Trop J Nat Prod Res, April 2021; 5(4):603-608 **ISSN 2616-0684 (Print)**
ISSN 2616-0692 (Electronic)

Tropical Journal of Natural Product Research

Available online at https://www.tjnpr.org

Review Article

Sea Lettuce (*Ulva lactuca*) as a Source of Dietary Antioxidant

Luh P. R. Sundari[1]* and Putu A. W. Wijaya[2]

[1]*Physiology Department, Faculty of Medicine, Udayana University, Bali, Indonesia*
[2]*Biomedic Science Postgraduate Program, Faculty of Medicine, Udayana University, Bali, Indonesia*

ARTICLE INFO

Article history:
Received 16 February 2021
Revised 19 March 2021
Accepted 11 April 2021
Published online 03 May 2021

ABSTRACT

Sea lettuce (*Ulva lactuca*) is a local food with high antioxidant activity. It exists as a green algae and lives in shallow waters, especially on rocky beaches. Several studies have demonstrated *Ulva*'s bioactive compounds and their antioxidant effect on several health parameters. The plant is also known to contain vitamin C, total phenolics, and Vitamin E (alpha-tocopherol), hence, it has anti-peroxidation and anti-hyperlipidemic effects. In addition, *Ulva lactuca* also has anti-inflammatory effect due to its ability to inhibit free radicals. This review will discuss how the active ingredients contained in *Ulva lactuca* act in the body that they can be a potential dietary source of antioxidants.

***Keywords*:** Sea lettuce, *Ulva lactuca*, Vitamin C, Vitamin E, Antioxidant.

Introduction

In Indonesia, sea lettuce is found on the east coast including the Bali Region, namely Serangan Beach, Sanur, Nusa Penida, Sawangan Beach, and Nusa Dua.[1] Several studies have demonstrated *Ulva*'s bioactive compounds and its antioxidant activity effect on several health parameters.[2-5] Previous research reported that sea lettuce contains vitamin C (35.64 mg / 100 g), total phenolic (694.57 mgGAE / 100 g), and α-tocopherol (308.54 mg / 100 g),[5] and showed that *Ulva lactuca* crude polysaccharide had anti-peroxidation and anti-hyperlipidemic effects in *D-Galactosamine* induced rat. Meanwhile, *D-Galactosamine* is an agent which induces inflammation in the liver. Previous studies have shown that *Ulva lactuca* prevents an increase in levels of *free fatty acids*, triglycerides, and total cholesterol in both tissue and serum.[2]

Ulva lactuca content which acts as anti-hyperlipidemic is vitamin E(or alpha-tocopherol) and its polyphenols.[2,3] Vitamin E is known to modify lipid metabolism through activation of Peroxisome proliferator-activated receptor alpha (PPARα) which incite an increase in β-oxidation of fatty acids.[6] Polyphenols demonstrate its anti-hyperlipidemic effect through *Carnitine Palmitoyltransferase* (CPT1A1) activation which also induce β-oxidation of fatty acids.[7] Besides, *Ulva lactuca* also possesses anti-inflammatory effect due to its ability to inhibit free radicals hence, preventing the activation of inflammatory cytokines and chemokines such as TNF-α, IL-1, IL-2, IL-4, IL-6, and IL-8.[8-10] *Ulva lactuca* has a hepatoprotective effect on *D-galactosamine* induction, in addition, the plant possess a strong inhibitory effect on superoxide formation and decreases intracellular ROS.[4] This indicates that *Ulva lactuca* possesses antioxidant effect. Several studies have also demonstrated the anti-oxidizing ability of Ulva lipids using *Malondialdehyde* (MDA) marker. Meanwhile, *Ulva lactuca* extract prevents MDA increase and intensify the activity of antioxidant enzymes *in vitro* and *in vivo*.[11,12]

*Corresponding author. E mail: luhputu_ratnafk@unud.ac.id
Tel: +6281933070077

Citation: Sundari LPR and Wijaya PAW. Sea Lettuce (*Ulva lactuca*) as a Source of Dietary Antioxidant. Trop J Nat Prod Res. 2021; 5(4):603-608. doi.org/10.26538/tjnpr/v5i4.1

Official Journal of Natural Product Research Group, Faculty of Pharmacy, University of Benin, Benin City, Nigeria.

Materials and Methods

The review was conducted from the available literature on the internet that discuss about discovery and development of *Ulva lactuca* as antioxidant. The researchers used the search terms sea lettuce, *Ulva lactuca*, Vitamin C, Vitamin E and antioxidant on Google Scholar, PubMed, ScienceDirect, directory of Open Access Journal (DOAJ), ResearchGate search engines. From the results, articles that have a definite relationship with the subject matter were included in this review and otherwise were excluded.

