CHAPTER TWO

Harvesting and potential uses of selected red seaweeds in the Philippines with emerging high-value applications

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Abstract

While seaweed cultivation is indeed practiced globally, it is by no means a mature industry. In part, this is because that in spite of the tremendous biodiversity available within this "polyphyletic rag bag" of distantly-related photosynthetic organisms, very

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few species have actually been studied sufficiently to bring them into domestication for production. This is not unlike the situation with terrestrial agronomy.

The history of extensive cultivation of seaweeds is several centuries old. One of the major, global centers for innovation and production of industrial-scale quantities of biomass for processing has been the Philippines and in turn the Coral Triangle.

However, the species and strains of seaweeds currently in cultivation, often clonally propagated on account of their relative ease of producing propagules, have been victim to their own success. Farmers and industry have simply used the same, limited pool of biomass and techniques for too long. This has led to declines in yield and quality of constituents due to loss of vigor and increased incidences of pests and diseases. Innovation is urgently required both in the choice candidate species for cultivation and also the necessary steps and techniques required for the reliable and sustainable production of industrial quantities of biomass.

Once again, the Philippines is at the forefront of leading technologies for the selection of novel candidate species for responsible, phyconomic activities. These species are economically valuable candidates, not only for their colloidal constituents, but also the more innovative applications of biologically active compounds from seaweeds used for the benefit of human, animal, plant and microbial products. Selected examples of these biologically active constituents and their applications are briefly reviewed.

This chapter summarizes advances being made in the Philippines and outlines developments in several candidate species as future cultivated, marine crops.

1. Introduction

The marine environment has much to offer mankind in terms of the benefits derived from the goods and services supplied by its varied flora and fauna. Seaweeds are one of the major components thriving abundantly, under suitable conditions, distributed from the intertidal to sub-tidal regions of the sea, with some being fully pelagic. Man has explored the sea in search for food, bioactive compounds with medicinal properties, as well as feedstocks for fuel. In spite of a tremendous amount of published work to date, there remains much to discover and develop for both societal and economic benefits to the world.

For more than four decades there has been a great deal of published works presented on economically important red seaweeds including the carrageenophytes – especially the genera *Kappaphycus* and *Eucheuma* (Hayashi et al., 2017). In spite of the fact that there are many success stories related to the socio-economic benefits of eucheumatoid farming in the Philippines and elsewhere, their extensive, open-water farming, for commerce (recently termed phyconomy by Hurtado et al. in press) has been seriously challenged with the deteriorating quality of propagules (seedlings) and lack of strain vigor (Ali, Yashir, Critchley, & Hurtado, 2018; Hurtado et al., 2012).

A number of reasons for this have been put forward including repeated vegetative propagation from a limited genetic stock. Although entirely predictable (with hindsight), the consequences of this practice have contributed to extensive and devastating pest and disease infestations (Critchley et al., 2004; Hurtado & Critchley, 2006; Largo, 2002; Vairappan et al., 2008). Reasons given for this included: increasing abiotic stresses, weak propagules and limited pools from which to select new strains and cultivars, poor crop management, and economic factors such as unstable market prices (Hurtado, 2018).

The rapid geographic expansion of new cultivation sites was the main reason for apparent successes and continued, overall increasing global production of eucheumatoids (FAO, 2017). This was in spite of declining productivity (as in kg per unit area) in some of the already established farming sites affected by pests and disease (Hayashi et al., 2017). Both *Kappaphycus* and *Eucheuma* are commercially cultivated in Southeast Asia and their combined production has come to dominate the rankings of global seaweed production; after 2010 to the present, even surpassing the extensive cultivation of brown seaweeds such as *Laminaria/Saccharina* and *Undaria* (FAO, 2014).

Global seaweed resources are increasingly coming under scrutiny. There are a number scientific reports on the collective biomasses of carrageenophytes which demonstrate their potential as sources of structurally diverse, biologically active compounds with potentially multiple pharmaceutical and biomedical applications (Pere Ribeiro-Claro, 2014; Pereira, 2018b). It must be remembered that seaweeds and their extracts are very complex and, as such, there is no one compound which conveys the many beneficial properties, rather that various seaweeds and their extracts contain many compounds which may work synergistically and/or antagonistically with biological processes. Some of the bioactivity of extracts is as a direct result of the chemical interactions between raw materials and the extraction processes. This is why, while there have been many reports citing beneficial applications of extracts, as demonstrated by model-organism responses and bioassays to date, there is a paucity of available literature on various modes of actions and identification of the constituent bioactive compounds. As an exception to this, some of the more recently published reports have provided an insight into biological activities and neuro-protective effects of marine algal extracts including: antioxidant, anti-neuro-inflammatory conditions, cholinesterase inhibitory activity and the inhibition of neuronal death. Taken together, these studies suggest that specific and selected seaweeds, and the cultivar/strains thereof, have considerable potential to be used as neuro-protective agents which can be assimilated in new products in pharmaceuticals, nutraceuticals, cosmetics and functional foods (Jin et al., 2006; Pangestuti & Kim, 2011).

2. The current status of seaweed resources in the Philippines

The Coral Triangle (CT) which includes: Indonesia, Malaysia, Papua New Guinea, the Philippines, the Solomon Islands and Timor-Leste is one of the most important reef systems in the world. It covers 132,636 km, extending across six countries and occupies just 1.5% of the total ocean area, yet represents 30% of the world's coral reefs. The CT has the highest coral diversity in the world, i.e. 76% of all coral species are found there. Fifteen species are endemic to the region (www.weforum.org). It is a biodiversity-rich region where there is a diversified marine flora and where tropical seaweed farming has become firmly established (Hayashi et al., 2017; Hurtado, Gerung, Yasir, & Critchley, 2014).

