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POTENTIAL OF MACROALGAE FROM TIDUNG ISLAND WATERS AS ACTIVE INGREDIENTS FOR FUNCTIONAL FOODS

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ABSTRACT

Macroalgae are valuable for functional foods due to their rich secondary metabolites which are greatly influenced by their environmental condition. This study evaluated the potential of Tidung Island's macroalgae as a source of bioactive compounds for functional food ingredients. Seventeen macroalgae samples were collected from Tidung Besar (TB) and Tidung Kecil (TK), Kepulauan Seribu, representing Chlorophyceae, Phaeophyceae, and Rhodophyceae. The macroalgae were extracted using ethanol and analysed for their total phenol using Folin-Ciocalteu method, antioxidant using Ferric Reducing Antioxidant Power (FRAP) assay, antibacterial using Resazurin-based Microtiter Dilution Assay, and anticancer activity using MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay. Result showed that total phenolic content varied among species (39.85–122.26 mg GAE g^{-1}). Antioxidant activity ranged from 16.43–96.58 mg mL^{-1}, with *Turbinaria ornata* exhibiting the strongest effect, while *Gracilaria debilis* showed the lowest. Species of Phaeophyceae generally displayed higher antioxidant capacity compared to the other groups. Antibacterial assays revealed minimum inhibitory concentrations (MIC) between 2.5 and 10 mg mL^{-1}, with *Halimeda gracilis* showing the strongest inhibition. Anticancer evaluation against MCF-7 breast cancer cells demonstrated inhibition ranging from 7.68–90.22%, with *H. gracilis* and *H. macroloba* being the most active. Phenolics correlated moderately with anticancer activity (r = 0.56) and weakly with antioxidant activity (r = 0.36), while antioxidant–anticancer correlation was strong (r = 0.76). In conclusion, *H. gracilis*, *C. sertularioides*, *P. australis*, and *A. muscoides* emerged as promising candidates for further development as natural sources of antioxidant, antibacterial, and anticancer compounds.

Keywords: seaweed, diversity, antioxidant, antibacteria, total phenol, anticancer

INTRODUCTION

The increasing demand for functional foods is driven by growing health awareness in society and a preference for products that offer benefits beyond basic nutrition (**Martirosyan & Stratton, 2023**). This trend presents both opportunities and challenges for researchers and the food industry to explore various types and develop functional food products. The Functional Food Centre (FFC) defines functional foods as "natural or processed foods that contain known or unknown biologically active compounds, which, in defined amounts, provide a clinically proven and documented health benefit for the prevention, management, or treatment of chronic diseases." (**Martirosyan & Singh, 2015**).

Marine ecosystems offer greater biodiversity than terrestrial ecosystems and provide many resources that are beneficial for human nutrition and health (**Suleria *et al*., 2015**). Macroalgae are known for their significant benefits as a source of raw materials for various food products, since they are rich in essential nutrients such as vitamins, minerals, and fiber, which have health benefits for humans (**Adarshan *et al*., 2024**). The consumption of macroalgae-based foods has increased, driven by growing awareness of their health benefits (**Lomartire & Gonçalves, 2022**).

Macroalgae are valuable nutritional source and offer antibacterial, antioxidant, and anticancer properties, along with high total phenol content, making them significant in modern nutraceutical diets (**Sheikh & Kaur, 2022**). Their bioactive compounds, including polysaccharides, pigments, fatty acids, polyphenols, and peptides, contribute to the development of functional foods and nutraceuticals (**Ganesan *et al*., 2019**). Antioxidants in macroalgae, such as fucoxanthin and fucoidan, protect cells from oxidative damage, which can cause premature aging and chronic diseases (**Meinita *et al*., 2022**). Additionally, macroalgae extracts have shown potential as anticancer agents by inhibiting cancer cell proliferation and inducing apoptosis (**Lee *et al*., 2021**).

Each type of macroalgae has unique characteristics and bioactive compounds, highlighting its significant potential applications in health as functional foods. These compounds, including polyphenols, polysaccharides, carotenoids, and omega-3 fatty acids, have demonstrated antibacterial, antioxidant, anti-inflammatory, and anticancer properties (**Cikoš *et al*., 2018**). The composition and effectiveness of these compounds can vary depending on the macroalgae species, harvest time, and environmental conditions, resulting in unique properties for each species (**El-Beltagi *et al*., 2022**). A study reported that red macroalgae contain various phycocyanins, mycosporins, unsaturated fatty acids, polysaccharides, minerals, and vitamins (**Torres *et al*., 2019**). Red and green macroalgae are rich in bromophenols, phenolic acids, and flavonoids, while brown macroalgae have high levels of phlorotannin (**Gómez-Guzmán *et al*., 2018**). Phenolic compounds are among the most commonly found groups of secondary metabolites in macroalgae. These compounds play a crucial role in the growth and development of macroalgae and terrestrial plants, and they also provide defence mechanisms against environmental stress (**Santos *et al*., 2019**). The phenolic content in macroalgae has been extensively studied for its potential as antioxidants and anticancer agents.

In Indonesia, macroalgae, including Chlorophyceae, Rhodophyta, and Phaeophyceae, are abundant in coastal areas such as Tidung Island in the Kepulauan Seribu, DKI Jakarta Province. Tidung Island, about 106 hectares in size, consists of Tidung Besar (TB), which is densely populated with around 4,000 residents, and Tidung Kecil (TK), which is uninhabited (**BPS-Statistic Indonesia, 2018**). Preliminary observations have noted various macroalgae in ecosystems like mangroves, seagrass beds, and coral reefs. However, the growing population on TB Island impacts macroalgae growth significantly.

