyta), or red seaweed (phylum Ochrophyta) based on their anatomy, type of pigments, and morphological and reproductive characteristics (Achmad *et al*. 2020).

Seaweed exhibits antioxidant properties. These antioxidant chemicals are useful for preventing the development of diseases such as cancer, inflammation, Alzheimer's disease, and aging. Factors such as chemical contamination, shortwave radiation, herbicides, and smoking can induce the development of free radicals that can destroy biochemicals, such as lipids, DNA, and proteins. The cumulative damage to proteins, lipids, and DNA is linked to the development of chronic diseases, including cardiovascular diseases, neurodegenerative disorders, cancer, and rheumatism. These disorders are mediated by the generation of "oxidative stress", and antioxidant molecules suppress the generation of free radicals or affect the generation of free radical chains by scavenging species. Hence, antioxidant molecules are critical in aging and cancer (Youssif *et al*. 2019). Among macroalgae, brown algae are among the major reservoirs of antioxidants due to their vast biodiversity and the presence of various secondary antioxidant metabolites. Brown seaweed contains antioxidant compounds such as proteins, pigments (*e.g.,* carotenoids), vitamins (*e.g.*, vitamins E and C), alkaloids, sulfated polysaccharides, glutathione, amines, amino acids, and phenolic compounds (El-Sheekh *et al*. 2020; El-Shafay *et al*. 2021; Fonseca-Barahona *et al*. 2025; Afrin *et al*. 2025). Seaweeds contain several bioactive secondary metabolites with antibacterial activities due to the presence of phenolic compounds, carotenoids, polysaccharides, phycobiliprotein pigments, and unsaturated fatty acids (Čmiková *et al*. 2022).

The prevalence of diabetes has increased in recent years, and the global diabetes incidence in 2021 was approximately 536.6 million people; approximately 10.5% of the population between the ages of 20 and 79 years; and it is expected to increase to 783.2 million in 2045 (Sun *et al*. 2022). Suppressing the postprandial blood glucose level is a promising method for the management and prevention of diabetes. Such suppression can be effectively achieved by inhibiting the activity of various carbohydrate enzymes, including α-glucosidase and α-amylase, in the gastrointestinal tract (Santos *et al*. 2022). The effective inhibition of these carbohydrate-digesting enzymes results in a delay in the digestion of polysaccharides to minimize the absorption level of glucose. Substances such as miglitol, acarbose, and voglibose are widely used to treat diabetes, and these compounds are considered α-amylase and α-glucosidase inhibitors. Moreover, these substances exhibit side effects such as flatulence and diarrhea (Martin and Montgomery 1996; Li *et al.* 2022). Owing to the severe side effects of synthetic enzyme inhibitors, natural α-glucosidase and α-amylase inhibitors from food sources have attracted attention because of their feasibility and safety. The daily uptake of these seaweeds could prevent and improve diabetes (Li *et al*. 2022).

Seaweed extracts are a reservoir of several phytochemical compounds. Metabolomic analysis has revealed inhibitory effects of seaweeds on α-glucosidase and α-amylase (Landa-Cansigno *et al*. 2020). In addition, seaweed phytochemicals have been shown to contribute to a reduction of weight gain by decreasing pro-inflammatory cytokine expression and the up-regulation of anti-inflammatory cytokine genes. Their health benefits have been seen in hepatic lipid profile and serum and determination of antioxidant enzymes, revealing the protective role of seaweeds against free radicals mediated

hyperglycemia and hyperlipidemia (Agarwal *et al*. 2023). Moreover, the in-depth analysis of the functional properties of brown algae needs to be explored further for their bioactive potential and wide application in pharmaceutical, nutraceutical, and food industries. The present study aimed to analyze the nutrient composition and the antioxidant, antibacterial, and antidiabetic potential of brown algae collected from the intertidal region of the sea.

EXPERIMENTAL

Macroalgae

The macroalga (seaweed) *Sargassum ilicifolium* was collected in May 2024 from the coast of Alkhobar city, Arabian Gulf, Saudi Arabia. The collected seaweed was rinsed with tap water, and the adhering sand particles were removed. The samples were air-dried between 30 °C and 35 °C. The samples were powdered in an electric grinder and stored at room temperature in airtight containers.

Soxhlet Extraction

The Soxhlet apparatus comprised a condenser, an extraction flask, and a Soxhlet chamber. A total of 50 g of powdered macroalgae was placed in a Soxhlet extraction flask and poured into 450 mL of solvent (methanol, ethyl acetate, or water) in the extraction flask. The extraction process was performed continuously, and the duration was fixed based on the time required for the descending solvent to become colorless. The final extract was placed in a rotary evaporator, and the yield was calculated *via* the following Eq. 1:

$$\text{Yield (\%)} = \frac{\text{Mass of dried extract (g)}}{\text{Mass of dried matrix (g)}} \times 100 \quad (1)$$

Proximate Nutrient Analysis

The amount of crude protein, moisture, crude fat, crude fiber, and ash content of *S. ilicifolium* powder was analyzed (Ahmad *et al*. 2019).

Determination of Total Phenolic Content

The total phenolic content (TPC) of the ethyl acetate extract of seaweed was determined *via* the Folin–Ciocalteu method (Odabasoglu *et al*. 2004). Gallic acid was used as the standard and was prepared at five different concentrations ranging from 0.2 to 2 mg/mL. The standard gallic acid solution was prepared in methanol and diluted appropriately before use. To the sample or standard (0.1 mL), 0.5 mL of water was added and mixed. Then, 0.1 mL of Folin–Ciocalteu reagent was added, and the mixture was incubated for 10 min at 28±1 °C. To the reaction mixture, 1 mL of 10% sodium carbonate was added, and the mixture was incubated at 28±1 °C for 30 min. The absorbance of the sample was read at 760 nm against a reagent blank using a UV–visible spectrophotometer (Thermo Scientific, USA). The total phenolic content was measured by calculating the amount of gallic acid equivalents (mg GAE/g) in the sample (Zohra *et al*. 2019).