The Philippines is an archipelagic country consisting of more than 7000 islands, the shore-lines and reefs of which are endowed with a considerable diversity of seaweeds. Ganzon-Fortes (2012) provided a comprehensive, historical account of studies in to the seaweed biodiversity in the Philippines. The article covered the period from 1750 to the end of the 20th century (1999). The review revealed that the earliest literature contained not only taxonomic studies of commercial species, but also included aspects of their population biology, seasonality, and the yield and quality of their phycocolloids. However, during the last decade of the 20th century, seaweed research trends shifted to more applied aspects of utilization (Buschmann et al., 2017).

The latest report on the seaweed resources of the Philippines was prepared by Trono and Largo (in progress) which provided information on the biodiversity of economically important species of the Philippines, their utilization as food and raw materials in processing and also use of their industrially extracted products such as: agar, carrageenans, alginates, fucoidans, etc. Trono (2010) discussed potential cultivation technologies for the red seaweed *Halymenia durvillei* utilizing both vegetative propagules and spores.

In spite of the tremendous marine biodiversity of the Philippines very few are actually grown commercially and these are really limited to just two genera, viz. *Kappaphycus* and *Eucheuma* (Hayashi et al., 2017). There are still several seaweeds which have a seemingly high potential as candidates for phyconomic development such as: *Asparagopsis taxiformis* (Cordero, 1977; Silva, Menez, & Moe, 1987), *Betaphycus philippinensis* (Doty, 1995; Dumilag, 2018; Dumilag, Liao, & Lluisma, 2014), *Callophyllis adnata* (Hurtado-Ponce, 1983), *Grateloupia filicina* (Hurtado-Ponce, 1983), *H. durvillei* (Trono, 2010) and *Pyropia acanthophora and Pyropia tanegashimensis* (Ame, Ayson, Okuda, & Andres, 2010; Dumilag et al., 2016, 2017).

This chapter presents the case for alternative red seaweeds to be brought on board as candidates to extend phyconomic activities to a greater range of "domesticated" species. Herewith, we discuss seven red seaweeds from the Philippines which are emerging with a high potential for further exploration leading to the development of the required phyconomic techniques for their production. This will ultimately feed a sustainable and reliable supply-chain of raw materials for industrial processing and value-chain-addition and novel applications leading to new products. Such developments have beneficial local, regional and global social and economic values.

3. Brief descriptions, local distribution and uses of red seaweeds with emerging potential applications

Fig. 1 and Table 1 show the distribution of Philippine red seaweeds which are suggested to have considerable potential. Of the seven species, four are restricted in their distribution (i.e. endemic) to northern-most Luzon, e.g. *C. adnata*, *G. filicina*, *Pyropia acanthophora and P. tanegashimensis*. The remaining three, i.e. *A. taxiformis*, *B. philippinensis* (= *Betaphycus gelatinus*) and *Halymenia durvillaei* are distributed around the country.

The marked seasonality of *C. adnata*, *G. filicina*, *P. acanthophora* and *P. tanegashimensis* has dictated their market value in the community (Table 2). These seaweeds are predominantly eaten as fresh, sea vegetable salad, especially by Filipinos in the northern-most part of Luzon. *C. adnata* and *G. filicina* cost around \$0.39 per 100 g or \$3.90/kg fresh weight in public markets, while *P. acanthophora* and *P. tanegashimensis* command the higher price \$15.68/ft^2 dry wt. The high cost of these seaweeds is primarily due to their limited supplies during the northeast monsoon (November – early March) in the northern part of the Philippines (Table 3).

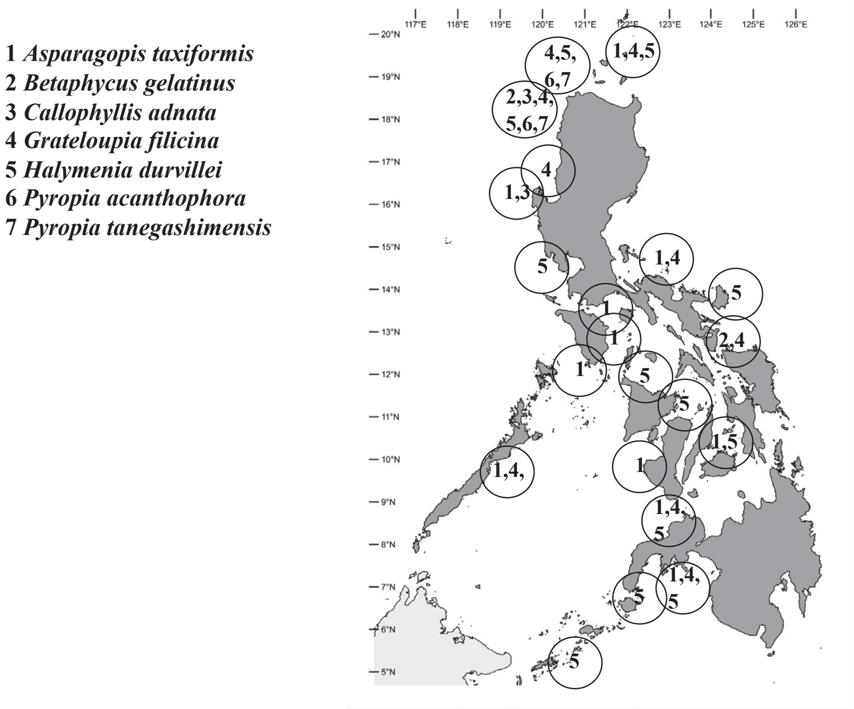

Fig. 1 Distribution of red seaweeds of emerging interest in the Philippines.

Table 1 Distribution of red seaweeds of emerging interest in the Philippines.