Dietary antioxidants

Antioxidants are compounds that counteract or reduce the negative effects of an oxidant. This compound act by donating an electron to the oxidant compound hence, inhibiting its oxidant effect. Furthermore, at certain levels, these compounds are able to inhibit the damage caused by oxidation processes and protect the body from free radicals.[13]

The body contain antioxidants in small amounts and has no reserves. Moreover, when the free radicals level increases, the body require additional antioxidants to inhibit the resultant effects. These additional antioxidants are obtained from exogenous antioxidants of food origin.[13,14]

Antioxidants possess several endogenous and exogenous components which function synergistically to inhibit free radicals. These antioxidants types include:[14]

Nutrient-derived antioxidants, such as ascorbic acid (vitamin C), tocopherols and tocotrienols (vitamin E), carotenoids and other low molecular weight compounds such as glutathione and lipoic acid.

Antioxidant enzymes, such as superoxide dismutase, glutathione peroxidase and glutathione reductase, catalyzes free radical reactions.

Metal-binding proteins, such as ferritin, lactoferrin, albumin and ceruloplasmin are capable of trapping free iron, and copper ions which also catalyzes oxidative reactions.

Phytonutrient antioxidants are present in large quantities in plants.

Dietary antioxidants are secondary metabolites, synthesized by plants to protect themselves from oxidative stress. Based on the chemical properties, dietary antioxidants are grouped into four namely, vitamin C (ascorbic acid), vitamin E (tocopherol), carotenoids (α and β-carotene, lycopene, lutein), and polyphenols. Meanwhile, each group differs in the average antioxidant potential, absorption, and availability to the environment. Phenols and flavonoids have with the highest environmental availability and are found in almost all types of food. These two compounds also have the highest antioxidant potential *in vitro*, followed by carotenoids, vitamin E, and vitamin C.[10,13,14]

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

The mechanism of action dietary antioxidant is to reduce oxidative stress by scavenging free radicals through three major pathways depending on the reactive species at play. Tocopherols and most polyphenols donate hydrogen ions, while carotenoids act by deactivating singlet oxygen and ascorbic acid by transferring electrons. Phenolic compounds inhibit free radicals by transfer of a hydrogen atom, from its hydroxyl group. The reaction mechanism of a phenolic compound with a peroxyl radical involves a concerted transfer of the hydrogen cation from the phenol to the radical, forming a transition state of an H-O bond with one electron. Carotenoids are characterized as excellent peroxyl radical scavengers. The polyunsaturated chains that make up the base structure of carotenoids give these compounds a lipophilic character. Carotenoids play an important role in the protection of cell membranes and lipoproteins against peroxyl radicals. Vitamin C is chemically capable of reacting with most of the physiologically important ROS and acts as a hydro soluble antioxidant. The antioxidant reaction mechanisms of vitamin C are based on the hydrogen atom transfer to peroxyl radicals, the inactivation of singlet oxygen, and the elimination of molecular oxygen.[14]

Characteristics of Ulva lactuca

Sea lettuce or *Ulva lactuca* is a marine macroalga which belongs to the phylum Chlorophyta. It thrives in shallow waters, especially on rocky beaches in America, Europe, Africa, the Caribbean, Indian Ocean, East and South Asia, Australia as well as Indonesia. Sea lettuce is found on the eastside coast of Bali, including Serangan Beach, Sanur, Nuda Penida, Sawangan Beach, and Nusa Dua.[1,5]
Furthermore, sea lettuce is widely used globally as a food ingredient. However, the *Ulva lactuca* species are not widely used despite its abundance and it is easy to obtain. Sea lettuce is high in carbohydrates (up to 60%), protein (10-47%), but low in fat content (1-3%). Several bioactive compounds are also contained in their extracts including vitamin C, phenol, and α-tocopherol.[5,15] Meanwhile, previous studies have shown that *Ulva lactuca* possesses antioxidant, anti-inflammatory, antihyperlipidemic and hepatoprotective effects.[2-4,9,12]
Ulva lactuca belongs to the Chlorophyta division with high chlorophyll content which gives it the green color. It is found in seawater and has the morphology of a thin and flat thallus like a sword consisting of two cellular layers. All cells are identical in shapes, except the basal cells which undergo elongation to form attached rhizoids. In addition, each cell consists of a nucleus, cup-shaped chloroplasts, and pyrenoids.[1] *Ulva lactuca* often reaches 100 cm in length and has an irregular round shape with smooth edges in form of rope-shaped blades (folded sword) with a blade diameter of 30-65 cm. The middle part is pale and it has darker edges (Figure 1). Generally, *Ulva lactuca* is yellowish-green to dark green. Besides, in tropical areas, this lettuce is usually found in shallow water (upper intertidal zone to a depth of 10m) while the Ulva species thrives at a temperature of 28-31^{0}C.[9]