Determination of Total Flavonoid Content

The total flavonoid content of each sample was determined following the aluminum chloride method. Briefly, 0.1 mL of extract or 0.1 mL of standard sample was mixed with 0.5 mL of double-distilled water and 0.1 mL of 5% sodium nitrate solution. The mixture

was left undisturbed for 10 min, after which 0.2 mL of 10% aluminum chloride solution was added and mixed. The mixture was further incubated for 6 min, and 0.2 mL of a 1 M sodium hydroxide solution was added. The absorbance of each sample was read at 510 nm against a reagent blank *via* a UV–Visible spectrophotometer (Thermo Scientific, USA). The total flavonoid content in the extract was determined as mg QE/g of quercetin equivalents (Zohra *et al*. 2019).

Alkaloid Content

The alkaloid content of the solvent extract was determined as described previously by Sreevidya and Mehrotra (2003), with slight modifications. Briefly, 0.1 mL of solvent extract was prepared in 95% ethanol. The pH of the mixture was adjusted to approximately 2.0 to 2.5. Then, 0.1 mL of the sample was mixed with 0.2 mL of Dragendorff's reagent and centrifuged at 4000 rpm for 10 min. The precipitate formed was collected and repeatedly washed with ethanol (95%). Then, 0.2 mL of 1% disodium sulfide was added, and the black precipitate was separated by centrifugation (4000 rpm for 10 min). The final pellet was suspended in concentrated HNO_3 and brought to 2 mL with double-distilled water. Then, 200 µL of the reaction mixture was pipetted and mixed with 1 mL of 3% thiourea, and the absorbance of the sample was read at 460 nm. The results are expressed as mg of equivalent piperine released per g of dry extract.

Phytochemical Screening

Five drops of hydrochloric acid were added to the solvent extracts. The development of red color indicates the presence of flavonoids. The alkaloid content of the extract was determined *via* Dragendorff's reagent method (Widowati *et al*. 2021). The saponin content of each sample was determined as described previously by Harborne (1998). The presence of phenol hydroquinone was detected by adding 2 drops of 5% $FeCl_3$ to the extract after adding 2 mL of 70% ethanol. The development of blue or green color indicated the presence of hydroquinone (Harborne 1998).

Antibacterial Activity Test

Bacterial strains such as *Klebsiella pneumoniae* (ATCC13883), *Enterococcus faecalis* (ATCC29212), *Pseudomonas aeruginosa* (ATCC27853), *Staphylococcus aureus* (ATCC25923), *Staphylococcus epidermis* (ATCC12228), and *Salmonella typhimurium* (ATCC14028) were used to test the antimicrobial activity of the seaweed extracts. The strains were maintained in broth culture media comprising 0.5% (w/v) yeast extract, 1% (w/v) sodium chloride, and 1% (w/v) peptone (pH 7.2). The antimicrobial activity of the solvent extracts of seaweed was tested following the disc diffusion method. Mueller Hinton agar medium (Himedia, India) was prepared and poured into a Petri dish. Solvent extracts (methanol, ethyl acetate, and water) were prepared at a concentration of 10 mg/mL and loaded onto 6 mm diameter filter paper discs. The mixture was placed on the surface of Mueller–Hinton agar media. Chloramphenicol (10 µg) was used as a positive control. The plates were incubated for 24 h, and the zone of inhibition (mm) was measured (Wu *et al*. 2020; Baazeem *et al.* 2021).

Analysis of Glucose Diffusion-Inhibitory Activity

A glucose diffusion inhibition assay was performed by using a dialysis bag as described previously (Mahalingam 2017), with slight modifications. The dialysis membrane (Himedia, India) was activated, and 5 mL of the extract (1 mg/mL) was loaded

onto an activated dialysis membrane with 5 mL of 300 µg/mL glucose solution. The sample was dialyzed against 0.15 M sodium chloride using a magnetic stirrer. The glucose concentration in each sample was determined *via* an enzymatic method. Distilled water was used as the control, and acarbose was used as the standard.

Antioxidant Activity

The total antioxidant activity of the extract was determined by the phosphor-molybdenum method, as described by Prieto *et al*. (1999). The DPPH (1,1-diphenyl-2-picrylhydrazyl) radical scavenging activity of the sample was detected *via* the method of Mensor *et al*. (2001). 2,2-Azino-bis-3-ethylbenzthiazoline-6-sulfonic acid (ABTS) scavenging activity of the extract was determined as described previously by Re *et al*. (1999), with slight modifications. The nitric oxide radical scavenging activity of the extract was tested with Griess reagent (Gulcin 2006). The ferrous ion chelating activity of the extract was evaluated as described by Decker and Welch (1990), with slight modifications. The extract was prepared at five different concentrations for antioxidant assays (0.5 to 2.5 mg/mL). Ascorbic acid (Sigma–Aldrich, MO, USA) was used as a standard for the antioxidant activity assay (Al-Ansari *et al*. 2021).

Analysis of *α*-Glucosidase Inhibition Activity

The influence of the solvent extract (0.5 to 3.0 mg/mL) on α-glucosidase activity was assayed as described previously by Hbika *et al*. (2022), with slight modifications. The reaction mixture was composed of 0.1 mL of sucrose solution (0.05 M), 1 mL of phosphate buffer (0.05 M, pH 7.5), and 0.1 mL of α-glucosidase prepared in buffer (20 IU). To the negative control, double-distilled water was added, and acarbose (control) was added. The mixture was incubated at 37 °C for 10 min, and the amount of released glucose was determined.

Analysis of *α*-Amylase Inhibition Activity

The *α*-amylase inhibition activity of the crude solvent extract was analyzed as described previously by Daoudi *et al*. (2022), with slight modifications. Briefly, 0.1 mL of extract (0.5 to 3.0 mg/mL) or acarbose (positive control, 0.5 mg/mL to 3 mg/mL), 0.3 mL of phosphate buffer (pH 7.0), and 0.1 mL of *α*-amylase (100 IU/mL) were mixed. The mixture was incubated for 15 min at 37 °C. Then, 0.1 mL of soluble starch solution was added, and the mixture was incubated for 30 min at 37 °C. Then, DNS reagent (1 mL) was added, and the mixture was placed in a boiling water bath for 10 min. The mixture was cooled, and 5 mL of double-distilled water was added to all test tubes. To the negative control, an enzyme mixture was added after the addition of the DNS reagent. The absorbance of each sample was read at 540 nm against a reagent blank, and the percentage inhibition was calculated using Eq. 2:

$$\text{Inhibition activity (\%)} = \frac{(ODc\ 540\ \text{nm} - ODc\ \text{blank}\ 540\ \text{nm}) - (ODs\ 540\ \text{nm} - ODs\ \text{blank}\ 540\ \text{nm})}{ODc\ 540\ \text{nm} - ODc\ \text{blank}\ 540\ \text{nm}} \times 100 \quad (2)$$

Acetylcholinesterase Inhibition Activity of the Algal Extracts

The acetylcholinesterase (AChE) inhibition activity of the algal extract (0.5 to 3.0 mg/mL) was detected. The amount of thiocholine released during acetylthiocholine hydrolysis under the influence of AChE was analyzed. For the control, the sample was not added; galantamine was used as the standard, and the percentage inhibition was analyzed.