Species	**Locations**	**References**
Asparagopsis taxiformis (Delile) Trevisan	LUZON: Batanes, Pangasinan, Quezon, Occidental Mindoro, Oriental Mindoro, Palawan	Silva et al., 1987
	ViSAYAS: Aklan, Cebu, Negros Oriental	Cordero, 1977
	MINDANAO: Zamboanga del Sur	Trono, 1977
Betaphycus philippinensis (=*B. gelatinus*) Doty	LUZON: Sorsogon	Doty, 1995; Dumilag et al., 2014
Callophyllis adnata Okamura	LUZON: Ilocos Norte	Hurtado-Ponce, 1983, 1984; Agngarayngay, 1984a,b
Grateloupia filiciina (Lamouroux) C. Agardh	LUZON: Batanes, Cagayan, Ilocos Norte, Pangasinan, Sorsogon	Hurtado-Ponce, 1983; Silva et al., 1987

Table 1 Distribution of red seaweeds of emerging interest in the Philippines.—cont'd

Species	**Locations**	**References**
	Palawan, La Union,	Trono, 1977
	VISAYAS: Negros Oriental	Trono, 1977
	MINDANAO: Zamboanga del Sur	Trono, 1977
Halymenia durvillei Bory de Saint-Vincent	LUZON: Batanes, Ilocos Norte, Cagayan, Bataan, Catanduanes, Quezon,	Cordero, 1977; Hurtado-Ponce, 1983
	Batangas,	
	VISAYAS: Iloilo, Aklan, Guimaras, Negros Oriental, Negros Occidental;	Cordero, 1977; Trono, 1977; Hurtado, Luhan, & Guanzon, 2006
	Cebu, Siquijor,	
	MINDANAO: Zamboanga City, Zamboanga del Sur, Sulu, Tawi-Tawi	Cordero, 1977; Trono, 1977
Pyropia acanthophora (E.C.Oliveira & Coll)	LUZON: Cagayan, Ilocos Norte	Dumilag et al., 2017
M.C.Oliveira, D.Milstein & E.C.Oliveira		Dumilag & Monotilla, 2018
Pyropia tanegashimensis (Shinmura)	LUZON: Cagayan, Ilocos Norte	Dumilag et al., 2016; Dumilag & Monotilla, 2018
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Table 2 Seasonality of red seaweeds of emerging interest in the Philippines.

Species	**Seasonality**	**References**
Asparagopsis taxiformis	Oct—Nov	Cordero, 1977
	Apr—May	Trono, 1977
Betaphycus philippinensis	Dec—Apr	Doty, 1995
Callophyllis adnata	Nov—Apr	Hurtado-Ponce, 1983 Marcos-Agngarayngay, 1984
Grateloupia filicina	Nov—Apr	Hurtado-Ponce, 1983
	Mar—Jul	Trono, 1977
Halymenia durvillaei	Jan—Dec	Hurtado-Ponce, 1983 Trono, 1977
Pyropia acanthophora	Oct—Mar	Ame et al., 2010
Pyropia tanegashimensis	Oct—Mar	Ame et al., 2010

Table 3 Summary of the utilization of red seaweeds of emerging interest in the Philippines.

				Applications			
Species	Carrageenan			Pharmaceuticals	Human food	Animal feed	Pigment
	Kappa	Lambda	Beta				
Asparagopsis taxiformis				▨		▨	
Betaphycus philippinensis (=B. gelatinus)			▨		▨		
Callophyllis adnata					▨		
Grateloupia filiciina		▨			▨		
Halymenia durvillei		▨			▨		▨
Pyropia acanthophora	▨				▨		
Pyropia tanegashimensis	▨				▨		

4. Sustainable harvesting and utilization of biomass removed from natural populations

Among those red seaweeds described in this paper with a high potential for further exploration and development, only *H. durvillei* has, so far, been scaled-up for phyconomic purposes. It is still in its infancy at the pilot-scale (Trono, 2010) in the Visayas. The under-lying feature has been the necessary research required for the sustainable and reliable production of healthy sporelings for land-based culture.

Unfortunately, all other raw materials of red seaweeds mentioned in this chapter are harvested manually and not necessarily sustainably. There are reports of the total removal of the whole, adult thalli (plant bodies), leaving no basal tissue for future regeneration. Likewise, large waves can bring a considerable amount of sand to areas where ephemeral seaweeds grow, thus covering and hampering the (re-)growth of the seaweed (Pers. Observation). Thus, the total biomass harvests have been rather unstable, unreliable and certainly not practiced in a sustainable manner. Furthermore, indiscriminate gathering of these seaweed resources will ultimately result in severe depletion, or even worse, local extinctions as personally observed.

Each of the emerging red seaweed candidates is dealt with individually regarding their descriptions, methods of production and value proposition in the following sections.

A. taxiformis (Fig. 2) is a tropical species widely distributed throughout the Philippines, as reported by Cordero (1977) and Trono (1977). It has a tri-phasic, diplo-haplontic, heteromorphic life cycle. The alga can be found almost year-round, from the upper inter-tidal to sub-tidal regions.

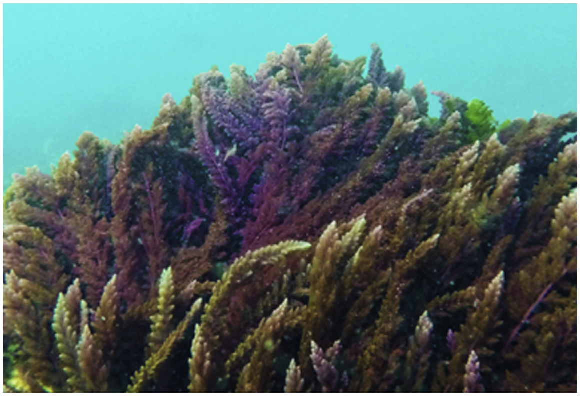

Fig. 2 Photo of *Asparagopsis taxiformis*. (Photo courtesy of N Paul).