Nutritional value of ulva lactuca

Ulva lactuca has various nutritional composition depending on several factors, including geographical origin, physiological factors, and environmental variations. In example, *Ulva lactuca* in Indonesia contains water, carbohydrates, protein, fiber, ash and vitamins. Several studies conducted in different countries have produced varying results. The difference composition of Ulva lactuca are shown in Table 1.[1, 9,16]
This plant also contains vitamins such as vitamin A, B1 and B2 (<0.5 IU / 100mg, 4.87 mg / kg and 0.86 mg / kg respectively) as well as calcium (1828 mg / 100g).[1] Meanwhile, the qualitative and quantitative phytochemical contents are presented in Table 2.[17]

Bioactive compound of ulva lactuca

Ulva lactuca also contains a lot of bioactive compounds. In addition, this sea lettuce is known to possess antioxidant, antimicrobial, antiviral, antihyperlipidemic, anti-tumor and anti-inflammatory effects.[9] Both original ingredients and chemical extracts have a fairly high antioxidant activity. A research by Yu Qing showed that chemically extracted *U. lactuca* has higher antioxidant activity compared to the original ingredients. By measuring IC50, the antioxidant potential was 16.5-18.7 µg / mL and about 34 bioactive components were obtained through HPLC *(High-Performance Liquid Chromatography)* and TLC *(Thin Layer Chromatography)* examinations.[9] The major bioactive components are presented in Table 3.[9]
A study in India showed that *Ulva lactuca* has a total antioxidant activity of 6.203% at a concentration of 1 mg/ml with ethanol extract (10 mg/ml) using DPPH radical scavenging activity method. The highest total phenol content was obtained using chloroform extract (26.53), ethanol extract (22.02) and ethyl acetate extract (21.25) at 765 nm.[18]
A study in Indonesia found that the antioxidant activity of *Ulva lactuca* with gallic acid and ethanol extract was 0.912 ug/ml and 1426.616 ug/ml using the ES50 value. Furthermore, *in vivo* test with malondialdehyde (MDA) as lipid peroxidation marker in rats administered with ethanol extract of *Ulva lactuca* at 200 mg/kg and 400 mg/kg doses were 2.57 and 4.76. Sea lettuce ethanolic extract has several bioactive compounds including vitamin C, total phenolic and α- tocopherol. At separate solvent concentrations, different levels of active compounds were obtained. However, the best levels were obtained at 90% solvent concentration.[5] In Table 4, the bioactive compounds were presented based on countries namely, India (methanol extract), Egypt (hot water extract) and Indonesia (ethanol extract).[5,17]

Potential utilization Ulva lactuca

Ulva lactuca is a local natural resource, it is easy to find and cultivate; and it has various potential usages. In general, different types of seaweed and sea lettuce are used as food ingredients. Furthermore, this lettuce is used pharmacologically as anti-inflammatory, antibacterial, antifungal, antiviral, cytotoxic, antioxidant, antihyperlipidemic and anti-tumor.[9,20] As a food ingredient, *Ulva lactuca* is processed into nori or dried seaweed. The high fiber content facilitates the digestive process. Furthermore, it contains high protein content hence, *Ulva lactuca* is the source of healthy food with great benefits for humans.[21]
In addition, Ulva is used as a bioethanol material due to its high mineral and polysaccharide content including cellulose and hemicellulose. It is also an alternative biomass source for various purposes in food and bioenergy fields.[22]
A study on *Ulva lactuca* extract taken from Iranian waters produced the highest antioxidant as well as the best radical scavenging effect compared to 3 other algae types namely, *U. intestinalis, P. pavonica and P. gymnospora*.[23] In addition, the solvent type also produces different levels of antioxidant activity. Several studies found that the methanol extract was the best, however, other studies found that the ethanol extract showed better antioxidant activity.[24] The high antioxidant activity was detected in this lettuce indicates a potential source of new marine supplements.[25]
Ulva lactuca contains high levels of vitamin C (35.64 mg / 100g), total phenolic (694.57 mg / 100g) and α-tocopherol (308.54 mg / 100g).[5] Meanwhile, the bioactive compounds in *Ulva* have antioxidant, anti-inflammatory and anti-hyperlipidemic effects.[2-5,9] *Ulva lactuca's* crude polysaccharide has anti-peroxidation and anti-hyperlipidemic effects in rats induced by *D-Galactosamine*, which triggers inflammation in the liver. It was found that *Ulva lactuca* prevents an increase in levels of *free fatty acids*, triglycerides and total cholesterol in tissues and blood serum.[2]
Ulva lactuca also demonstrated antioxidant and hypolipidemic effects in a study on hypercholesterolemic rat model. Extract administration showed a decrease in serum fat (-61%), total cholesterol (-49.6%), triglycerides (-66%) and LDL cholesterol (-93%) compared to the control which was given atorvastatin as drug of choice for hypercholesterolemia. In addition, treatment with *Ulva* extracts also inhibited the increase in hepatic *thiobarbituric acid reactive species* (TBARS), where TBARS indicated lipid oxidation in the liver.[3]