Tyrosinase Inhibition Properties of the Seaweed Extract

The tyrosinase inhibition activity of the seaweed extract was determined as described previously by Masuda *et al*. (2005). The seaweed extract was substituted at various concentrations (0.5 to 3.0 mg/mL), and L-DOPA was added. L-DOPA and buffer were added to the control. Kojic acid was used as a positive control, and the percentage of enzyme inhibition was determined.

RESULTS AND DISCUSSION

Proximate Composition of the *Sargassum ilicifolium* Seaweed

The proximate composition of the seaweed is described in Fig. 1. The ash content of the seaweed *S. ilicifolium* was 38.2±1.1%, which is higher than the ash content of *B. bifurcata* seaweed that ranges from 30.15% to 34.31% dry weight (DW) (Gómez-Ordóñez *et al*. 2010; Alves *et al*. 2016). Additionally, the ash content of *F. vesiculosus* (21% to 19% DW) (Peinado *et al*. 2014) was lower than that in the present study. Increased ash content is an important characteristic of seaweed, and seaweeds are generally richer in minerals compared to vegetables (Shek Mohamed Ibrahim *et al*. 2025). High ash contents are associated with high mineral contents in a sample. The moisture content of *S. ilicifolium* was 9.3±0.9% DW, which was similar to the results reported earlier for dried *Gracilaria gracilis* (8.0 g/100 g dry weight) and for dried *Osmundea pinnatifida* (11.8 g/100 g dry weight) (Rodrigues *et al*. 2015). The present findings are in very close agreement with previous reports by Gómez-Ordoñez *et al*. (2010) on edible seaweeds collected from the northwestern Spanish coast. *Sargassum ilicifolium* seaweed presented 23.4±1.1% total protein in the dried powder.

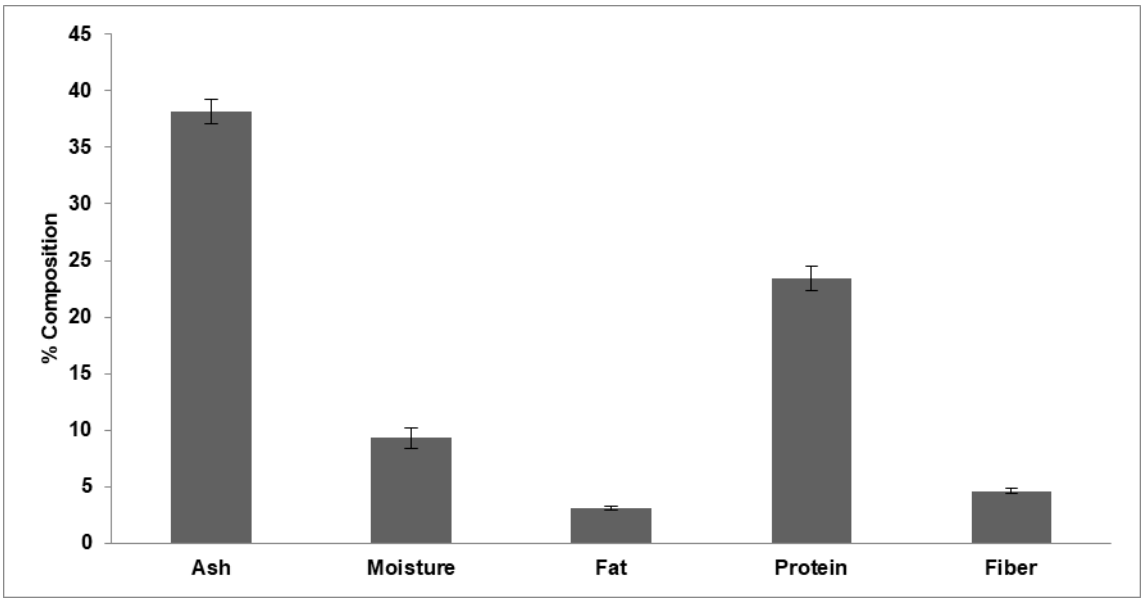


Fig. 1. Proximate analysis of the seaweed *Sargassum ilicifolium*

The values obtained in this study were similar to those reported for red seaweed (20.2 to 23.8 g/100 DW) and higher than those reported for brown seaweed (14.4 to 16.9 g/100 DW) and green seaweed (18.8 g/100 DW) (Rodrigues *et al*. 2015). However, the

total protein content detected in this study was lower than that reported by Fleurence (1999) in *Palmaria palmata* (35 g/100 DW) and *Porphyra tenera* (47 g/100 DW). In this study, the fat content was analyzed, and it was determined to be 3.1±0.2%, which agrees with previous reports. Seaweeds have very low-fat content, and most seaweeds have <4% fat content; however, fat content varies based on environmental and climatic conditions (Herbreteau *et al*. 1997; Manivannan *et al*. 2008). A low-fat content is preferable for the preparation of seaweed-based nutrients. The fat content of the seaweed *B. bifurcata* ranges from 5.67% DW to 5.81% DW (Gómez-Ordoñez *et al*. 2010; Alves *et al*. 2016).