Surprisingly there are several reports on the multiple uses of *A. taxiformis*, yet there is no information related to its harvesting, nor commercial cultivation in the Philippines. Recently, *A. taxiformis* became infamous (with considerable global, media attention) in relation to being a potential contributor to the mitigation climate change. A. taxiformis, as a dietary supplement, was found to reduce methane production in cows by more than 99% in laboratory evaluation (Machado, 2015). The mode of action was suggested to be due to the almost total disruption of methanogenic enzymes in the treated animal's gut. This also preserved feed energy for the treated cows which could then be allocated for health and production and not lost as energy/methane gas in to the atmosphere. Ruminant emissions of methane account for approximately 10% of all greenhouse gases (GHGs) each year in Australia (Kinley, de Nys, Vucko, Machado, & Tomkins, 2016). Reports on the intensive culture of *A. taxiformis* in tanks in Australia are known (Paul, Pers. Comm), however, its commercial, extensive open-water cultivation has yet to be piloted. Furthermore, *in situ* studies have to be made on the biology and eco-physiology of A. taxiformis, especially its heteromorphic alternation of generations, in the Philippines. This information is required in order to understand the needs for up-scaling, as required to provide high quality, consistent and regular, large, industrial volumes of material to service the livestock feed and supplements industry. This seaweed has huge potential value to the Philippines in particular since it is endemic and application of best-practice, phyconomic principles (Hurtado, Neish, & Critchley, 2019) for cultivated production could lead to the reliable supply of raw materials to the livestock industry, which in turn could have a significant impact on reduction of methane GHG in the atmosphere.

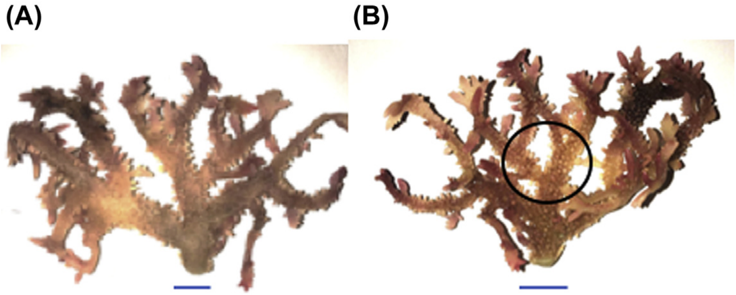

Fig. 3 Photo of *Betaphycus philippinensis*, (A) dorsal, (B) ventral (bar = 1 cm).

B. philippinensis (=*B. gelatinus*) (Fig. 3) thrives on hard coral substrata by means of well-developed haptera; branches are irregular with flattened segments provided with numerous spinous processes at the margin (Cordero, 1977; Doty, 1995; Trono, 1977). Gathering from wild populations of this seaweed is limited to utilization as a source of sea vegetable, especially in northern Luzon (Agngarayngay, 1984b).

C. adnata (Fig. 4) has been reported in Ilocos Norte (Cordero, 1980; Hurtado-Ponce, 1983, 1984; Agngarayngay, 1984a,b). This species grows mostly at the lower edge of the intertidal region where there is moderate wave action. The thallus of *C. adanata* is erect; a flabellate blade arises from a small disc; cystocarps are borne at the margin. This species occurs during the north-east monsoon from December—May. Gathering starts in January reaching a peak in March and April. This seaweed is sold locally in public markets in its fresh form and eaten as a sea vegetable salad. It is a

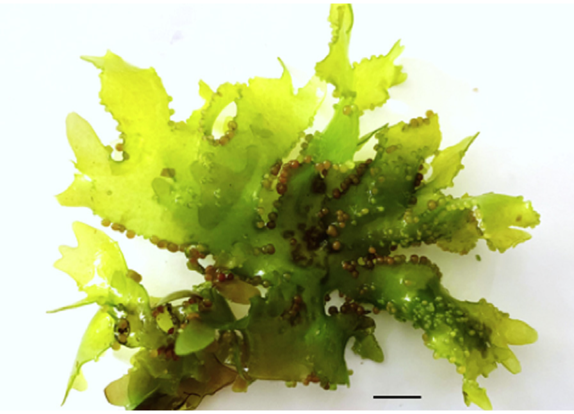

Fig. 4 Photo of *Callophyllis adnata* bearing cystocarps (bar = 1 cm).

special dish at important parties and occasions. The presence of *C. adnata* in the northernmost part of Ilocos Norte from March—April results in abundant harvests by local people which are preserved by sun-drying (Garcia, pers. comm).

The presence of cystocarps during March—April indicates a potential method of generating new plants from spores. However, there are no known studies in the Philippines on its biology and eco-physiology which would be required to develop methods for its commercial cultivation. This seaweed has much promise due to its relatively high market.

G. filicina (Fig. 5) is a red seaweed which can be found in the northernmost part of Luzon (Agngarayngay, 1984a; Hurtado-Ponce, 1983) and other areas such as Sorsogon, Palawan and Zamboanga del Sur (Trono, 1977) during the colder months of the year (i.e. November—March). This red seaweed is purplish to greenish in color, thin, gelatinous and slippery, erect, caespitose, growing on intertidal rocks or in shallow tide pools. Gatherers start collecting in December reaching a peak in February and the material is normally sold in local markets as a sea vegetable salad.

H. durvillaei (Fig. 6) is a red seaweed, indigenous to the Philippines, which has gained increasing attention because of its high demand in the market as a result of its source of phycobiliproteins (i.e. red-phycoerythrin; R-PE) which has important applications in value-added products such as natural coloring agents in cosmetics, pharmaceuticals and food. Successful

Fig. 5 Photo of *Grateloupia filicina* (bar = 1 cm).

Fig. 6 Photo *Halymenia durvillei* (bar = 1 cm).

attempts to generate new plants from spores was reported by Trono (2010), which led to pilot-scale field cultivation in Luzon and the Visayas. It is expected that this seaweed will be of increasing value and importance in the near future and is one to watch!

There are 10 published species of *Porphyra* in the Philippines (Ame et al., 2010; Codero, 1974, 1976; Tungpalan, 1984). However, out those listed and described species, eight were omitted from the list and only two are confirmed, namely: *Pyropia acanthophora* and *P. tanegashimensis*. These confirmations were based on the comparative analyses of plastid *rbc*L and mitochondrial COI-5P gene sequences (Dumilag et al., 2016, 2017). Furthermore, phylogenetic analysis revealed that Philippine populations of *P. tanegashimensis* were indeed endemic and distinct from the other known endemic populations from Japan and also an introduced strain found in Brazil (Milstein, Madeiros, Oliveira, & Oliveira, 2015).