Previous studies have reported the biological activities of several seaweed species from the Kepulauan Seribu, particularly Pulau Tidung. For instance, **Handayani *et al*. (2020)** examined the phytochemical composition, antibacterial, and antioxidant activities of three Phaeophyceae macroalgae (*Hormophysa triquerta, Padina australis, and Sargassum binderi*) collected from the Tidung coastline. Similarly, **Widowati *et al*. (2021)** investigated the phytochemicals and antioxidant properties of Gracilaria salicornia, *Halimeda gracilis*, *H. macroloba*, and *Hypnea* *asperi* from the same region. Comparisons between Tidung Besar (a densely populated island) and Tidung Kecil (an uninhabited island) remain unexplored, despite the potential influence of anthropogenic pressure on the composition and efficacy of macroalgal metabolites. Consequently, a comprehensive assessment that integrates antioxidant, antibacterial, and anticancer activities along with phenolic content across diverse macroalgae from these two contrasting environments is needed to fill this gap and to better inform the development of functional food ingredients in Indonesia. This study aims to evaluate the potential of macroalgae around Tidung Island as functional food ingredients, focusing on their antibacterial, anticancer, and antioxidant properties and phenol content. The findings are expected to provide valuable information for the functional food industry in Indonesia.

MATERIALS AND METHODS

Materials

Various macroalgae were collected from the waters around Tidung Island in the Kepulauan Seribu, DKI Jakarta, in December 2019. Tidung Island consists of Tidung Kecil (TK) with sampling coordinates at latitude 5° 48.0' 12" and longitude 106° 31' 21.37", and Tidung Besar (TB) with sampling coordinates at latitude 5° 47' 57.65" and longitude 106° 29' 44.87". Figure 1 shows the locations where samples were collected.

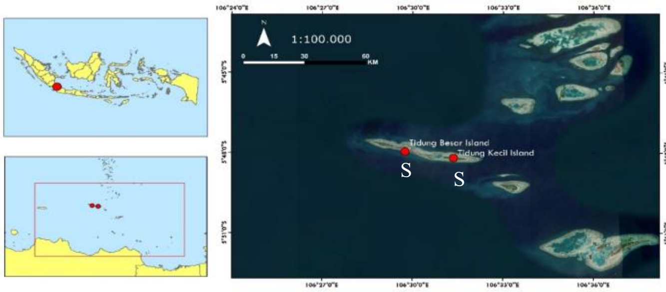

Figure 1 Sampling points (st-1) Tidung Besar Island (TB) and (st-2) Tidung Kecil Island (TK)

Preparation and Identification of Samples

The collected macroalgae samples were washed with distilled water to remove sand and invertebrates (**Tolpeznikaite *et al*., 2021**). The macroalgae were then cut into pieces and weighed at 10 grams, followed by maceration in 10 ml of ethanol (Sigma-Aldrich, USA), at 4°C for 24 hours. One milliliter of the maceration solution was centrifuged (Eppendorf Centrifuge 5430/5430 R, Germany) using single fixed rotor at 10,000 rpm for 15 minutes, and the supernatant was evaporated in a vacuum concentrator (Eppendorf Concentrator Plus EP5305000100, Germany) for approximately 24 hours. After drying, the extracts were re-dissolved in ethanol and re-evaporated. This procedure was repeated twice to minimize residual salts and to ensure that only ethanol-soluble compounds were retained. The resulting dry extract was subjected to bioactivity analysis. The taxonomy and identification of the macroalgae samples were verified based on morphological characteristics and species names using the Macroalgae Base website (**Ismail et al., 2023**).

Total Phenol Analysis

The total phenolic content was determined following the method by **Oki *et al.* (2002)**. The dried extracts (1 mg/mL) were dissolved in ethanol, and 50 µl of the solution was added to a 96-well microplate. Then, 50 µl of 10% Folin-Ciocalteu reagent (Sigma-Aldrich, USA) was added, followed by a 3-minute incubation at 37°C. Afterward, 100 µl of 10% Na_2CO_3 (Merck, Germany) solution was added, and the plate was incubated for 60 minutes. Absorbance was measured at 750 nm using a microplate reader (Thermo Scientific Multiskan GO, USA). The total phenolic content was calculated using a gallic acid standard curve (20 to 500 mg/mL), and results were expressed as milligrams of gallic acid equivalents (mg GAE/g). The standard curve equation was $Y = 0.0078x + 0.1138$ ($R^2 = 0.9843$).

Antioxidant Analysis

The antioxidant analysis followed the Ferric Reducing Antioxidant Power (FRAP) assay by **Benzie & Strain (1996).** The FRAP solution was prepared by mixing 300 mM acetate buffer (pH 3.6) (Merck, Germany), 10 mM 2,4,6-tripyridyl-s-triazine (TPTZ) (Sigma-Aldrich, USA) and 20 mM ferric chloride hexahydrate ($FeCl_3 \cdot 6H_2O$) (Sigma-Aldrich, USA) in a 10:1:1 ratio. The assay was conducted in a 96-well microplate with 150 µl of the FRAP solution and 20 µl of ethanol extract (1 mg/ml) in each well. After 8 minutes of incubation in the dark at 37°C, absorbance was measured at 595 nm using a microplate reader (Thermo Scientific Multiskan GO, USA). A standard curve was created with ferrous sulphate heptahydrate ($FeSO_4 \cdot 7H_2O$) (Sigma-Aldrich, USA) at concentrations between 0.01 and 0.5 mg/ml, and the FRAP value (µM) was calculated using the equation $Y = 0.002x + 0.0167$ ($R^2 = 0.9979$).