Phytochemical Composition of *Sargassum ilicifolium*

Soxhlet extraction showed 9.43±0.26% yield of phytochemical compounds from the seaweeds. The results revealed that the water extract of *Sargassum ilicifolium* contained fewer bioactive secondary metabolites. However, the flavonoid content of the water extract was comparable to that of the methanol and ethyl acetate extracts. The methanol extract had a greater yield of phytochemicals than did the ethyl acetate in terms of color intensity. The methanol extract contained alkaloids, steroids, flavonoids, and phenols, and these phytochemicals were detected in ethyl acetate, but the color intensity was lower. The ethyl acetate and alcohol fractions of the seaweed contained flavonoids, tannins, steroids, phenols, and alkaloids as summarized in Table 1. The phytochemical content in the extract varied based on the solvent used for extraction and the particle size of the biomass. The smaller particle size expressed richer phytochemical compounds than the larger particle size algal samples (Prasedya *et al*. 2021)

Table 1. Phytochemical Content of the Solvent Extract of *Sargassum ilicifolium*

Test	Ethyl Acetate	Methanol	Water
Alkaloids	++	+	+
Steroids	++	+++	+
Saponins	-	-	-
Triterpenoids	-	-	-
Flavonoids	++	++	++
Tannins	+	-	+
Phenols	++	+++	+

- =Negative;+=Weak positive; ++=Strong positive; and +++=Very strong positive

Alkaloids, Flavonoids, and Phenols in Seaweed Extracts

The amounts of total alkaloids, flavonoids, and phenols in the seaweed extract were determined, and the results are presented in Table 2. The alkaloid content was 26.3±0.9 g PE/g, and the maximum amount was detected in the methanol extract (71.4±0.8 g PE/g). The methanol extract presented the maximum phenol content (145±3.1 mg GAE/g), followed by the water extract (130.2±3.3 mg GAE/g), and the ethyl acetate extract (109±4.2 mg GAE/g). The flavonoid content of the solvent extract ranged from 75.2±1.1 to 97.5±3.1 mg QE/g. Among the extracted solvents, the methanol extract presented the highest total phenolic content, with values of 97.5±3.1 mg QE/g. The phenolic compounds and alkaloids were extracted from the seaweeds such as *Sargassum vulgare*, *Sargassum muticum*, *Cystoseira humilis*, *Cystoseira tamariscifolia*, *Bifurcaria bifurcata*, and *Laminaria ochroleuca*. This phytochemical-rich seaweed extract has been found to exhibit antibacterial and antifungal activities (Tarhzouti *et al*. 2024).

Table 2. Alkaloids, Flavonoids, and Phenols of Solvent Extracts of *Sargassum Ilicifolium*

Solvent	Alkaloid (g PE/g)	Phenols (mg GAE/g)	Flavonoids (mg QE/g)
Methanol	71.4±0.8	145±3.1	97.5±3.1
Ethyl acetate	59.5±1.2	109±4.2	76.5±1.2
Water	26.3±0.9	130.2±3.3	75.2±1.1

PE: Piperine equivalent per gram of dry weight; GAE: Gallic acid equivalent per gram of dry weight; QE: Quercetin equivalent per gram of dry weight

Antibacterial Activity

The methanol extract of *S. ilicifolium* had weak effects on *K. pneumoniae*, *P. aeruginosa*, and *S. epidermis*, with zones of inhibition of 14±1 mm, 15±0 mm, and 13±0 mm, respectively. The ethyl acetate fractions had weak effects on *S. epidermis*, *K. pneumoniae*, and *P. aeruginosa*, with zones of inhibition of 10±1 mm, 13±1 mm, and 14±1 mm, respectively (Fig. 2). The water extract exhibited weak activity against *S. epidermis* and *K. pneumoniae*. The zones of inhibition were 9±0 mm and 12±0 mm. The water extract exhibited moderate activity toward *S. aureus* (18±0 mm zone of inhibition) (Table 3).

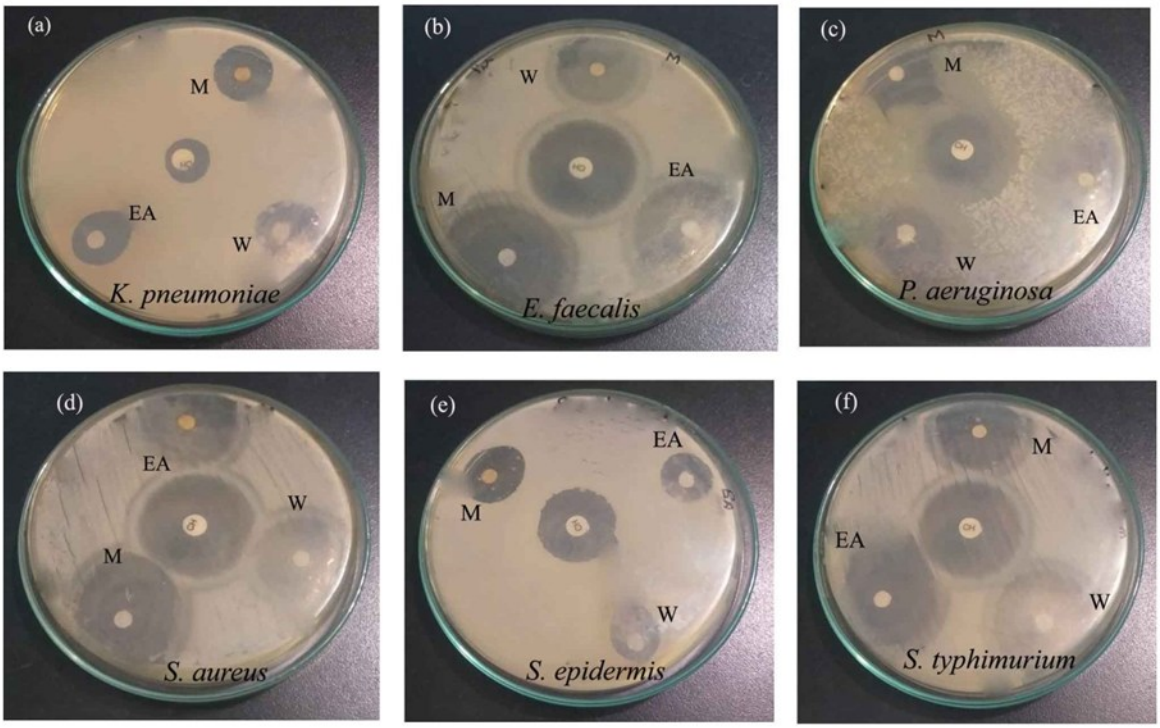


Fig. 2. Effect of seaweed extract on bacterial pathogens. The solvent extract was loaded on a sterile disc (6 mm) and dried. The mixture was placed on Mueller–Hinton agar plates and incubated for 24 h, after which the zone of inhibition was assayed. M: methanol extract; EA: ethyl acetate extract; W: water extract. (a): *Klebsiella pneumoniae*; (b): *Enterococcus faecalis*; (c): *Pseudomonas aeruginosa*; (d): *Staphylococcus aureus*; (e): *Staphylococcus epidermis*; (f): *Salmonella typhimurium*