Vitamin E (α-tocopherol) in Ulva lactuca

Apart from the high fiber and amino acid content, *Ulva lactuca* also contains high α-tocopherol.[26,27] Meanwhile, the antioxidant activity was found to be related to the content of vitamin E (*the major lipid soluble antioxidant).*[10,14,28] Alpha-tocopherol is the most active form found in tissue and blood plasma. It acts as a breaker of oxidant chains by donating hydrogen atoms from its phenolic hydroxyl groups to bind lipid *peroxyl radicals.* Other mechanisms of action sometimes interact with other cellular components thereby increasing antioxidant coverage. Vitamin E increases *superoxide dismutase* (SOD), the body's antioxidant enzyme, which works by breaking down superoxide radicals into oxygen and hydrogen peroxide. Moreover, Vitamin E also suppresses peroxidation and inhibits the expression of transforming growth factor beta (TGF-β) associated with

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

hepatic fibrosis and apoptosis as well as hepatic stellate cell activation.[10,28] Apart from the antioxidant properties, vitamin E has also exhibit anti-inflammatory and anti-hyperlipidemic effects. Several studies have shown that vitamin E is associated with increased levels of mRNA and adiponectin protein. Meanwhile, adiponectin is an important molecule which suppresses liver fatty acid synthesis and reduces inflammation in nonalcoholic steatohepatitis (NASH) patients.[8,10,29] Vitamin E also prevents NF-kB nuclear localization, suppresses COX-2 expression, as well as cytokines TNF-alpha, IL-1, IL-2, IL-4, IL-6 and IL-8 to prevent inflammatory response to non-alcoholic fatty liver disease (NAFLD).[8,10,30]

Alpha-tocopherol execute its anti-hyperlipidemic effect through the peroxisome proliferator-activated receptor (PPAR) alpha mechanism which is also involved in the NAFLD pathogenesis. Furthermore, PPAR is an intracellular transcription factor included in the nuclear hormone receptor superfamily, it is activated by ligands and it consists of three subtypes namely; PPARα, PPARγ and PPARβ. In general, PPAR plays a role in energy homeostasis and metabolism. PPARα modifies free fatty acids β-oxidation and regulates lipogenesis-related genes thereby, triggering a decrease in serum TG lipid levels.[3,6]

Administration of alpha-tocopherol was found to reduce serum and liver malondialdehyde (MDA) levels, increase PPAR-α expression, decrease PPAR- expression and also improve insulin resistance, serum triglyceride (TG) levels as well as very-low-density lipoprotein-cholesterol (VLDL-C) in rats treated with high-fat diet.[6,12] Increasing the PPAR-α expression also lead a rise in β-oxidation of fatty acids in the liver, resulting to the up-regulation of uncoupling protein-2 (UCP2) mRNA. In addition, activation of this factor causes rapid usage of liver lipids hence, it is capable of reducing TG levels.

Meanwhile, PPAR-γ expression decreases with alpha-tocopherol administration. Figure 2 shows the role of PPAR in liver fat metabolism.

Vitamin C in Ulva lactuca

Vitamin C is one of the bioactive compounds found in *Ulva Lactuca* and broadly regarded as an antioxidant.[5,14] It is a water-soluble *dietary antioxidant* capable of neutralizing ROS in the aqueous phase before lipid oxidation. This occurs by capturing free radicals and plays a role in several enzymatic reactions as a reducing agent. Vitamin C decreases the formation of mitochondrial ROS and increases the activity of *manganese superoxide dismutase* (SOD) and *glutathione peroxidase* (GPx). It also influences adiponectin which tends to reduce hepatic lipid accumulation, systemic insulin resistance, inflammation and inhibit NAFLD.[31,32]

A study conducted with vitamin C supplements on NAFLD showed that vitamin C reduce NAFLD especially in middle age and elderly.[32] Moreover, other studies have also shown that the combination of vitamin C and E tends to reduce inflammation and fibrosis in NASH patients.[2,33]

Polyphenols in Ulva lactuca

Polyphenols are antioxidants with the highest environmental availability, found in almost all types of food. Generally, the mechanism of action is to donate hydrogen ions hence, to reduce oxidants.[9,13,14] A study in Egypt indicated high phenol content (0.75 $\pm$ 0.05 mg / 100g) in *Ulva lactuca* obtained from the Abu-Qir Bay during the summer.[34] It is confirmed that *Ulva* as a potential antioxidant as well as a healthy food source capable of being developed into food coloring and food preservatives.[34-36]

Ulva lactuca contains high levels of macromolecular anti-oxidants up to about 42% of the total polyphenol content. Therefore, apart from the high fiber content which is good for nutrition, it also exhibits antioxidant activity which inhibits free radicals.[37] It was supported by a research which reported that beside of the high polyphenol levels, *Ulva lactuca* also contains amino acids and fatty acids, which are useful as anti-free radicals.[38] A study on the benefits of *Ulva lactuca* in rats administered with high doses of paracetamol indicate significant results as a hepato-protector and an antioxidant, hence, it was concluded that polyphenol act as an antioxidant which stimulates an increase in the glutathione enzyme in the liver as well as the total plasma protein.[39]