Antibacterial Analysis

The antibacterial test followed the procedure by **Sarker *et al.* (2007)**. The dried extracts (10 mg/ml) were dissolved in 10% dimethyl sulfoxide (DMSO) (Sigma-Aldrich, USA) and tested using a 96-well microplate. A 100 µl of the extract was added to the first well, with 50 µl of sterile water in the others. Serial dilutions were performed from the first to the twelfth well. Then, 30 µl of nutrient broth (Oxoid, UK), 10 µl of bacterial suspension, and 10 µl of resazurin (Sigma-Aldrich, USA) were added to each well. The negative control used sterile water, while the positive control used chloramphenicol (Merck, Germany) (1 mg/ml). The microplate was incubated at 37°C for 18-24 hours. A pink color indicated no antibacterial activity, and a purple color indicated antibacterial activity. The bacteria used for testing were *Staphylococcus aureus* (ATCC25923), a Gram-positive bacterium, and *Escherichia coli* (ATCC25922), a Gram-negative bacterium.

Anticancer Analysis

The anticancer analysis was performed at the Primate Studies Center, IPB University, Bogor, Indonesia, using MCF-7 human breast adenocarcinoma cells (ATCC HTB-22). MCF-7 is considered an ideal model for studying hormone-responsive breast cancer, owing to its ability to form tumours in vivo with estrogenic support, and many in vitro therapeutic findings using this cell line have been successfully translated into clinical trials and anticancer drug development (**Robertson *et al.* 2003; Ismail *et al*., 2020**). Cells were maintained in Roswell Park Memorial Institute medium (RPMI 1640) supplemented with 10% fetal bovine serum (FBS) (Gibco, USA), penicillin (Sigma-Aldrich, USA) (100 U/mL), and streptomycin (Sigma-Aldrich, USA) (100 µg/mL) at 37 °C in a humidified atmosphere containing 5% CO_2. For the assay, dried extracts were dissolved in cell culture media, in the same RPMI 1640 medium. Cells were cultured at 5000 cells per 100 µL of media and treated with the extract once they reached 50% confluence (after 24 hours). After three days of incubation, cell viability was assessed using a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay, which was conducted by adding 10 µL of MTT (Thermo Fisher Scientific, USA) solution (5 mg/mL) per well and incubating for 4 hours at 37°C. The resulting formazan (Sigma-Aldrich, USA) crystals were dissolved in ethanol, and absorbance was measured at 595 nm using a microplate reader (Thermo Scientific Multiskan GO, USA), with the extract concentration set at 100 mg/L.

RESULTS AND DISCUSSION

Identification of Macroalgae in Tidung Island Waters

A total of 18 macroalgal species were identified from Tidung Besar (TB) and Tidung Kecil (TK) Islands, distributed across both sites (Tables 1 and 2). Based on their pigment composition, these macroalgae comprised six species of Chlorophyceae (green algae), four species of Phaeophyceae (brown algae), and eight species of Rhodophyceae (red algae). Among these three groups, the Rhodophyceae class exhibited the highest species diversity compared to the other two classes. A previous study by **Ruslian (2017)** conducted at the same location reported five Chlorophyceae species and six Phaeophyceae species. The current findings indicate a difference in the number of Chlorophyceae and Phaeophyceae species compared to the earlier study. This may be due to to changes in environmental conditions and varying ecological pressures at the time of sampling. The distribution of macroalgae in marine environments is strongly influenced by ecological factors and interspecific competition within their habitats. Abiotic factors such as wave intensity, salinity, temperature, and substrate type, as well as biotic factors such as herbivory and competition, play crucial roles in shaping algal communities, thereby determining species abundance and composition in each area **(Forslund et al., 2010).** That study also described specific interactions between herbivorous biota and marine algae, such as those between *Fucus* species (*F. radicans*, *F. evanescens*, *F. vesiculosus*) and marine isopods *Idotea* spp., *Gammarus* spp., and *Theodoxus fluviatilis* in Swedish waters.

In addition, anthropogenic pressures also have a significant impact on algal diversity in marine environments. Consistent with the findings of **Langoy et al. (2011),** high levels of human activity can reduce algal diversity through alterations in environmental quality, increased turbidity, and disturbances to natural habitats in North Sulawesi, Indonesia. This condition was observed on TB Island, which showed lower algal diversity and higher human activity compared to TK Island. Based on the identification results, four species of macroalgae were found exclusively on TB Island, namely *Sargassum binderi*, *Eucheuma cotonii*, *Gracilaria debilis*, and *Halimeda macroloba*. In contrast, TK Island exhibited higher diversity, with several distinctive species such as *Acanthopora spicifera*, *Eucheuma spinosum*, and *Plocamium cornutum* that were not found on TB Island. In addition, the Rhodophyceae group (red algae) dominated on TK Island with six species, whereas only five species were identified on TB Island. This pattern indicates that the environmental conditions on TK Island are more favorable for macroalgal growth, particularly for red algae, which are generally sensitive to changes in water quality and habitat disturbances.

Table 1 Distribution of macroalge in TB and TK islands

NO	Species	TB island	TK island
	Chlorophyceae		
1	*Halimeda macroloba*	-	+
2	*Boergesenia forbesii*	+	+
3	*Chaetomorpha crassa*	+	+
4	*Caulerpa sertulariodes*	+	+
5	*C. racemosa*	+	+
6	*Halimeda gracilis*	+	+
	Phaeophyceae		
7	*Padina australis*	+	+
8	*Sargassum natans*	+	+
9	*S. binderi*	+	-
10	*Turbinaria ornata*	+	+
	Rhodophyceae		
11	*Acanthopora muscoides*	+	+
12	*A. spicifera*	-	+
13	*Eucheuma spinosum*	-	+
14	*E.cotonii*	+	-
15	*Galaxaura rugosa*	+	+
16	*Gracilaria debilis*	+	-
17	*G. salicornia*	+	+
18	*Plocamium cornutum*	-	+