Table 3. Antibacterial Activity of *Sargassum ilicifolium* Solvent Extracts against Pathogenic Bacteria

Bacteria	Zone of Inhibition (mm)			
	Methanol	Ethyl acetate	Water	Chloramphenicol (10 µg)
Gram-positive				
S. aureus	22±0	20±1	18±0	20±1
S. epidermis	14±0	10±1	9±0	18±1
Gram-negative				
S. typhimurium	21±1	19±0	20±1	20±1
P. aeruginosa	14±0	13±1	15±1	18±1
E. faecalis	27±2	22±1	17±1	20±1
K. pneumoniae	14±1	13±1	12±0	9±1

The methanol extract exhibited strong activity, with a zone of inhibition of 27±2 mm against *E. faecalis* and a 22±0 mm zone of inhibition against *S. aureus*. The water extract had very strong activity against *S. typhimurium*; the zone of inhibition was 20±1 mm, and it had moderate activity against *E. faecalis* and *S. aureus*. The methanol extract and ethyl acetate extract had strong antibacterial activity against *S. aureus*. Seaweed extracts have antibacterial activity against gram-positive bacteria, including *S. aureus* (Emu *et al*. 2023). *G. lemaneiformis* seaweed extract has very strong activity against *E. coli* and *S. aureus* (Stirk *et al*. 2007). *Sargassum ilicifolium* is an important brown seaweed that contains several antimicrobial compounds, including antibacterial proteins (Mousaie *et al*. 2022) and fucoidan (Tsou *et al*. 2022). The acetone and chloroform extracts of seaweed, *Sargassum muticum*, have antibacterial activity toward *Micrococcus* sp., *Shigella flexneri*, and *Salmonella paratyphi* (Moorthi and Balasubramanian 2015). The water extract of *Sargassum ilicifolium* had inhibitory activity against bacterial pathogens, including *E. coli*, *P. aeruginosa*, and *S. aureus* (Tanniou *et al*. 2014).

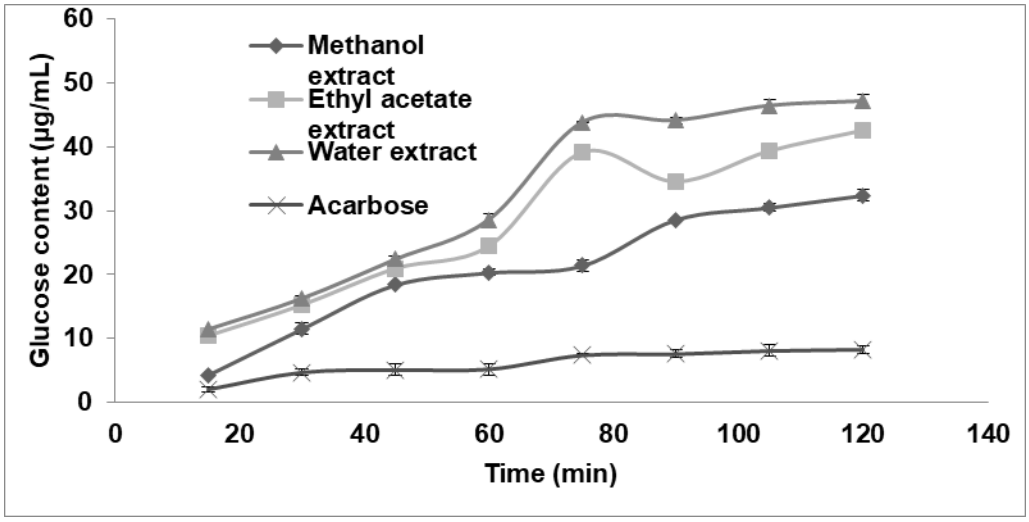


Fig. 3. Effect of the solvent extract of *Sargassum ilicifolium* on glucose diffusion inhibitory activity. The dialysis membrane was filled with glucose (300 µg/mL) and sample (1 mg/mL) or standard (1 mg/mL) and incubated for 120 min under continuous stirring. The glucose content in the external medium was assayed, and the results are presented as µg/mL.

Glucose Diffusion Inhibitory Assay

The algal extract was incubated with a glucose solution and maintained in a dialysis tube. The amount of glucose in the external medium was analyzed every 15 min. The effects of the solvent extracts on glucose diffusion inhibitory activity are presented in Fig. 3. The methanol extract showed maximum inhibition of glucose diffusion after 120 min of incubation, and the glucose content in the external medium was 32.4±1.1 µg/mL. At this same incubation time, the glucose content was 8.3±0.61 µg/mL in the standard (acarbose). The ethyl acetate and water extracts presented moderate effects compared with the methanol extract, and the glucose content in the external solution was high.

Antioxidant Activity of the Solvent Extract

The total antioxidant activity and DPPH, ABTS, and nitric oxide radical scavenging activities were analyzed. These methods are rapid, easy, and comparatively sensitive compared with other methods. In this study, solvent extracts at various concentrations (0.5 to 2.5 mg/mL) were used to analyze their antioxidant activity, and the results were compared with those of ascorbic acid. The antioxidant activity data presented in Table 4 indicate that the methanol extract exhibited greater potential antioxidant activity than the ethyl acetate and water extracts did. Compared with the ethyl acetate extract (49.4±0.4%), the methanol extract had a greater total antioxidant capacity (58.2±0.8%), and the water extract (44.6±0.3%) had a greater total antioxidant capacity at a concentration of 2.5 mg/mL. At this concentration, ascorbic acid presented 64.8±0.1% antioxidant activity. However, this seaweed extract showed potential activity against DPPH radicals at selected concentrations. The DPPH activity of the methanol extract was 53.8±0.5%, whereas that of the ethyl acetate extract and water extract was 51.2±0.1% and 49.3±0.3%, respectively. At this concentration, ascorbic acid presented 50.3±0.4% antioxidant activity (Table 4).