A research using a rat model for NAFLD reported that *dietary polyphenols* inhibit intracellular steatosis with some polyphenols (resveratrol, quercetin, catechin) and also protects against mitochondrial dysfunction as well as anaerobic metabolic disorders. Furthermore, curomanin and berberine inhibit steatosis more specifically by modulating lipid metabolism (lipogenesis and lipid oxidation).[7]

The antisteatotic effect of polyphenols is due to the increased expression of the enzymes involved in fat oxidation, such as hepatic mitochondrial enzyme CPT1A1 (*Carnitine Palmitoyl-transferase*) and decreased expression of the lipogenic enzyme, FAS (*Fatty Acid Synthase Complex*). Furthermore, the increase in CPT1A1 expression was found to intensify β-oxidation of mitochondrial fatty acids. This is consistent with previous studies in which *flavonoid-rich extracts* were found to induce *dose-dependent* CPT1 mRNA increase in samples of a high-fat diet.[7,40]

PPARα is a transcription control gene which plays an important role in lipid metabolism, inflammation and fibrosis. When it is activated, it induces f*atty acid oxidation-related genes*, such as CPT1A1. Polyphenols were reported to sufficiently trigger PPARα expression.[40] Figure 3 below shows a mechanism of action polyphenol compounds, tocopherols and other antioxidants.

Figure 1: *Ulva lactuca* [1]

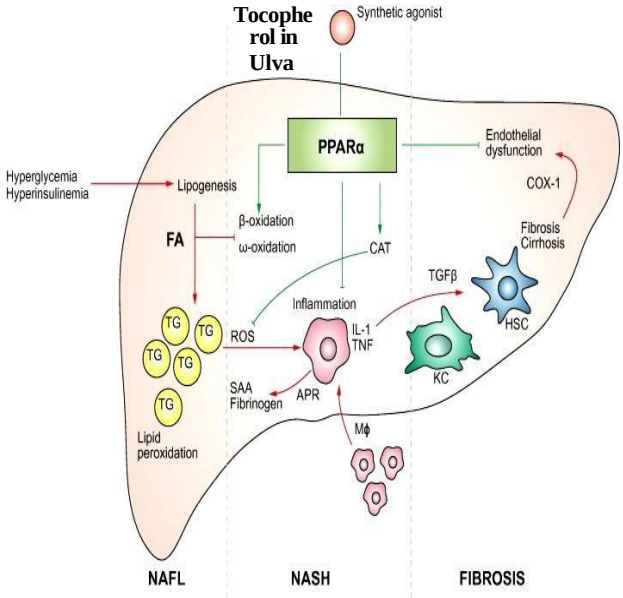

Figure 2: Role of PPARα on Fat Metabolism. PPARα plays a role in *β*-fatty acid oxidation by preventing triglycerides build-up.[6,12]