Note: (+) = present, (−) = absent

Table 2 Species of Macroalgae in TB and TK islands

Species of Macroalgae		
Chlorophyceae		
		
Boergesenia forbesii	***Chaetomorpha crassa***	***Caulerpa sertulariodes***
		
Caulerpa racemosa	***Halimeda macroloba***	***Halimeda gracilis***
Phaeophyceae		
		
Padina australis	***Sargassum natans***	***Sargassum binderi***
		
Turbinaria ornata		
Rhodophyceae		
		
Acanthopora muscoides	***Acanthopora spicifera***	***Eucheuma spinosum***
		
Eucheuma. cotonii	***Galaxaura rugosa***	***Gracilaria debilis***
		
Gracillaria salicornia	***Plocamium cornutum***	

Total Phenol Content

The total phenol contents in macroalgae from both islands (TB and TK) are varies (Figure 1). *Acanthopora muscoides* from TK Island has the highest total phenol content at 122.26 ± 13.57 mg GAE/g, which is higher than the 46.19 mg GAE/g reported by **Akbar *et al.* (2018)** for *A. muscoides* using n-hexane. This difference is attributed to the varying solvent treatments, which affect solvent polarity. Extraction and purification of phytochemicals are influenced by factors such as time, temperature, solvent concentration, and polarity (**Nawaz *et al.*, 2020**). The high phenol content in the methanol extract of Acanthophora indicates a higher concentration of polar compounds. Ethanol extracts both polar and semi-polar compounds, while a mix of polar solvents like methanol, acetone, and water can improve flavonoid extraction and antioxidant capacity (**Chaves *et al.*, 2020**).

Polyphenols act as reducing agents that protect body tissues from oxidative stress damage. In seaweed, polyphenols' antioxidant activity is linked to phenolic and flavonoid compounds, which scavenge free radicals and reduce iron ions (**Kasanah *et al.*, 2022**). Phenolic compounds with hydroxyl groups at ortho and para positions are more effective at enhancing antioxidant capacity than those with meta substitutions (**Parcheta *et al.*, 2021**). Among phenolic acids, derivatives with three hydroxyl groups on the aromatic ring, such as 3,4,5-trihydroxybenzoic acid (gallic acid), are the most potent antioxidants. Phenolic acids with two hydroxyl groups on the ortho ring, like dihydrocinnamic acid and 3,4-dihydroxybenzoic acid, also exhibit significant antioxidant activity. Conversely, compounds with only one hydroxyl group, such as 2-hydroxybenzoic acid, show the lowest antioxidant activity (**Tung *et al.*, 2009**).

The antioxidant bioactivity of phenolic compounds is related to their ability to scavenge free radicals. However, the total phenol content in *A. muscoides* samples does not show a direct correlation with antioxidant activity. The results indicate that the antioxidant activity of the methanol extract of *A. muscoides* is lower compared to other macroalgae species, with a value of 19.49–19.49 µM/µg (Figure 1). This suggests that *A. muscoides* may contain other antioxidant compounds besides phenolic compounds. According to **Aljadi & Kamaruddin (2004)**, phenolic compounds are the main substances responsible for antioxidant effects, but non-phenolic compounds are often also involved in scavenging free radicals.

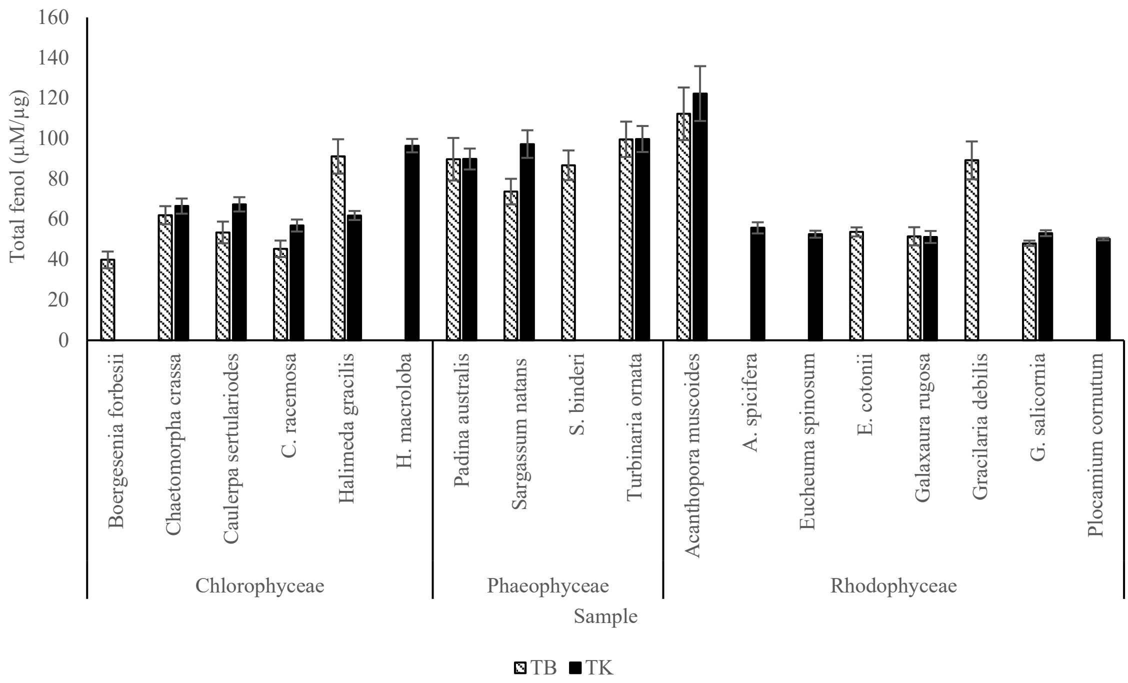

Figure 1 Total phenol content of macroalgae in TB and TK islands. Note: The bar shows the presence of macroalgae at the locations according to the legends

Antioxidant Activity

Eighteen macroalgae species with varying antioxidant concentrations were identified on Tidung Besar (TB) and Tidung Kecil (TK) islands (Figure 2). Based on pigment color, the macroalgae can be categorized into three divisions: Chlorophyceae (green macroalgae) with six species, Phaeophyceae (brown macroalgae) with four species, and Rhodophyceae (red macroalgae) with eight species. According to **Campbell *et al*. (2023)**, the distribution of macroalgae in a water body is greatly influenced by ecological factors such as wave action, salinity, temperature, substrate, and competitors in their habitat, which determine the abundance and composition of macroalgae in an area.