Pyropia spp. (Fig. 7) are found at the upper inter-tidal on rocks and barnacles in the northernmost part of the Philippines, notably: Claveria, Sta. Prexedes, Sta. Ana and Calayan in Cagayan (Ame et al., 2010) and Burgos and Pagudpud, in Ilocos Norte (Cordero, 1977). These thalli are abundant during the northeast monsoon (December—February) when seawater temperatures drop to 17—18°C. This relatively low, local seawater temperature

Fig. 7 Photo of *Pyropia sp.* (bar = 1 cm).

is believed to be influenced by the cold Kuroshio Current which originates from southeastern Japan and passes by the northernmost part of the Philippines during the northeast monsoon. Gathering of *Pyropia* spp. is restricted to December—February since at other times of the year this seaweed only exists as its microscopic, conchocelis stage of growth and development, which happens to be endolithic, or endo-conchocelic (i.e. living within the protection of porous rocks or shell matrices). The only post-harvest processing of *Pyropia* spp. in the Philippines is sun-drying and bundling into crude sheets for local markets (Agngarayngay, Llaguno, Aquino, Taclan, & Galacgac, 2005). Though some studies have been reported on the biology and ecophysiology of *Pyropia* in the Philippines (Monotilla & Notoya, 2010, 2004), its rearing as a crop within commercial hatcheries and out-door cultivation, has never been introduced in the Philippines. This is in marked contrast to the billion dollar nori industries of China, Japan and Korea (Kim, Yarish, Hwang, Park, & Kim, 2017). In mitigation, one must understand the prevailing characteristics of the sea bordering the Cagayan and Ilocos Norte provinces on the west of the Philippines which during southwest monsoon, and the onset of northeast monsoon, are subject to large, rough waves derived from the Trade Winds. Thus, current methods and technologies for extensive nori cultivation would be too fragile for such conditions.

5. Biochemical compositions

5.1 Protein and amino acids

Generally, red seaweeds are found to be higher in protein content and amino acid composition, as compared to the green and brown algae (Hamed, Özogul, Özogul, & Regenstein, 2015). Sources of variability in algal composition can broadly be divided into taxonomic, ecological and ambient environmental factors (Stengel, Connan, & Popper, 2011). The protein content of various macroalgae differs significantly by: phylum, species, geographic location, season, and environmental parameters (Hamed et al., 2015). However, they have all the essential amino acids, in reasonable proportions. Generally, green or red seaweeds are found to have 10%–47% protein by dry weight, while brown seaweeds contain protein levels as low as 3%–15% on a dry weight basis (Fleurence, 2004). Among red algae, according to McDermid and Stuercke (2003), the highest protein content was found to be in *Halymenia formosa* (21.2%), followed by *Porphyra vietnamensis* (16.5%), and a not insubstantial value for *A. taxiformis* (9.4%). The protein contents of *Porphyra tenera* (up to 47% dry weight) and *Palmaria palmata* (around 35% dry weight) were found to be highest (Fujiwara-Arasakil, Minol, & Kuroda, 1984) and are both comparable to the protein content of soybean; *Grateloupia turuturu* has a reported protein content of up to 27.5% dry weight (Fleurence, 1999). A recent study of three *Halymenia* species from the Philippines found that *Halymenia durvellaei* had the highest protein content (13.02%), followed by *Halymenia maculata* (11.07%), and *Halymenia dilatata* (9.99%) (Kho, Orbita, & Manting, 2016).

The amounts of total protein and profiles of amino acids in red seaweeds of the Philippines makes them interesting sources for use in the industrial food and even aquaculture feed sectors (Baweja, Kumar, Sahoo, & Levine, 2016; Hamed et al., 2015). The percentage proportion of essential amino acids (EAAs) available from red seaweeds (40.4%), was found to be the highest, as compared to greens (38%), and brown (38.9%) seaweeds (Dumay & Morançais, 2016). *Porphyra acanthophora* has a reported EAA of 48% (Lourenço, Barbarino, De-Paula, Pereira, & Marquez, 2002) suggesting that red seaweeds had the highest EAA content per 1 mg of protein in relation to dry algal matter. The dominant forms of algal amino acids are aspartic and glutamic, while other acids (e.g., valine, leucine, and lysine) are in sufficient concentrations (Baweja et al., 2016). In red edible Japanese algae such as *Gloiopeltis tenax*, *G. furcata*, *Gracilaria textorii*, and *Gr. vermiculophylla* have relatively high concentrations of taurine that may be used to create functional foods that are rich in such naturally occurring compounds. In contrast, the taurine content was low or undetectable in brown and green algae (Kawasaki et al., 2017).

5.2 Carbohydrates

Various seaweeds can be a most abundant source of: alginic acid, agar, agarose, and carrageenans — collectively called structural polysaccharides. There are also storage polysaccharides, such as laminarin (*Laminaria* sp., brown seaweeds), ulvan (members of the Ulvales, green seaweeds), and floridean starch (*Porphyra* sp., found in members of the Florideophycidae, red seaweeds) are an accumulation of metabolites with no obvious immediate role and assumed to be useful in some later event (Stiger-Pouvreau, Bourgougnon, & Deslandes, 2016). These polysaccharides are regarded as dietary fibers and cannot be digested by humans due to the general lack of required enzymes (Baweja et al., 2016; Hamed et al.,2015; Mendis & Kim, 2011; Mišurcová, Kráčmar, Klejdus, & Vacek, 2010). There are two groups of dietary fiber, soluble and insoluble. Soluble fibers can form viscous gels in the intestinal tract, which are reported to lower blood cholesterol and glucose levels; whereas insoluble fibers are reported to regulate ingested materials in the digestive tract, thereby increasing faecal-bulking capacity, which can relieve constipation and irregular stools (Baweja et al., 2016; Hamed et al., 2015). Soluble carbohydrates of *A. taxiformis* were determined to comprise 13.2% of dry weight (McDermid & Stuercke, 2003). Consumption of selected seaweeds has been demonstrated to have beneficial effects with anti-tumor, anti-coagulant, and anti-viral properties (Hamed et al., 2015), and through eliminating unnecessary substances by dietary (insoluble) fibers binding to *toxic* compounds from the consuming organism. The total dietary fiber content of some seaweeds was found to be relatively high (25%—75% dry weight) as compared to most fruits and vegetables (MacArtain, Gill, Brooks, Campbell, & Rowland, 2007). Utilization of non-digestible soluble fiber (polysaccharides/oligosaccharides), in the large intestine, can produce short chain fatty acids (SCFAs) (e.g., butyrate, propionate and acetate) which are important, host health-promoting products of beneficial gut bacteria (Cornish, Mouritsen, & Critchley, 2019; Liu et al., 2015). Members of the red algal genus *Porphyra/Pyropia* contain the polysaccharide porphyran, which can make up to 48% of thallus dry weight, and therefore have useful properties for food applications (MacArtain et al., 2007). *P. tenera* had a carbohydrate value (44%—56%), total dietary fiber (34.7%), soluble fiber