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

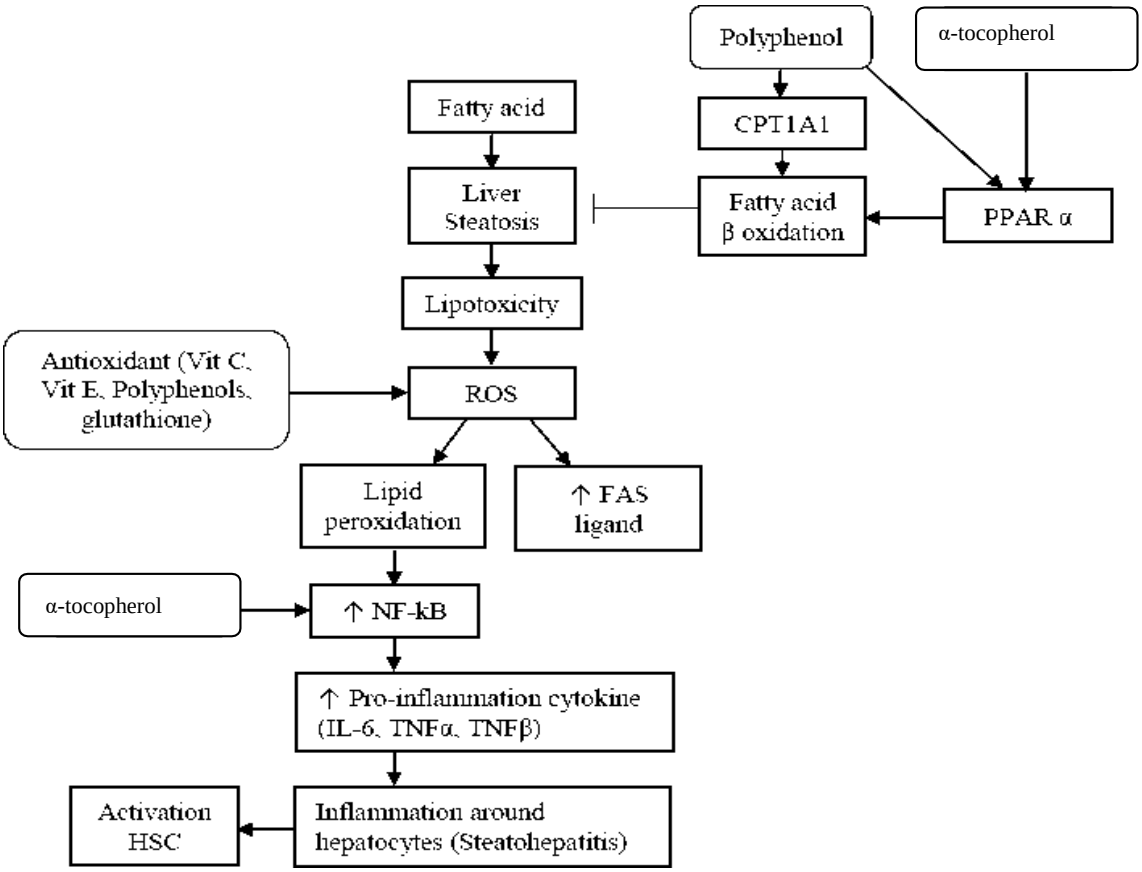

Figure 3: Mechanism of Action for Polyphenols, Vitamin E, and Vitamin C Compounds. [7,32,40]

Table 1: Nutritional Composition of *Ulva lactuca* Found in Indonesia, Tunisia and China

Nutritional Composition	Indonesia	Tunisia Values (%)	China
Protein	15-16	27.2	8.46
Fat	0.1-0.7	0.3	7.87
Carbohydrate	46-51	61.50	59.10
Fiber	2-5	60.50	54.90
Ash	16-23	19.59	-

Table 2: Phytochemical Contents of *Ulva lactuca*

Compound Tested	Qualitative	Quantitative (mg/100g)
Alkaloids	+	75.58 ± 4.5
Tannins	-	
Plobatin	-	
Saponins	+	0.03 ± 0.0002
Flavonoids	+	2.36 ± 0.04
Terpenoids	+	
Cardiac glycosides	+	
Total phenol (mg/ml)	+	14.233 ± 1.2

Table 3: Major Fractions of *Ulva lactuca* Bioactive Components

Bioactive Compounds	Content
Chlorophyll-a	15.60-30.90%
Chlorophyll-b	12.20-14.89%
α-carotene	11.44-11.47%
β-carotene	6.16-29.70%
α-tocopherol	14.4 µg/ml
Butylated hydroxyanosil (BHA)	13.1 µg/ml
Butylated hydroxytoluene	13.1 µg/ml

Table 4: Bioactive Compounds of *Ulva lactuca* Extract [2,5,17]

Bioactive Compounds	Country		
	India (mg/g)	Egypt (mg/ml)	Indonesia (mg/100g)
Vitamin C	4.29	-	35.64
Total Phenolic	-	14.22	694.57
Vitamin E	1.73		308.54

Conclusion

Based on the results, *Ulva lactuca* contains components such as Vitamin C, alpha tocopherol, total phenol which have high antioxidant, anti-oxidation, anti-hyperlipidemic and anti-inflammatory effects. Apart from being a food source, it also acts as an antioxidant hence, provides great health benefits. It is expected that the use of *Ulva lactuca* as a source of antioxidant becomes widely known in the future.

