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Potential Antioxidant and Anti-Proliferative Activities of Biologically Active Marine Algae Extracts

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Authors' contributions

This work was carried out in collaboration between all authors. Authors TAK, KSB, YAM and SSM designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors OASB, MZ, SSY, AHA, WYA, MHAZ and RRAR managed the analyses of the study. Authors WYA, AHA and SSY and managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: Marine microorganisms such as algae were identified a rich sources of biologically active compounds. This study was designed to explore the *in vitro* antioxidant, anti-apoptotic and anti proliferative activities of different algae *[Gracilaria dendroides (GD), Dictyota ciliolata (DC) and Cladophora socialis* (CS)] extracts obtained from Red sea at Jeddah.
Materials and Methods: Algae extracts (ethanol, chloroform and water) were tested for antioxidant activity for free radical scavenging and secondly as anti-apoptotic and anti-proliferative activity against different cell lines. Antioxidant capacity was detected by evaluation superoxide anion radicals, reducing potential and assay of phenolic and flavonoid content in extracts.
Results: Chloroform extract of DC (CEDC) was found to have a better free radical scavenging activity (IC50= 310.58 g/ml) than methanol extract (MEDC). MEDC (IC50= 522 g/ml). The phenol level in CEDC and MEDC were 50.1 and 38.18 mg, while flavonoids were 65.58and 41.74 /mg.EDC and EDC were showed ant proliferative against MC7 and HALA 1.
Conclusion: The solvents extracts exhibited promising biological activity as antioxidants and ant proliferative action.

Keywords: Algae extract; antioxidant; antiproliferative.

1. INTRODUCTION

Free radicals are the main cause of various chronic diseases, such as cardiac, inflammation, hypertension, diabetes mellitus and neoplasia [1-3]. The damage subsequently leads to degenerative diseases [4,5]. The drug discovery using natural products such as medicinal plants or marine organism still as an important target for recent research. Marine microorganisms such as green and blue algae were identified as rich sources of biologically active compounds [6]. Nowadays, some countries during food processing add a variety of algae, which have high contents of fiber, minerals, vitamins and scavenging activity against free radicals [7]. Marine algae considered as reservoir of raw active materials which important in pharmaceutical biology, complementary medicine, food supplements, antibacterial and safe cosmetics [8].

The Saudi coast lines in Red Sea contain different species of marine algae, however; there are a few studies on the biological effects of the marine algae in this region. This study will design to explore *in vitro* antioxidant and antiproliferative activity of the algae extract. The main objective is to investigate the possibility of using different algae extracts that posses biological activity as antioxidant, antiproleferative. Secondly identification the active ingredients related to their biological activity to be used as complementary and alternative medicine in different diseases.

2. RESEARCH DESIGN

2.1 Materials and Methods

Samples of different types of algae were becollected from red sea at Jeddah city and were identified by Stuff members of marine biology at King Abdulaziz University.

2.1.1 Preparation of algae extracts

The algae samples (*Gracilaria dendroides* - Rhodophyta, *Dictyota ciliolata* - Phaeophyceae, and *Cladophora socialis* - Chlorophyta)were air-dried at room temperature, grounded to powder with glass homogenizer. Twenty grams of each sample were extracted with 400 ml Methanol-H2O (70:30) at room temperature. Then evaporated under vacuum. The residues were extracted in 100 ml chloroform and then the solvent will be evaporated under vacuum. The residue were be dissolved in 100 ml of distilled water and stored at 20°C till use [9]. The different extracts (methanol, ethanol and water were tested) for antioxidant and antiproliferative activity.

2.2 Methods

2.2.1 Toxicity test (determination of LD50)

Algal toxins are considered as a public health problem. For this reasons, toxicity will be measured by cell count viability [10].

2.2.2 Determination of superoxide radicals Inhibition

Superoxide radical produced by the xanthine oxidase will be measured by its capacity to reduce nitroblue tetrazolium [11]. Percent scavenging of superoxide radical will be calculated by comparing treated and untreated with extract.

2.2.3 Diphenylpicrylhydrazyl assay

The antioxidant activity of algae extract will be evaluated by the inhibition percent of oxidation of DPPH reagent in methanol [12].