(17.9%), and insoluble fiber (16.8% of seaweed dry weight) (Fleurence, 2004). The carbohydrate contents of three *Halymenia* species from the Philippines were reported as: *H. durvillaei* (53.65%), *H. maculata* (51.18%) and *H. dilatata* (40.53%). While its carrageenan yield content comprised about 74% of the carrageenan content of *Kappaphycus alvarezii*, of these *H. durvillaei* had the highest (28.4%), which differed significantly with *H. maculata* (11.5%), and *H. dilatata* (9.7%) (Kho et al., 2016). These data suggested that *H. durvillei* could be a potential source of future carrageenan production.

5.3 Lipid and fatty acid content

In general, total lipids (TLs) and fatty acids (FAs) in seaweeds are characterized by total lipid content which ranges in 1–6% dry weight of TL (Rodrigues et al., 2015), a relatively low content of saturated fatty acids (SFAs), and a substantial amount of polyunsaturated fatty acids (PUFAs) such as omega 3 and omega 6, as compared to land vegetables (Mendis & Kim, 2011).

TL and FA composition may vary during the life cycles of various seaweeds which may be seasonal, geographical, or growth conditions (Melo et al., 2015). For instance, the TL of *Ulva pertusa*, *Laminaria religiosa*, *Undaria pinnatifida*, and *Hetrochordaria obietina* appeared to decrease as depth increased (Ito, Tsuchiya, & Tohoku, 1977). These observations could be linked to light intensity whereby the TL content and FA composition of *G. turuturu* (Hotimchenko, 2002) and *Chondrus crispus* (Koch, Hagen, Graeve, & Bischof, 2017) increased when light intensity decreased, or changes in other abiotic factors (e.g. nutrients, salinity, temperature) and its interactions can affect or influenced lipid metabolism (Schmid, Guihéneuf, & Stengel, 2014). The mean TL content of those Rhodophyceae tested, SFA (42%), PUFA (36%), MUFA (13%), and several red seaweeds (e.g. *A. taxiformis*, *B. philippinensis*, *G. filicina*, *Pyropia acanthophora*, *P. tanegashimensis*, *H. durvillaei*) species varied from less than 0.1%–2.0% (Wielgosz-Collin, Kendel, & Couzinet-Mossion, 2016). The mean TL content of *A. taxiformis* was reported as being 4% (McDermid & Stuercke, 2003), and 12% (Ragonese et al. 2014), and for *G. filicina* as 22% dry weight (Tsai & Sun Pan, 2012). Three *Halymenia* species from the Philippines had a TL content of 1.3% as the highest for *H. durvillaei*, which differed significantly with *H. maculata* (1.1%), and *H. dilatata* (0.3%) (Kho et al., 2016). These are considered beneficial for human health as their consumption reportedly reduced the risk of cardiovascular diseases and osteo-arthritis (Hamed et al., 2015; Poudyal, Panchal, Ward, & Brown, 2013), decreased blood pressure and also improved heart and liver function in animal trials (Poudyal et al., 2013), as well as reducing the risks of diabetes, as long as they are not oxidized or converted into saturated lipids (Hamed et al.,2015). Various seaweeds can also be major sources of long-chain PUFAs (Lordan, Ross, & Stanton, 2011). Since humans are incapable of synthesizing PUFAs with more than 18 carbons, e.g., long-chain fatty acids such as: eicosapentaenoic acid (EPA, ω3 C20:5) and arachidonic acid (AA, ω6 C20:4). EPA and AA are present in red seaweeds, some notable examples are: *Porphyra dioica* (17.0 ± 6.1, 19.7 ± 3.7), *Ceramium virgatum* (17.4 ± 3.7, 3.7 ± 0.6), *C. crispus* (14.8 ± 0.9, 22.5 ± 1.5), *Gracilaria gracilis* (2.6 ± 1.5, 30.8 ± 6.6), *and P. palmata* (36.8 ± 4.3, 1.4 ± 1.2) (Schmid et al., 2014), and docosahexaenoic acid (DHA, C22:6) from *U. pinnatifida* and *U. pertusa* as anti-allergic (Hamed et al., 2015). Certain red seaweed species (*P. palmata*) may be rich sources of PUFAs (up to 20 carbons), with four or five double bonds, e.g. 20:5 n-3 (EPA) with levels ranging from 0.4% to 0.6% of dry weight (Schmid et al., 2014), palmitic (16:0) and oleic (18:1) acids. In *G. turuturu* two unusual non-methylene interrupted (NMI) dienoic FA were identified: (1) the 5,11-octadecadienoic (18:2*n*-7,13) had an equivalent chain length (ECL) value of 17.75 as FAME, firstly characterized in the green seaweed *Cladophora rupestris* and identified through oxidative ozonolysis. It is also known to occur in numerous mollusks; and (2) the 5,9-nonadecadienoic (19:2*n*-10,14) had an ECL value of 19.08 as FAME, was firstly identified in lipids from terrestrial flowers (Kendel, Barnathan, Fleurence, Rabesaotra, & Wielgosz-Collin, 2013).