The characteristics of TK Island, which is uninhabited, and TB Island, which is densely populated, show variations in the distribution of macroalgae. **Okuhata *et al*. (2023)** stated that anthropogenic pressure due to human activities influences the growth and diversity of macroalgae. Human activities in densely populated transition zones between terrestrial and marine ecosystems subject macroalgae to various levels of anthropogenic stress. Global climate changes, such as increased UV radiation, CO2 levels, rainfall, temperature, wind direction, storm frequency, and sea-level rise, also impact their life cycles and development (**Veluchamy *et al*., 2023**).

The diversity of antioxidant concentrations on Tidung Island (TK and TB) showed the values range from 16.43±1.20 to 94.94±2.74 µM Fe^{2+}/g dw (dry weight). Macroalgae from the division Phaeophyceae exhibited higher antioxidant activity compared to Chlorophyceae and Rhodophyceae. The average antioxidant activity for Phaeophyceae ranged from 26.29–96.58 µM Fe^{2+}/g dw, while that Chlorophyceae ranged from 19.49–77.27 µM Fe^{2+}/g dw, and Rhodophyceae from 16.43–40.56 µM Fe^{2+}/g dw. Comparison between locations revealed that most species had higher antioxidant activity in TK than in TB. This result likely relates to TK environmental conditions, which include environment condition due to higher sunlight exposure due to minimal vegetation and lower sedimentation compared to TB, which is more densely populated and experiences increased turbidity from anthropogenic sedimentation. Statistical analysis showed that several species, including *T. ornata*, *S. natans*, *Caulerpa sertularioides*, *C. racemosa*, and *A. muscoides* had significant differences between locations ($p < 0.05$). These findings supported the hypothesis that local environmental factors, such as light intensity and sedimentation, played important roles in influencing the biosynthesis of antioxidant compounds in macroalgae.

The highest activity was recorded in *T. ornata* with values of 96.58 µM Fe^{2+}/g dw (TK) and 91.18 µM Fe^{2+}/g dried extract (TB). In contrast, the lowest activity was observed in *G. debilis*, with 16.43 µM Fe^{2+}/g dw (TB), while this species was not found in TK. Some species, such as *H. gracilis* (77.27 µM Fe^{2+}/g dw in TB and 52.06 µM Fe^{2+}/g dw TK) and *S. natans* (52.68 µM Fe^{2+}/g dw in TB and 66.69 µM Fe^{2+}/g dw in TK), showed relatively high antioxidant activity, indicating variability among species and possibly reflecting the influence of environmental factors on antioxidant compound production. Species of *Turbinaria.* sp. (Phaeophyceae) is known for their high capacity to produce antioxidant compounds, particularly phlorotannins and carotenoids such as fucoxanthin, which are effective lipophilic antioxidants that neutralize reactive oxygen species (ROS) (**Begum *et al.* 2021**). High light exposure serves as an oxidative stressor that triggers endogenous antioxidant production as a protective mechanism against ROS formation. These antioxidants play a crucial role in protecting macroalgal cells from UV radiation damage, lipid peroxidation, and structural cellular disruption (**de Almeida *et al.* 2022**). ROS are reactive molecules or free radicals generated as byproducts of normal cellular metabolism or environmental stressors such as UV radiation, high salinity, extreme temperatures, or dehydration (**Madkour et al. 2019**). In shallow tropical waters like TK, intense sunlight exposure, particularly in the UV-A and UV-B ranges, can enhance intracellular ROS formation in macroalgae. The major ROS formed in macroalgal tissues include superoxide anions (O_2^-), hydrogen peroxide (H_2O_2), hydroxyl radicals (•OH), and singlet oxygen ($^1O_2$) (**Xue *et al.* 2022**). ROS formation mainly occurs in the chloroplasts during photosynthesis, where excessive light energy absorbed by photosystem II (PSII) may not be fully transferred to the Calvin cycle, leading to electron leakage that reacts with oxygen to produce O_2^-. This radical is then converted to H_2O_2 by superoxide dismutase (SOD), and subsequently to highly reactive •OH through Fenton reactions (**Noctor *et al.* 2018**).

Under stress conditions, ROS accumulation causes lipid peroxidation, protein denaturation, and DNA damage. Consequently, macroalgae develop biochemical defense systems by producing antioxidant enzymes (SOD, catalase, peroxidase) and non-enzymatic antioxidants such as ascorbic acid, glutathione, tocopherols, flavonoids, and polyphenols (**Hasanuzzaman *et al.* 2020**). Phlorotannins and fucoxanthin serve as primary ROS scavengers and membrane stabilizers. Fucoxanthin is known to donate electrons to neutralize singlet oxygen and hydroxyl radicals efficiently and prevent oxidation of linoleic acid and cholesterol in model biological systems (**Nomura *et al.* 2013).** High light exposure can also up regulate genes involved in antioxidant biosynthesis. Several previous studies have demonstrated the strong antioxidant potential of brown macroalga commonly found in tropical and subtropical coastal regions. An antioxidant value of acetone and ethanolic extract of *Sargasum olygocystum* were respectively 14.45±1.425 and 9.09±0.876 µM Fe^{2+}/g (**Sanger *et al*., 2024**),