2.2.4 Hydroxyl radical ($OH^{\bullet}$) scavenging

Hydroxy radical ($OH^{\bullet}$) could be measured at 532 nm [13].

2.2.5 Anti-proliferative activity of algae extract

Differnet cell lines (MB-231 and MCF-7) will be obtained from the Excellence center of human genome at KFMRC, king Abdulaziz University. Cells will be grown in RPMI media with 10% fetal bovine serum. Cell growth inhibition following exposure to algae extract will be determined by tetrazolium MTT assay [14]. The number of viable cells will be proportional to the extent of formazan formed. The antiproliferative potency of algea extracts was measured using MTT (3-(4, 5-dimethylthiazol- 2-yl)-2,5-diphenyltetrazolium bromide) assay.

2.2.6 Anti-apoptotic activity of algae extract

The cell line will be collected and DNA will be separated and subjected for DNA fragmentation by diphenylamine assay and detection of P53 [15].

3. RESULTS

Fig 1. Comparison of means of % reducing power capacity of *Dictyota ciliolate.* at different weights of extracts resulting from three solvents in comparison to the reference of Vitamin C. The labels on the graph are as follows: A, Vitamin C as reference; B, Methanol extract (ME); C, water extract (WE); D, Chloroform extract (CE). The alphabet labels of the curves, with different asterisk's superscripts, indicate significant differences of all means that established the curves ($P< 0.05$).

Fig. 2. The labels on the graph correspond to the following: A, Gallic acid used as a reference; B, ME; C, water extract (WE)(CE). The alphabet labels of the curves, with different asterisk's superscripts, indicate significant differences of means that established the curves between scavengers' concentrations of 20-80 mcg/ml ($P< 0.05$). Fig. 3. Comparison of the mean % scavenging activity against hydroxyl radical at different concentrations of the three different extracts of *Dictyota ciliolata*and the control-Vitamin C. The labels on the graph correspond to the following: A, Vitamin C; B, (ME); C, (WE); D, (CE). The values that constructed the curves represent Means ± SD of three samples of the plant material, analyzed individually in triplicate (n = 1x3x3). The alphabet labels of the curves, with different asterisk's superscripts, indicate significant differences of means that established the curves between scavengers' concentrations of 20-60 mcg/ml ($P< 0.05$). Fig. 4. Comparison of the mean % scavenging activity against nitric oxide radical at different concentrations of the three different extracts of *Dictyota ciliolate* and the control-trolox. The labels on the graph correspond to the following: A: control-Trolox; B, (ME); C, (WE); D, (CE). The alphabet labels of the curves, with different asterisk's superscripts, indicate significant differences of means that established the curves between scavengers' concentrations of 20-100 mcg/ml ($P< 0.05$).

4. DISCUSSION

New strategy for chemotherapy depend on their efficacy and lower side effect and increased its bioavailability in target tissues. In addition complementary medicine is important in cancer therapy. Increasedprevalence of cancer due to exposure to environmental pollution and treatment with chemotherapy lead to undesired side effects (as hair falling and affect blood components) in addition to psychological effects. Recent research was focused on medicinal plants as source of antitumor of natural product. For this reason we are looking for a new source as marine algae extract as a potential natural antioxidant and anti-proliferative activity with lowest side effects. The antitumor metabolites of natural products extracted from marine algae depend on the presence of bioactive molecules that have.

Flavonoids are considered as functional foods widely distributed in different species of plant. These active compounds exert a potent biological effects on target tissues and binds to biomolecules showed free radical scavenger, anticancer, hypocholeserolemic and antiobese action [15].

Table 1. The impact of different solvents on the recovery of phenolics and flavonoids from *Dictyota ciliolata (DC)*(Mean ±S.D)

Extracts	Phenolic (mg/g)	Flavonoids (mg g)
methanol	79.3±2.9[a]	80 ±7.0 [a]
water	25.5±3.2[b]	14.5±4.8[b]
Chloroform	58.9±4.8[b]	51.2±3.3[b]

[a-b] significantly different at P< 0.05)