Table 4 shows the percentages of saturated and unsaturated fatty acids of some selected examples of red seaweeds (Tables 5 and 6).

The galactolipids, monogalactosyl diacylglyceride (MGDG), digalactosyl diacylglyceride (DGDG), sulfoquinovosyl monoacylglyceride (SQMG), and sulfoquinovosyl diacylglyceride (SQDG) were recorded to be present in *G. filicina* (Arao & Yamada, 1989), *Porphyra crispata* (Tsai & Sun Pan, 2012), and *Gracilaria* sp. which was reported with anti-proliferative and anti-inflammatory properties, as determined by monitoring cell viability in human cancer lines. Also, a lipid extract (sulfoglycolipid) from *P. crispata* was demonstrated to inhibit the growth of the human hepato-cellular carcinoma cell-line (HepG2) (Tsai & Sun Pan, 2012), and also decreased cell viability of human T-47D breast cancer cells and of 5637 human bladder cancer cells (da Costa et al., 2017). Furthermore, SQDG is a potent telomerase inhibitor that may act as anti-cancer agent (Eitsuka, Nakagawa, Igarashi, & Miyazawa, 2004; Tsai & Sun Pan, 2012).

Table 4 Biochemical composition (% dw) of selected red seaweeds.

Group/Species	Proteins	Essential AA	TL	Carbohy-drates	Carrageenan	References
Asparagopsis taxiformis	9.4		0.1–12	13.2		(McDermid & Stuercke, 2003; Ragonese et al., 2014; Wielgosz-Collin et al., 2016)
Halymenia formosa	21.2		2.9	16.9		
Porphyra vietnamensis	16.5		4.4	30.5		
Porphyra acanthophora		48				(Lourenço et al., 2002)
Porphyra tenera	47			44–56		(Fujiwara-Arasakil et al., 1984)
Palmaria palmata	35	26.50				(Fleurence, 2004; Okolie, Mason, & Critchley, 2018)
Grateloupia turuturu	27.5					(Joël Fleurence, 1999; Okolie et al., 2018)
Grateloupia filicina			2.2	22		(Tsai & Sun Pan, 2012)
*Halymenia durvellaei**	13.02		1.29	53.65	28.41	(Kho et al., 2016)
*Halymenia maculata**	11.07		1.09	51.18	11.50	
*Halymenia dilatata**	9.99		0.29	40.53	9.7	

TL, total lipid; *AA*, amino acid; *, data obtained in Mindanao, Philippines.

Table 5 The variations in the percentage content of saturated and unsaturated FA of the following class, orders and species of red algae.

Group	No. of studied species	Fatty acids	SFA	MUFA	PUFA	Mean TL (% dw)	References
Class Rhodophyceae			42%	13%	36%		(Wielgosz-Collin et al., 2016)
		C16			1.8		
		C18			4%		
		C20			3.4%		
		C22			1.9%		
Order Bonnemaisoniales	2	from C6 to C28	73.80%			0.1 and 4.0	(Wielgosz-Collin et al., 2016)
A. taxiformis	1		52.47%		1.80%	12.22	(Ragonese et al., 2014)
		C14:0	18.17%				
		C16:0	48.9%				
		EPA			0.96%		
		Linoleic			0.84%		
Order Rhodymeniales	2	from C14 to C24		30.1%		0.1 and 1.4	(Wielgosz-Collin et al., 2016)
Order Halymeniales	11					1.9 (0.1–3.9)	(Wielgosz-Collin et al., 2016)
G. filicina	1	C14:0	13.8%				(Arao & Yamada, 1989)
		C16:0	50.8%				
		C18:1		11.2%			
		AA			9.3%		
G. filicina	1	EPA			43.7%		(Trono, 1977)
H. sinensis		EPA			42.2%		(Trono, 1977)

SFA, saturated fatty acid; *MUFA*, monounsaturated fatty acid; *PUFA*, polyunsaturated fatty acid; *TL*, total lipid.

Table 6 Biological activity of selected red seaweeds.

Species	Fraction	Activity against	IC50 (μg mL^{-1})	References
Asparagopsis taxiformis	Sulfated polysaccharides	Anticoagulant		(Pereira, 2018a)
Gigartina skottsbergii	Carrageenans, ($1C_3$, and $1T_{1,}$ λ)	Anticoagulant, Antiviral (HSV-1&2)	(0.7,0.5 and 0.6, 0.4)	(Carlucci et al., 1997)
Gymnogongrus torulosus	DL-galactan	Anticoagulant, HSV-2 and DENV-2	0.6–16.0, & 0.19–1.7	(Pujol et al., 2002)
Porphyra yezoensis	Carrageenans, Glycoprotein	Anticoagulant, Antiradical Antiangiogenic, Anti-inflammatory		(Liu et al., 2019; Pereira, 2018a, 2018b; Torres, Flórez-Fernández, & Domínguez, 2019)
Gracilaria birdiae	Carrageenans Sulfated polysaccharides	Anticoagulant, Antiradical		
Grateloupia turuturu	carrageenans	Anticoagulant		(Pereira, 2016, 2018a)
Halymenia floresii	Sulfated polysaccharides	Anticoagulant		(Pereira, 2018a)
Kappaphycus alvarezii	*k*-carrageenan Water extract	Apoptotic induction Anti-inflammatory Superoxide, hyroxyl, and lipid peroxidation	0.00011, 0.00033, & 0.00032	(Ariffin et al., 2014; Pereira, 2018b, 2018a)
Gymnogongrus griffithsiae	Kappa/iota/nu carrageenan *G3d* and DL-galactan hybrid *C2S-3*	DENV-2, DENV-3,	1.0, 13.9–14.2	(Talarico et al., 2005)
Porphyra crispata	SQDGs	*HepG2*	126.0	(Tsai & Sun Pan, 2012)
Gigartina tenella	SQDG KM043	*DNA* polymerase α, *DNA* polymerase β, and HIV-reverse transcriptase type 1	0.21, 3.02, & 9.42	(Plouguerné et al., 2014)
Callophycus serratus	Polysaccharides, lipids	anti-thrombotic		(Lin et al., 2010)

$1C_3$, cystocarpic fraction; *$1T_1$*, tetrasporic fraction; *SQDG*, sulfoquinovosyldiacylglycerols; *SQDG KM043*, a new sulfolipid extract belonged to sulfoquinovosyldiacylglycerols; *HSV*, herpes simplex virus; *DENV*, dengue virus; *HepG2*, human hepatocellular carcinoma cell line; *HIV*, human immunodeficiency virus.