Nevertheless, not all macroalgae from TK showed higher values than TB. For example, *H. gracilis* (64.67 µM Fe^{2+}/g dw) and *G. salicornia* (33.62 µM Fe^{2+}/g dw) from TB displayed relatively high antioxidant activity despite growing under conditions of limited light penetration. This suggests that beyond light, other factors such as osmotic stress, interspecies competition, and nutrient availability in the aquatic environment also modulate antioxidant production. A study by **Kamal *et al.* (2023)** showed that antioxidant enzyme activity in *Mastocarpus stellatus* and *Chondrus crispus* increased in winter compared to summer, indicating that seasonal and thermal variations affect secondary metabolic activity. Furthermore**, Shanab & Shalaby (2021)** emphasized that solvent type significantly influences measured antioxidant activity, as seen in *Enteromorpha compressa*, which exhibited antioxidant values of 50 mg/mL using ethanol and 47 mg/mL with chloroform. **Rattaya *et al.* 2015** found that methanolic extracts of *T. ornata* contained the highest total phenolic content (2.07 mg µM catechin/g dw). **Chakraborty &Joseph (2016)** identified major phenolic compounds such as quercetin and salicylic acid in the ethyl acetate fraction of *T. ornata* and *T. conoides* which exhibited higher antioxidant activity than other solvent fractions. This result showed that tropical macroalgae, particularly *Tornata*, have high potential as natural sources of antioxidant compounds.

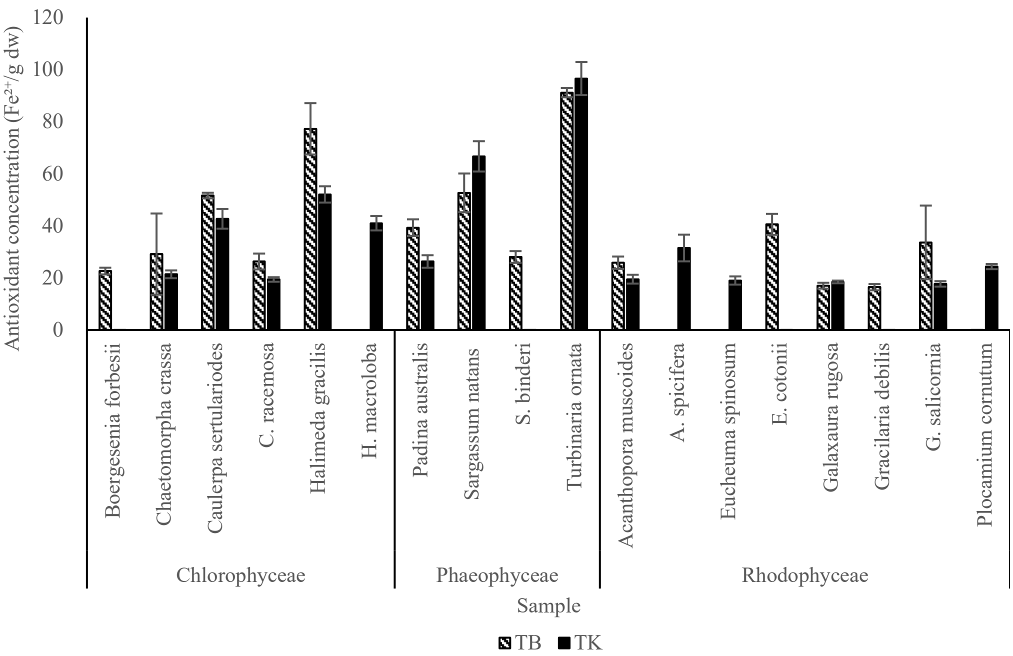

Figure 2 Antioxidant activity of macroalgae extracts in TB and TK islands. Note: The bar shows the presence of macroalgae at the locations according to the legends

Antibacterial Activity

Table 3 shows that out of eighteen macroalgae species tested, six were effective against *S. aureus* (gram-positive) and six against *E. coli* (gram-negative), while the rest were inactive. Green macroalgae (Chlorophyceae) had varied antibacterial activities, unlike brown (Rhodophyceae) and red macroalgae (Phaeophyceae). The cell wall composition impacts antibacterial efficacy: gram-positive bacteria have peptidoglycan and teichoic acids, whereas gram-negative bacteria also have lipopolysaccharides and lipoproteins (**Bogler *et al.*, 2019**). Gram-negative bacteria are less permeable to antimicrobials and produce β-lactamase enzymes that are more effective in the periplasmic space, making them generally more resistant to antibiotics (**Nurmala *et al*., 2015; Breijyeh *et al*., 2020**).

The antibacterial activity of various macroalgae extracts collected from TB and TK showed that methanol extracts of *H. gracilis* had the highest activity, with a MIC of 2.5 mg/mL against *S. aureus* at both locations. This indicates a significant potential as an antibacterial agent. *Padina australis* also demonstrated fairly strong activity against *E. coli* at both locations, with a MIC of 10 mg/mL. This is in line with the research by **Basir *et al.* (2020)**, which found that methanol extracts of the green macroalgae *H. gracilis* had higher antibacterial activity compared to *H. macroloba*. While *H. gracilis* showed potential antibacterial activity against *S. aureus*, it did not exhibit activity against *E. coli*. The Halimeda genus of macroalgae contains secondary metabolites such as halimedatrial and halimedatetraacetate, which have potential as antibacterial agents (**Suganya *et al*., 2019**).

The green macroalgae *Caulerpa sertulariodes* from TK had a MIC of 5 mg/mL against *E. coli*. Bioactive compounds from macroalgae with antimicrobial activity include various metabolites such as polysaccharides, polyunsaturated fatty acids, phlorotannins, other phenolic compounds, and carotenoids (**Perez *et al.,* 2016**). Research on antibacterial bioactivity in macroalgae shows a wide range of antibacterial values. **Kosanić *et al.* (2015**) reported that macroalgae species *Ulva lactuca* and *Enteromorpha intestinalis* had MIC values of 0.625 and 1.25 mg/mL (*S. aureus*) and 2.5 and 5 mg/mL (*E. coli*) using the microdilution resazurin method. Overall, this study indicates that certain macroalgae species have higher antibacterial potential compared to others, which may be influenced by species, location, and target organisms.