Conflict of interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

References

1. Dewi NNDT, Wrasiati LP, Putra GPG. Pengaruh Konsentrasi Pelarut etanol dan Suhu Maserasi terhadap Rendemen dan Kadar Klorofil Produk Enkapsulasi Ekstrak Selada Laut (Ulva lactuca L.). JRMA. 2016; 4(3):59-70.
2. Sathivel A, Raghavendran HR, Srinivasan P, Devaki T. Anti- peroxidative and Anti-hyperlipidemic Nature of *Ulva lactuca* crude polysaccharide on D-Galactosamine induced hepatitis in rats. Food Chem Toxicol. 2008; 46:3262-3267.
3. Hassan S, El-Twab SA, Hetta M, Mahmoud B. Improvement of Lipid Profile and Antioxidant of Hypercholesterolemic Albino Rats by Polysaccharides Extracted from Green Alga *Ulva lactuca* Linnaeus. Saudi J Biol Sci. 2011; 18:333-340.
4. Sathivel A, Balavinayagamani, Hanumantha Rao BR, Devaki T. Sulfated Polysaccharide isolated from Ulva lactuca attenuates D-galactosamine induced DNA fragmentation and Necrosis during Liver Damage in Rats. Pharm Biol. 2014; 52(4):498-505.
5. Yunita D, Wrasiati LP, Suhendra L. Karakteristik Senyawa Bioaktif Ekstrak Selada Laut (Ulva lactuca L.) pada Konsentrasi Pelarut Etanol dan Lama Ekstraksi. JRMA. 2018; 6(3):189-195.
6. Kim DY, Kim J, Ham HJ, Choue R. Effects of d-α-tocopherol supplements on lipid metabolism in a high-fat diet-fed animal model. Nutr Res Pract. 2013; 7(6):481-487.
7. Rafiei H, Omidian K, Bandy B. Dietary Polyphenols Protect Against Oleic Acid-Induced Steatosis in an *In Vitro* Model of NAFLD by Modulating Lipid Metabolism and Improving Mitochondrial Function. Nutr. 2019; 11(3):541.
8. Chen G, Ni Y, Nagata N, Xu L, Ota T. Micronutrient Antioxidants and Nonalcoholic Fatty Liver Disease. Int J Mol Sci. 2016; 17(9):1379.
9. Yu-Qing T, Mahmood K, Scehzadi R, Asharf MF. Ulva lactuca and Its Polysaccharides: Food and Biochemical Aspects. J Biol Agric Health. 2016; 6(1):140-151.
10. Perumpail BJ, Li AA, John N, Sallam S, Shah ND, Kwong W, Cholankeril G, Kim D, Ahmed A. The Role of Vitamin E in the Treatment of NAFLD. Dis. 2018; 6(4):86.
11. Widyaningsih W, Sativa R, Primardiana I. Efek Antioksidan Ekstrak Etanol Ganggang Hijau (Ulva lactuca L.) terhadap Kadar Malondialdehid (MDA) dan Aktivitas Enzim Superoksida Dismutase (SOD) Hepar Tikus yang Diinduksi CCl_4. Media Farmasi. 2015; 12(2):163-175.
12. Kammoun I, Ben-Salah H, Ben-Saad H, Cherif B, Droguet M, Magné C, Kallel C, Boudawara O, Hakim A, Gharsallah N, Ben Amara I. Hypolipidemic and cardioprotective effects of Ulva lactuca ethanolic extract in hypercholesterolemic mice. Arch Physiol Biochem. 2018; 124(4):313-325
13. Tariq A, Athar M, Ara J, Sultana V, Ehteshamul-Haque S, Ahmad M. Biochemical Evaluation of Antioxidant Activity in Extracts and Polysaccharide Fractions of Seaweeds. Global J Environ Sci Manage. 2015; 1:47-62.
14. Pizzino G, Irrera N, Cucinotta M, Pallio G, Mannino F, Arcoraci V, Squadrito F, Altavilla D, Bitto A. Oxidative Stress: Harms and Benefits for Human Health. Oxid Med Cell Longev. 2017; 2017:8416763.
15. Dominguez H and Loret EP. *Ulva lactuca*, A Source of Troubles and Potential Riches. Mar Drugs. 2019; 17(357):1-20.
16. Yaich H, Garna H, Bichir B, Besbes S, Paquot M, Richel A, Blecker C, Attia H. Chemical Composition and Functional Properties of Dietary Fiber Extracted by Englyst and Porsky Method from the Alga *Ulva lactuca* Collected in Tunisia. Algal Res. 2015; 9:65-73.
17. Elmegeed DFA, Ghareeb DA, Elsayed M, El-Saadani M. Phytochemical Constituents and Bioscreening Activities of Green Algae (*Ulva lactuca*). Int J Agric Pol Res. 2014; 2 (11):372-378.
18. Whankatte VR and Ambhore JS. Research Article: Phytochemical Screening and Antioxidant Activity of *Ulva lactuca*. Int J Curr Res. 2016; 8(9):38265-38269.
19. Mahmud I, Pertiwi R, Azis NR, Reviana DN. Pemanfaatan Potensi ganggang Hijau (Ulva lactuca) sebagai Antioksidan Alami pada Pencegahan Infark Miokard Akut. E-Proceeding PIMNAS PKM-P Ditjen Dikti Kmdikbud RI. [Online]PKM-P 2014. Available at: http://artikel.dikti.go.id/index.php/PKM-P/issue/view/35 downloaded on: 21st March 2018.
20. Ktari, L. Pharmacological Potential of Ulva Species: A Valuable Resource. J Anal Pharm Res. 2017; 6(1):00165.
21. Rasyid, A. Evaluation of Nutritional Composition of The Dried Seaweed Ulva lactuca from Pameungpeuk Waters, Indonesia. Trop Life Sci Res. 2017; 28:119-125.
22. Prasedya E, Martyasari NW, Apriani R, Mayshara S, Fanani R, Sunarpi H. Antioxidant activity of Ulva lactuca L. from different coastal locations of Lombok Island, Indonesia. AIP Conf Proc. 2019; 2199:020003.
23. Kokabi M, Yousefzadi M, Ahmadi A, Feghhi-Amin M, Keshavarz and Mousa. Antioxidant Activity of Extracts of Selected Algae from the Persian Gulf, Iran. Ulum Va Tiknuluzhii Khaliji Fars. 2013; 4:45-50.
24. Alagan V, Rajesh NV, Rajesh KD. Bioactive Chemical Constituent Analysis, *in vitro* Antioxidant and Antimicrobial Activity of Whole Plant Methanol Extracts of *Ulva lactuca* Linn. Br J Pharm Res. 2017; 15:1-14.
25. Zubia M, Robledo D, Freile-Pelegrin Y. Antioxidant activities in tropical marine. Macroalgae from the Yucatan Peninsula, Mexico. J Appl Phycol. 2007; 19(5):449-458.
26. Ortiz J, Romero N, Robert P, Araya J, Lopez-Hernandez J, Bozzo C, Navarrete E, Osorio A, Ríos A. Dietary fiber, amino acid, fatty acid and tocopherol contents of the edible seaweeds *Ulva lactuca* and *Durvillaea antarctica*. Food Chem. 2006; 99.
27. Wrasiati LP, Yunita NLGD, Suhendra L, Wijaya IMAS. Optimization of material concentration and extraction time on yield and α-tocopherol content of sea lettuce (Ulva lactuca L.) IOP Conf Ser Earth Environ Sci. 2019; 230: 012054.
28. Sundari LPR, Adiputra N, Dinata IMK. Supplementation of Vitamin E 400 IU Decreases Malondialdehyde Level of Obese Women Staff at School of Medicine Udayana University. Asian J Pharm Clin Res. 2017; 10(9):61-63.
29. Nan YM, Wu WJ, Fu N, Liang BL, Wang RQ, Li LX, Zhao SX, Zhao JM, Yu J. Antioxidants vitamin E and 1-aminobenzotriazole prevent experimental non-alcoholic steatohepatitis in mice. Scand J Gastroenterol. 2009; 44(9):1121-1131.
30. Rimbach G, Moehring J, Huebbe P, Lodge JK. Gene-