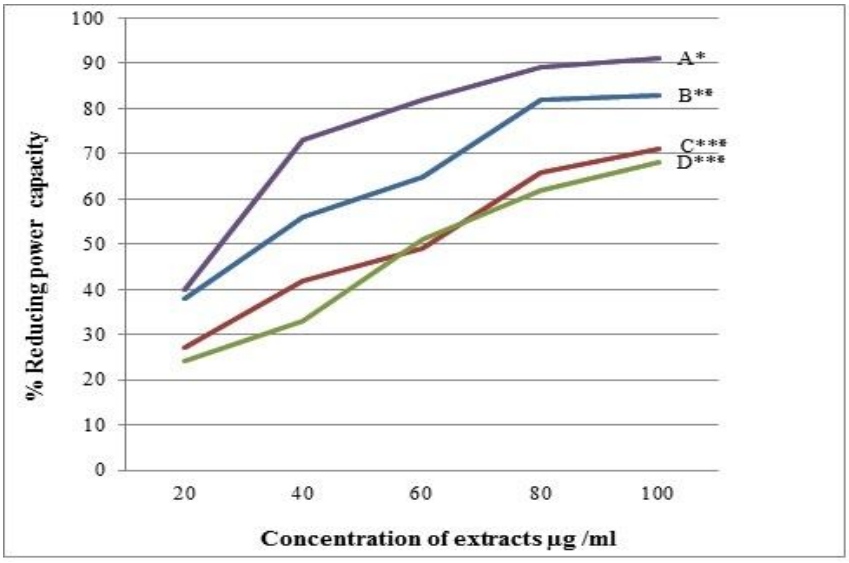

Fig. 1. Comparison of means of % reducing power capacity of *Dictyota ciliolata*

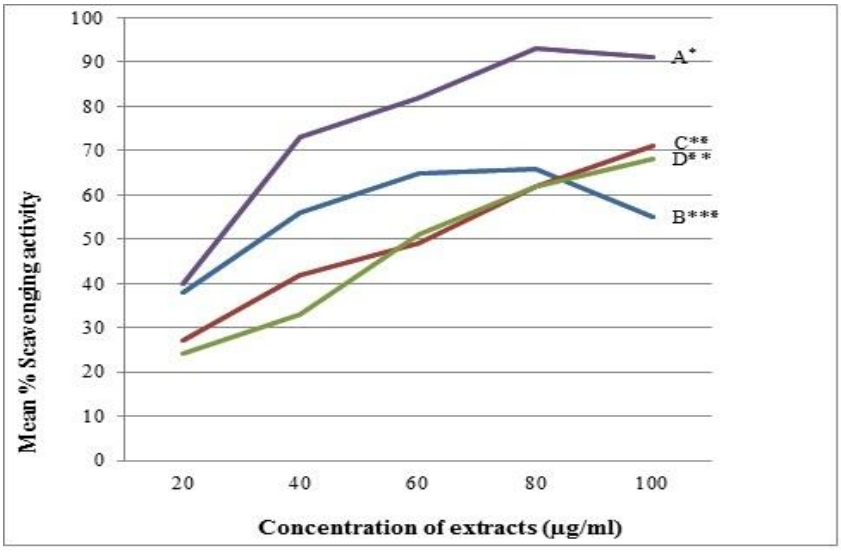

Fig. 2. Comparison of mean % radical scavenging activity against DPPH

According to the previous reports in literature algaeare considered as a main source of fiber, high proteins and, trace elements, probiotics and showed a potent health promotion. Moreover, the results of this study suggested that flavonoids exert cell cycle arrest by inhibiting cell proliferation on different cell lines [16,17]. In addition, Quercetin and showed antitumor action

Table 2. Caspase-8 and caspase-9 levels treated cell line with *Dictyota ciliolata* (CEDC) or vincristine (Mean ±SD)

Parameter	No treatment	CEDC	Vincristine
Caspase-8			
Mean±SD	0.41±0.23	0.785±0.16[a,b,c]	1.3±0.28 [a,c]
Caspase9			
Mean±SD	0.37±0.01	0.95±0.17 [a,b,c]	1.09±0.18[a,c]