Table 3 Antibacterial activity of macroalgae extracts from TB and TK islands

NO	Filum/species	Tidung Besar (TB) (mg/ml)		Tidung Kecil (TK) (mg/ml)	
		EC	SA	EC	SA
	Chlorophyceae				
1	*Boergesenia forbesii*	NA	NA	-	-
2	*Chaetomorpha crassa*	NA	10	NA	10
3	*Caulerpa sertulariodes*	NA	NA	5	10
4	*C. racemosa*	NA	NA	10	NA
5	*Halimeda gracilis*	NA	2.5	10	2.5
6	*H. macroloba*	-	-	NA	5
	Phaeophyceae				
7	*Padina australis*	10	NA	10	NA
8	*Sargassum natans*	NA	NA	NA	NA
9	*Sargassum binderi*	NA	NA	-	-
10	*Turbinaria ortana*	NA	NA	NA	NA
	Rhodophyceae				
11	*Acanthopora muscoides*	NA	TA	10	NA
12	*Acanthopora spicifera*	-	-	NA	NA
13	*Eucheuma spinosum*	-	-	NA	NA
14	*Eucheuma cotonii*	NA	NA	-	-
15	*Galaxaura rugosa*	NA	10	NA	NA
16	*Gracilaria debilis*	NA	NA		
17	*Gracillaria salicornia*	NA	NA	10	NA
18	*Plocamium cornutum*	-	-	NA	10

Note: (EC) = E. coli, (SA) = S. aureus, (NA) = Not Active, (-) = Species Not Found. The MIC control values for *E. coli* and *S. aureus* are 0.01 mg/mL and 0.03 mg/mL, respectively.

Anticancer Activity

Figure 3 shows the percentage inhibition of macroalgae extracts against cancer cells of various macroalgae samples across three groups (Chlorophyceae, Phaeophyceae, and Rhodophyceae). The following observations show among the green macroalgae (Chlorophyceae), *H. gracilis* and *H. macroloba* exhibit high anticancer inhibition activity, with inhibition rates of 90.22% and 83.69%, respectively. In contrast, other macroalgae in the Chlorophyceae group show lower inhibition activity, with inhibition values below 20%, indicating low anticancer potential. Previous studies have reported that *Halimeda sp.* exhibits cytotoxic activity against several types of cancer cells. **Nazarudin *et al.* (2020, 2022)** found that the methanolic extracts of *H. macroloba* had cytotoxic effects on MCF-7 cancer cell lines, with an IC50 value of 37.25 µg/mL, while *H. opuntia* resulted in an IC50 value of 25.14 ± 1.02 mg/mL. Morphological observations from the in vitro anticancer assay indicate that treatment with *Halimeda* extracts induces notable structural alterations in MCF-7 cells compared with both the untreated baseline (A) and the control group (B) (Figure 4). Cells exposed to *H. macroloba* (C) and *H. gracilis* (D) at 100 ppm exhibit reduced cell density, loss of typical epithelial morphology, membrane irregularities, and evidence of cell shrinkage, suggesting cytotoxic and possibly apoptotic effects. These visible changes support the antiproliferative potential of the extracts and align with their proposed anticancer activity.
Brown macroalgae (Phaeophyceae) show relatively high anticancer inhibition activity overall. *Turbinaria ornata* has the highest inhibition percentage among the brown macroalgae, at 71.25%, indicating a strong anticancer potential. *S. natans* also demonstrates significant inhibition activity at 53.64%. *Padina australis* and *S. binderi* show nearly identical inhibition activities, around 43%. Red macroalgae (Rhodophyceae) display a range of anticancer inhibition activities, with values ranging from 18.87% to 49.89%. *Plocamium cornutum* shows the highest inhibition activity among Rhodophyceae macroalgae, at 49.89%, indicating a relatively strong anticancer potential. *Eucheuma spinosum* and *G. salicornia* also show relatively high activity, with inhibition values of 34.09% and 39.94%, respectively.
Some studies report that marine natural products, which contain numerous biologically active substances with novel chemical structures, can be utilized to halt the progression of various diseases and provide protection against different types of cancer. Bioactive compounds from algae can induce cytotoxicity in various ways, including inhibition of tumor growth, invasion, metastasis, and through apoptosis in cancer cells (**Minhas *et al.*, 2024**). Carotenoids and chlorophylls can prevent oxidative damage caused by free radicals and play an essential role in inhibiting cell proliferation, making them useful for reducing cancer risk (**Rowles & Erdman, 2020**). However, antioxidant and cytotoxic activities may not be entirely related to a single specific compound, such as carotenoids, but rather to a mixture of compounds, as these mixtures may work synergistically (**Phan *et al.*, 2018**).