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

regulatory activity of alpha-tocopherol. Molecules. 2010; 15(3):1746-1761.
31. Ipsen DH, Tveden-Nyborg P, Lykkesfeldt J. Does Vitamin C Deficiency Promote Fatty Liver Disease Development? Nutr. 2014; 6:5473-5499.
32. Wei J, Lei GH, Fu L, Zeng C, Yang T, Peng SF. Association between Dietary Vitamin C Intake and Non-Alcoholic Fatty Liver Disease: A Cross-Sectional Study among Middle-Aged and Older Adults. PloS One. 2016; 11(1):e0147985.
33. Foster T, Budoff MJ, Saab S, Ahmadi N, Gordon C, Guerci AD. Atorvastatin and antioxidants for the treatment of nonalcoholic fatty liver disease: the St Francis Heart Study randomized clinical trial. Am J Gastroenterol. 2011; 106(1):71-77.
34. Khairy HM and El-Sheikh MA. Antioxidant activity and mineral composition of three Mediterranean common seaweeds from Abu-Qir Bay, Egypt. Saudi J Biol Sci. 2015; 22(5): 623-630.
35. El baky H, El-Baz F, El baroty G. Evaluation of Marine Alga *Ulva lactuca* L. as A Source of Natural Preservative Ingredient. Am-Euras J Agric Environ Sci. 2008; 3:434-444.
36. Zaatout H, Ghareeb D, Abd-Elgwad A, Ismael A. Phytochemical, antioxidant, and anti-inflammatory screening of the Egyptian Ulva lactuca methanolic extract. Rec Pharm Biomed Sci. 2019; 33-38.
37. Sanz-Pintos N, Pérez-Jiménez J, Buschmann AH, Vergara-Salinas JR, Pérez-Correa, JR, Saura-Calixto F. Macromolecular antioxidants and dietary fiber in edible seaweeds. J Food Sci. 2017; 82:289-295.
38. Fomenko SE, Kushnerova NF, Sprygin VG, Drugova ES, Lesnikova LN, Merzlyakov, V.Yu, Momot TV. Lipid Composition, Content of Polyphenols, and Antiradical Activity in Some Representatives of Marine Algae. Russ J Plant Physiol. 2019; 66:942-949.
39. Ravindran NT and Sadiq M. Pharmacological Activity of Ulva Lactuca Polyphenols Fraction: Hepatoprotective and Antioxidant Activities Against Paracetamol-Induced Liver Damage In Rats. Asian J Pharm Clin Res. 2019; 12:55-58.
40. Yang CQ, Shu L, Wang S, Wang JJ, Zhou Y, Xuan YJ, Wang SF. Dietary Patterns Modulate the Risk of Non-Alcoholic Fatty Liver Disease in Chinese Adults. Nutr. 2015; 7(6):4778-4791.