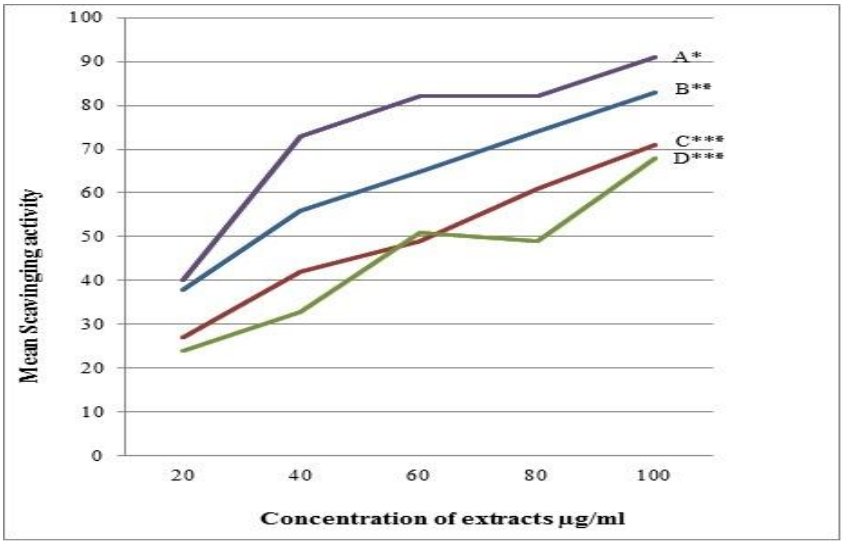

Fig. 3. Comparison of the mean % scavenging activity against hydroxyl radical

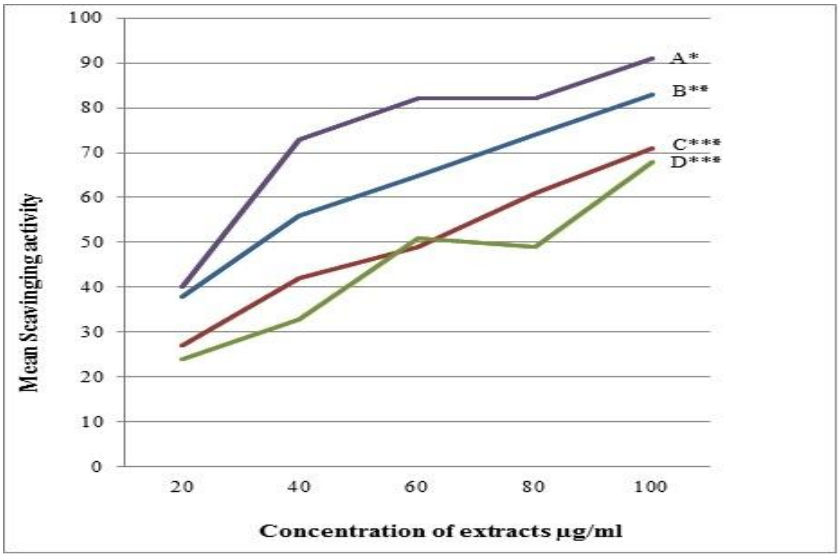

Fig. 4. Comparison of the mean % scavenging activity against nitric oxide radical

in vivo and *in vitro* trails. Further results of the present study also indicated remarkable differences in antibacterial activities among the tested bacterial pathogens which may be attributed to the exposure of marine algae to the combined effect of light and oxygen, this

generate the formation of reactive oxygen radicals. But seaweeds suggested that their protective antioxidative defense systems [18]. Indeed, marine algae containpolyphenols, carotenoids and flavonoids referred to as antioxidants, protect the body's tissues against oxidative stress and associated pathologies such as cancer and inflammation [19].

It was found that, MEDC can stimulate programme cell death via activation of caspase in cell line. The antiproliferative action of algae extracts are mediated via cell cycle arrest, which analog to Trolox. This is in agreement with Scagel [20] who reported that apoptosis is detected by cell shrinkage, membrane blebbing, DNA fragmentation [21,22].

MEDC has promising anti-cancer activity with higher activity than CDDC extracts.

The Red sea marine environment of the Jeddah Seashore has potential to return pharmaceutically useful seaweeds which can be harnessed for the development of drugs for use in management of human cancer, There is great scope for further investigations toward drug development

5. CONCLUSION

Usefulness and utilization of environmental natural product marine sources that are rich with active ingredients may act as free radical scavenger and anti-proliferative potential against different types of tumors. This will spotlight on new drug discovery with lowest side effects of chemotherapy.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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