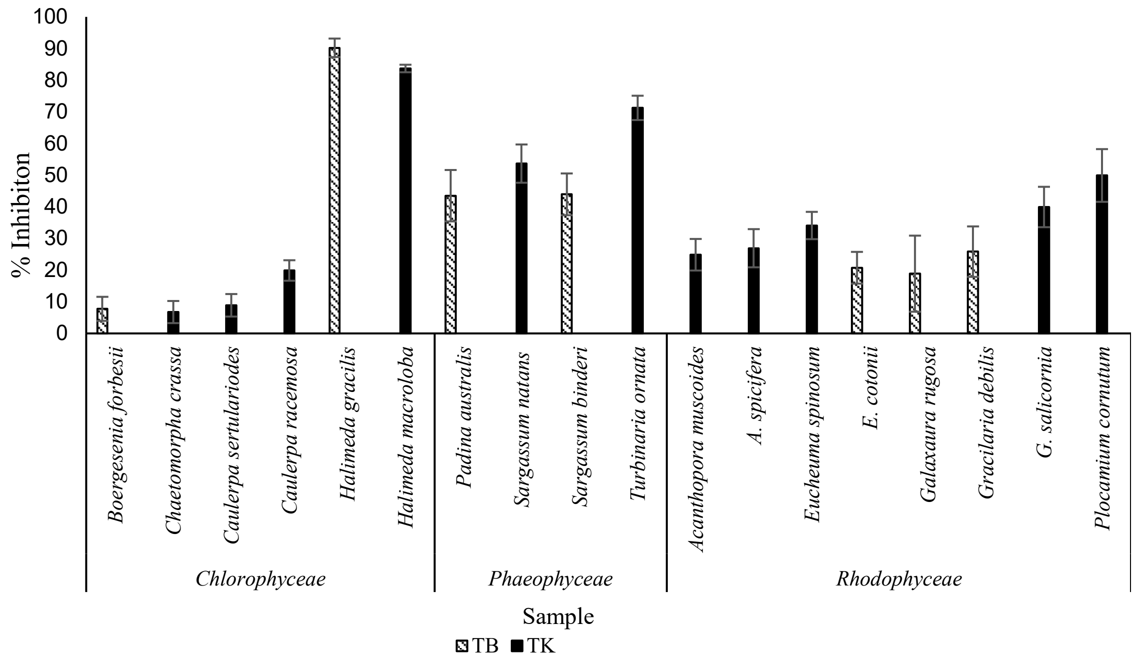

Figure 3 Percentage inhibition of macroalgae extracts against cancer cells in TB and TK islands. Note: The bar shows the presence of macroalgae at the locations according to the legends

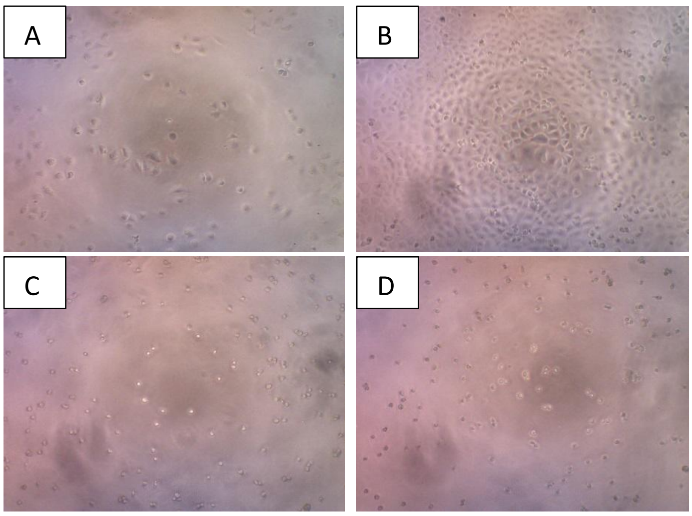

Figure 4 Results of *in vitro* anticancer assay showing morphological changes in the specified cell line (e.g., MCF-7 human breast cancer cells). Panel (A) shows the cells prior to treatment, while panels (B–D) show the cells after 24 hours under different treatments: control cells without treatment (B), cells treated with *H. macroloba* extract (100 ppm) (C), and cells treated with *H. gracilis* extract (100 ppm) (D). The images illustrate the effects of the extracts on cell morphology and viability.

T.ornata, H. gracilis, Halimeda spp., and *A. muscoides* collectively represent promising candidates for the development of functional food ingredients, supported by their distinctive biochemical profiles, broad-spectrum bioactivities, and documented ethnoculinary utilization in tropical coastal regions. *T. ornata*, a brown macroalga enriched with fucoidan, laminarin, and alginate, has demonstrated potent antioxidant, anti-inflammatory, and immunomodulatory activities (**Ishmayana et al., 2025**). In addition, fucoidan derived from Turbinaria species has been reported to exert antidiabetic and anti-obesity effects through enhanced insulin sensitivity, modulation of glucose transporter expression, and suppression of lipid accumulation (**Magwaza et al., 2023**). The long-standing traditional use of *T. ornata* as a boiled vegetable and herbal preparation in Indonesia further supports its cultural acceptability and dietary safety (**Sinay & El-Sheekh, 2023**). Similarly, *H. gracilis* and other *Halimeda sp.* are calcareous green macroalgae that naturally accumulate substantial amounts of calcium carbonate and magnesium, in addition to phenolic constituents and other secondary metabolites known to contribute to antioxidant, antibacterial, and cytotoxic activities (**Hemamalini et al., 2025**).

In contrast, *A. muscoides*, a red macroalga rich in sulfated galactans, agar, and phycobiliproteins, exhibits well-documented antiviral, anticoagulant, anti-inflammatory, and antioxidant properties in both *in vitro* and *in vivo* assays (**Balkrishna et al., 2025**). Species of Acanthophora have also been traditionally consumed in the Philippines and are attributed with therapeutic benefits for digestive and glandular disorders (**Tahiluddin et al., 2025**). Overall, these four macroalgae exhibit substantial potential as high-value resources for the formulation of tropical macroalgae-based functional foods and nutraceutical products.

CONCLUSION

Macroalgae possess a significant potential for functional foods since they contain various bioactive compounds. Tidung Island holds significant potential as a major center for macroalgae due to the diversity of macroalgae that grow and thrive in its aquatic environment. The secondary metabolites of macroalgae from Tidung Island present valuable potential as functional food sources, particularly those offering benefits as antioxidants, antibacterial agents, and anticancer agents. *Turbinaria ornata*, *Halimeda gracilis*, *Acanthophora muscoides*, and *Halimeda sp.* extracts showed the highest results of FRAP antioxidant value, antibacterial activity against *E.coli* and *S.aureus*, total phenolic content, and anticancer activity against breast cancer cell MCF7, respectively. Further research on the applications of these species into various functional foods with their effects are important to be conducted to enhance the development of functional foods industry in Indonesia.

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