Compared with standard ascorbic acid, the extracted algal phytochemicals exhibited a lower ability to chelate ferrous ions, nitric oxide radical scavenging activity, and ABTS scavenging activity. The results obtained in this study were similar to those of previous investigations on various seaweed species, such as *Sargassum vulgare*, *S. vachellianum*, *S. swartzii*, *Chaetomorpha antennina*, and *Ulva fasciata*, which have shown significant DPPH free radical scavenging activity (Arguelles *et al*. 2018; Jesumani *et al*. 2020). In addition, these findings revealed that seaweed extracts with increased phenolic contents presented increased antioxidant activity, which is similar to the trends detected in the present study. Solvent extracts of *S. ilicifolium* have been shown to have greater antioxidant activity than seaweed, *Turbinaria decurrens*, *Sargassum oligocystum*, and *H. macroloba* (Sanger *et al*. 2019).

The antioxidant properties of brown algae are associated with bioactive compounds from the extract, such as sulfated polysaccharides, phenolic compounds, pigments, vitamins, lipids, and terpenoids. The presence of these bioactive compounds is responsible for their metal-chelating ability, radical-scavenging ability, and peroxidation properties (Arguelles *et al*. 2018). The crude lipid extract and fucoidan derived from *Sargassum ilicifolium* had antioxidant activity (Saraswati *et al*. 2021; Lakshmanan *et al*. 2022). In addition, polysaccharides isolated from seaweed from the genus *Sargassum* have antioxidant activity (Flores-Contreras *et al*. 2023). The brown alga *Sargassum polycystum* C. Agardh, which was collected from Port Dickson, Peninsular Malaysia (Nazarudin *et al*. 2021), has antioxidant activity.

Table 4 Antioxidant Activity of Seaweed Extracts at Various Concentrations

	Total Antioxidant Activity (%)			
Sample (mg/mL)	ME Extract	EA Extract	WA Extract	Ascorbic acid (50 µg/mL)
0.5	15.7±1.2	13.1±0.4	14.8±0.9	18.5±0.2
1	26.2±0.9	19.5±0.7	20.3±0.4	27.5±0.9
1.5	39.4±0.3	37.5±0.5	35.2±0.6	47.5±0.5
2	45.1±0.7	40.9±0.2	39.4±0.2	52.3±0.2
2.5	58.2±0.8	49.4±0.4	44.6±0.3	64.8±0.1
DPPH Radical Scavenging Activity				
Sample (mg/mL)	ME Extract	EA Extract	WA Extract	Ascorbic Acid (50 µg/mL)
0.5	8.4±0.2	10.1±0.2	11.4±0.2	10.3±0.1
1	25.3±0.1	17.2±0.3	16.9±0.1	15.4±0.1
1.5	37.4±0.8	28.4±0.5	26.9±0.2	33.4±0.5
2	43.1±0.2	40.5±0.2	38.5±0.8	38.5±0.4
2.5	53.8±0.5	51.2±0.1	50.3±0.4	49.3±0.3
ABTS Scavenging Activity				
Sample (mg/mL)	ME Extract	EA Extract	WA Extract	Ascorbic Acid (50 µg/mL)
0.5	7.4±0.1	6.3±0.5	1.4±0.1	5.3±0.2
1	33.7±0.4	19.5±0.1	19.5±0.2	17.5±0.1
1.5	30.3±0.1	31.5±0.2	27.5±0.1	22.9±0.2
2	40.2±0.2	37.4±0.1	35.4±0.2	36.3±0.5
2.5	49.5±0.2	41.5±0.2	40.5±0.1	42.7±0.3
Nitric Oxide Radical Scavenging Activity				
Sample (mg/mL)	ME Extract	EA Extract	WA Extract	Ascorbic Acid (50 µg/mL)
0.5	3.1±0.2	4.1±0.2	8.5±0.2	4.2±0.1
1	10.3±0.3	8.5±0.1	13.5±0.5	15.2±0.2
1.5	19.5±0.4	15.3±0.2	22.5±0.4	23.4±0.3
2	21.6±0.1	20.3±0.5	23.1±0.1	25.1±0.2
2.5	26.3±0.2	22.5±0.3	24.8±0.2	28.4±0.3
Ferrous Ion Chelating Activity				
Sample (mg/mL)	ME Extract	EA Extract	WA Extract	Ascorbic Acid (50 µg/mL)
0.5	2.2±0.2	1.8±0.1	2.7±0.3	2.7±0.1
1	11.7±0.3	10.5±0.3	12.5±0.2	10.2±0.3
1.5	18.1±0.3	12.3±0.2	17.4±0.1	19.5±0.2
2	27.2±0.3	26.5±0.1	25.3±0.2	22.9±0.0
2.5	35.4±0.4	34.8±0.2	37.5±0.1	33.2±0.1

ME: Methanol Extract; EA: Ethyl Alcohol Extract; WA: Water Extract

In Vitro Enzyme Inhibitory Effects of Seaweed Extracts

In the present study, the enzyme inhibitory effects of the seaweed *S. ilicifolium* extract on α-glucosidase and α-amylases were analyzed. The solvent extract of *S. ilicifolium* exhibited α-glucosidase inhibition activity, and the results were compared with those of a positive control (acarbose). The present study revealed that all the selected extracts effectively inhibited α-glucosidase activity in a dose-dependent manner. The results showed that the methanol extract exhibited maximum enzyme inhibition activity (54.7±0.9%) at a concentration of 3 mg/mL. At the same concentration, 43.7±0.6% inhibition was achieved with the water extract, and 40.4±0.9% inhibition was achieved with the ethyl acetate extract (Fig. 4a). These findings are similar to those of previous reports that seaweed from the genus *Sargassum* has glucosidase inhibitory properties (Nagappan *et al*. 2017). The hexane fraction of the seaweed *S. buxifolium* has glucosidase inhibitory properties (Landa-Cansigno *et al*. 2020), and isolated palmitic acid has been reported as one of the most effective glucosidase inhibitors (Xie *et al*. 2021). These findings are in agreement with previous reports on the hypoglycemic properties of bioactive secondary metabolites from seaweed (Zhao *et al*. 2022).

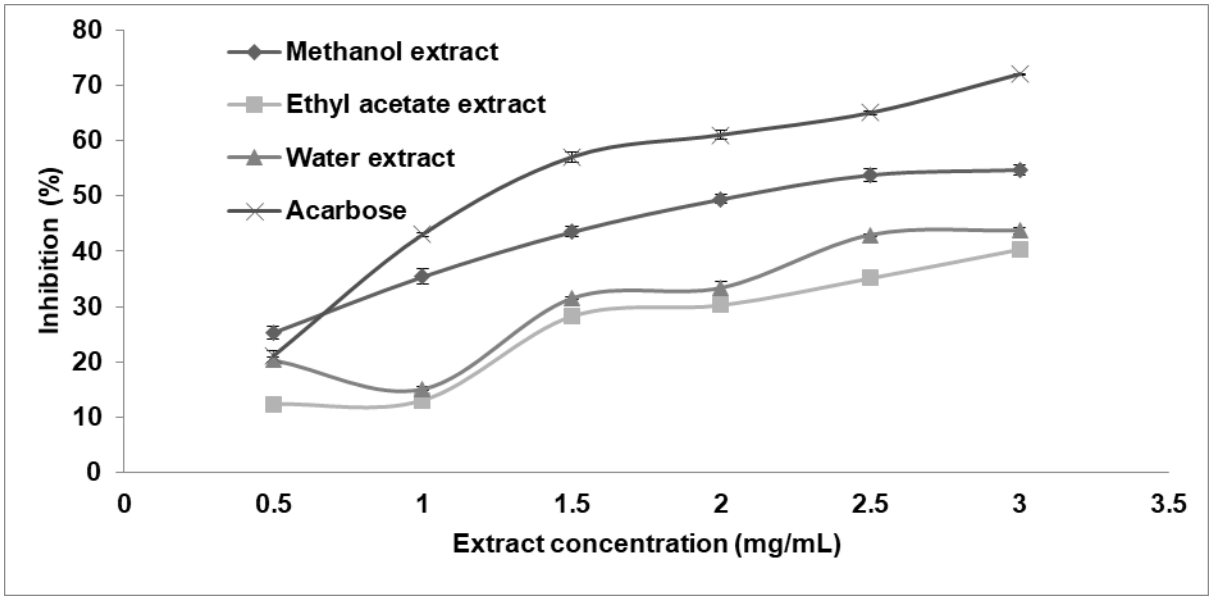
The bioactive compounds from seaweed, including *Sargassum* species, exhibit antidiabetic activity. Antidiabetic activity has been shown for *Sargassum hystrix* extracts (Gotama and Husni 2018), *Sargassum wightii* (Renitta *et al*. 2020), *Sargassum fusiforme* (Jia *et al*. 2020; Zhao *et al*. 2022), and *Sargassum pallidum* (Cao *et al*. 2019). Figure 4b shows the inhibitory activity of the seaweed extract on amylase. The methanol extract presented 64.8±0.72% inhibition at a 3 mg/mL concentration, which was similar to that of acarbose (65.1±1.1% inhibition) at a 3 mg/mL concentration. The other solvent extracts, ethyl acetate, and water extracts presented 62.9±0.9% and 61.8±0.3% inhibition, respectively, at a 3 mg/mL concentration in the reaction mixture. The inhibition of intestinal α-glucosidase and pancreatic α-amylase activity is an important strategic approach to delay the absorption of glucose in the digestive tract, which results in the prevention of rapid increases in blood glucose levels in the blood after food consumption, greatly contributing to better glycemic control (Haguet *et al*. 2023). The use of acarbose reduces glucose absorption and is a known α-glucosidase and α-amylase inhibitor (Li *et al*. 2018). The use of acarbose is associated with various side effects, including flatulence and diarrhea (Scheen 2015). This has prompted researchers to search for enzyme inhibitors from natural resources.

Among the available natural resources, marine algae are significant alternatives to chemical inhibitors (Animish and Jayasri 2023). In this study, antidiabetic activity was established in water, methanol, and ethyl acetate extracts. This finding was similar to the findings of studies of *Sargassum ringgoldianum* methanol extract (Lee and Han 2012), *Hydroclathrus clathratus* aqueous extract (Nagy 2015), and *Sargassum longiotom* methanolic extract (Selvaraj and Palanisamy 2014). The acetylcholinesterase inhibition activity of the solvent extracts of *S. ilicifolium* is presented in Fig. 4c. The acetylcholinesterase inhibition activity was greater in the ethyl acetate extract than in the methanol and water extracts. At a concentration of 0.5 mg/mL seaweed extract, 10.5±0.8% inhibition was achieved with the ethyl acetate extract, and this value increased to 59.1±0.9% at a 3% seaweed extract concentration.

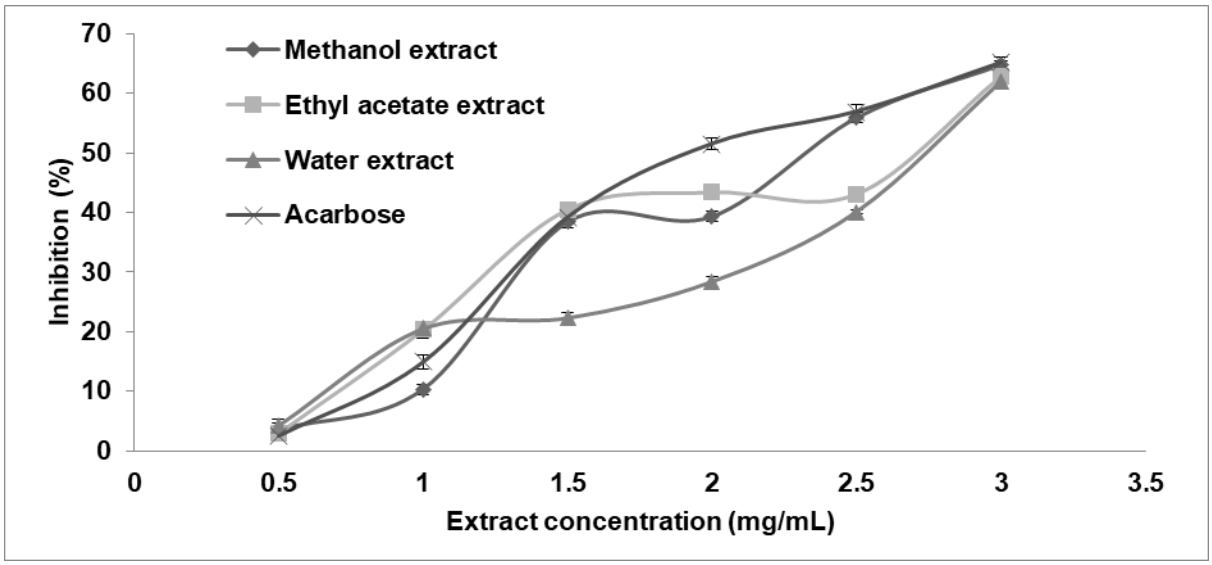
Neurodegenerative diseases are major disorders; as populations age, and the prevalence of neurological disorders such as Parkinson's disease and Alzheimer's disease is also increasing continuously (Feigin *et al*. 2019). Depression is considered a mental disorder and is associated with neurodegenerative disorders (Gelenberg 2010). The

tyrosinase inhibition activity of the solvent extract of *S. ilicifolium* is reported in Fig. 4d, which shows that 59.7±0.72% inhibition was achieved at 3 mg/mL in the reaction mixture. Cholinesterase inhibitors, including *Gracilaria gracilis*, *Sargassum* (Natarajan *et al*. 2009), and *Sargassum angustifolium* (Hosseinpouri *et al*. 2022), have been identified from seaweed. Kojic acid was used as a positive control and presented 64.5±0.9% inhibitory activity at a concentration of 3 mg/mL. There is increasing interest in natural products capable of effectively decreasing the occurrence of neurodegenerative disorders. Tyrosinase is an important enzyme associated with the development of Parkinson's disease. It is involved in the generation of neuromelanin, which subsequently decreases the amount of the neurotransmitter dopamine and induces neuronal death (Pinteus *et al*. 2021; Nagatsu *et al*. 2022).

a



b



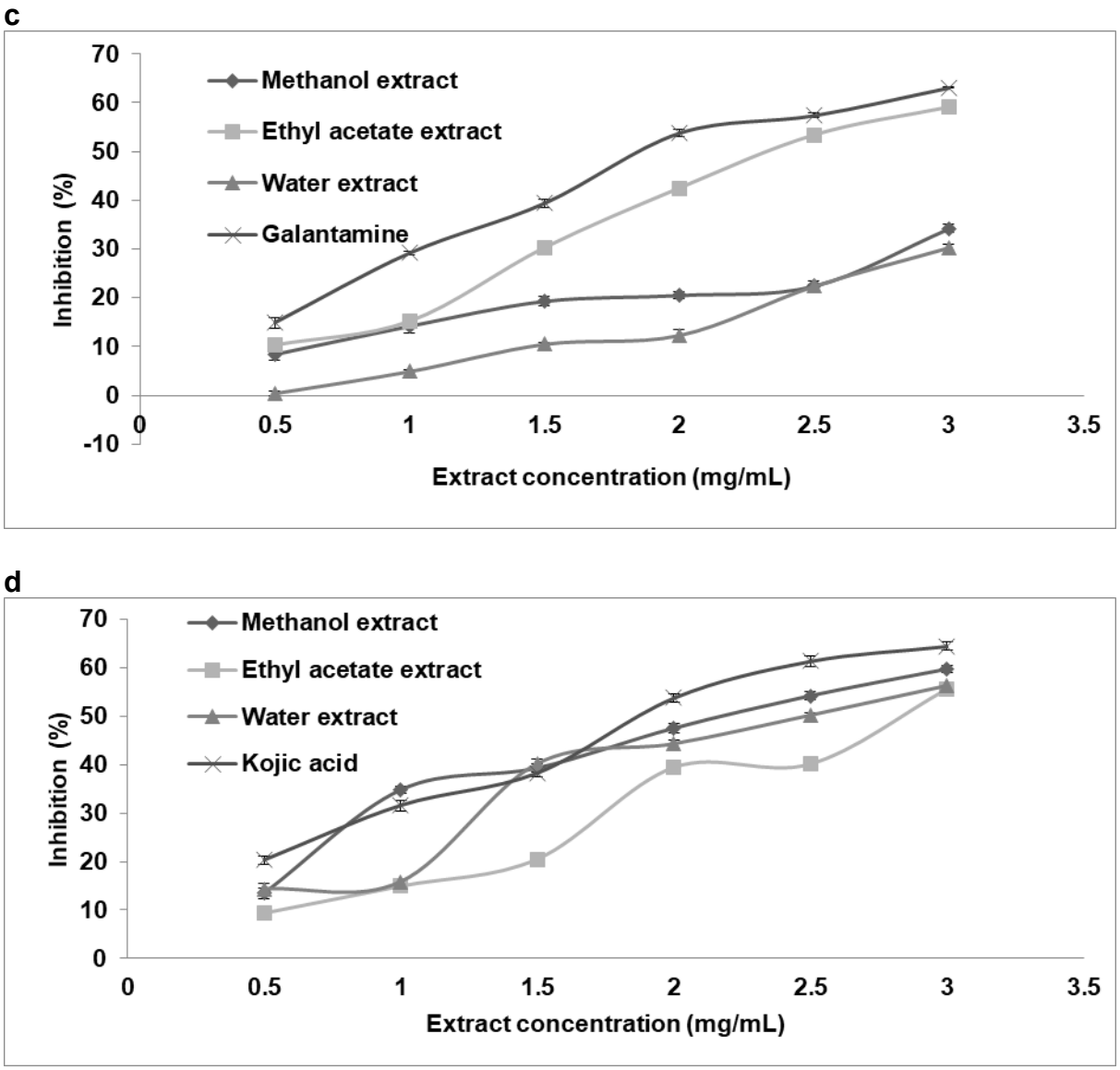


Fig. 4. Enzyme inhibitory effect of the solvent extracts of the seaweed *Sargassum ilicifolium*. Inhibitory effects of various concentrations of α-glucosidase (a), amylase (b), acetylcholinesterase (c), and tyrosinase (d). The results are expressed as the mean±SD percentage of the enzyme inhibitory effect.

CONCLUSIONS

1. The results of this study revealed that *Sargassum ilicifolium* seaweed contains bioactive materials that are capable of preventing the growth of bacteria.
2. The potential antioxidant properties of the *Sargassum ilicifolium* seaweed extracts were obtained in this study. These extracts were evaluated as a natural source of organic antioxidants.
3. The methanol, ethyl acetate, and water extracts presented α-glucosidase and α-amylase inhibitory activities. The antidiabetic property of this suggests the potential of *Sargassum ilicifolium* seaweed as a phytomedicine to regulate blood sugar levels in diabetic patients.
4. The *Sargassum ilicifolium* seaweed extracts inhibited tyrosinase and acetylcholine-esterase activity. Hence, these extracts may contribute to the treatment of neurodegenerative disorders.

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