6. Biological activity and potential applications

6.1 Anti-coagulant properties

Anti-coagulants or blood thinners are chemical substances which prevent or reduce the coagulation of blood or which prolongs clotting time. The anti-coagulant activity of various seaweed extracts depends on there being, preferably two sulfate groups and a glycosidic linkage on the pyranose ring of its sulfated polysaccharides (Ciancia, Quintana, & Cerezo, 2010), in order to interact with basic groups of proteins. It was suggested that in this interaction, one or more proteases were targeted and that the major components of these activities were thrombin inhibition, as mediated by anti-thrombin and/or heparin co-factor II (Mohamed, Hashim, & Rahman, 2012). An example of anti-coagulant activity by carrageenans extracted from the red seaweeds *Gigartina skottsbergii* (Carlucci et al., 1997), and DL-galactan hybrids isolated from *Gymnogongrus torulosus* (Pujol et al., 2002) were found to have less anti-coagulant action. Another is of agaran fractions from *Acanthophora spicifera* which reportedly largely depended on the interaction affinity of protein-polysaccharide, which varies according to the seaweed-derived, sulfated polysaccharide. Several modes of action(s) were reported for anti-coagulant activities of various seaweed extracts, i.e. direct inhibition of thrombin, catalysis of thrombin inhibition via anti-thrombin and/or HCII, inhibition of protease generation and active complexes of blood coagulation, and interference by fibrin polylmerization (Duarte et al., 2004).

Sulfated galactans from the green alga *Codium fragile* were shown to have no anti-coagulant effects, while its highly sulfated arabinans were reported to have important anti-coagulant activity, with a different mode of action from that of heparin (Pengzhan et al., 2003).

The total sulfate content of the brown seaweed *Dictyopteris delicatula* was not correlated to the anti-coagulant activity of its sulfated polysaccharides (i.e. the heterofucans) which were reported to inhibit the coagulation pathways of both common and intrinsic, but not the extrinsic coagulation pathways (Magalhaes et al., 2011). Anti-coagulant activities were determined using activated partial thromboplastin time (aPTT) and prothrombin time (PT) coagulation assays. Anti-coagulant activity was reported for four fucans from the brown seaweed *Canistrocarpus cervicornis* (with only 0.1 mg/mL of plasma a result similar to that of Clexane, a commercial, low molecular weight heparin) at 1.25-fold less potency than Clexane, but with no clotting inhibition observed in six fucans tested for prothrombin time (PT) (Camara et al., 2011). Brown seaweed fucoidans were as effective as heparin and dermatan sulfate in the potentiation of heparin co-factor II. These anti-coagulant fucoidans might therefore be an alternative source of a cheaper and sustainable resource of alternative drugs, as compared to synthetic anticoagulants (Colliec et al.,1991). Fucoxanthin, a carotenoid from various brown algae was reported to have anti-inflammatory effects (Wijesinghe & Jeon, 2011). The biological effects of these compounds vary from species to species and due to their chemical structure (Cumashi et al., 2007). Philippine seaweeds could be a potential, rich natural resource and used to produce a beneficial and novel new products in the field of biomedical industry.

6.2 Anti-angiogenic properties

Anti-angiogenic compounds are chemical substances that prevent the growth of new blood vessels that provide cells with an adequate supply of oxygen and nutrients, as well as removing waste products. These compounds find applications in preventing cancerous tumors from growing their own blood vessels, or by blocking the vascular, endothelial growth factor (VEGF), a cancer-cell protein, from attaching to receptors lining the blood vessels.

A fucoxanthin extract of the brown seaweed *U. pinnatifida* was found to suppress the development of endothelial progenitor cells and the formation of new blood vessels in cultured human, umbilical vein endothelial cells. It was also observed to reduce the tube length of endothelial cells of a rat aortic ring (Sugawara, Matsubara, Akagi, Mori, & Hirata, 2006). Similar activity was reported from a fucoxanthin extract of *Sargassum* sp. which suppressed expression of VEGF on xeno-grafted, sarcoma 180 (S180) cells in mice (Wang et al., 2012). Another anti-angiogenic effect of a fucoxanthin extracts was proposed to be a molecular mechanism which suppressed fibroblast growth factor 2 (FGF-2) and its receptor (FGFR-1) (Ganesan, Matsubara, Sugawara, & Hirata, 2013). Anti-angiogenic effects of an enzyme-digested fucoidan extracted from *Cladosiphon novae-caledoniae* was reported for human uterine carcinoma HeLa cells by suppressing VEGF. Similar results were also reported with HT1080 human fibrosarcoma cells where the fucoidan extract (commercially known as "Pöwer fucoidan") promoted the VEGF suppression of the matrix metallo-proteinases (MMP-2/9) (Ye et al., 2005).

Carrageenans, from selected red seaweeds are linear, hydrophilic, sulfated polysaccharides (Campo, Kawano, Braz da Silva, & Ivone, 2009), and some have been reported to have anti-angiogenic effects in mice (Dias et al., 2004).

Only a few studies have suggested that carrageenans may have anti-tumoral activities. A study of human intestine (Caco-2) and hepatic (HepG2) cell lines showed apoptotic induction using *k*-carrageenan [from *K. alvarezii* (cottonii)], while no toxicity was observed in corresponding normal and cancerous intestinal and liver cell-lines, using non-degraded carrageenan (Ariffin et al., 2014). According to (Murad, Ghannam, Al-Ktaifani, Abbas, & Hawat, 2015), a pro-apoptotic activity of ι-carrageenan [from *Eucheuma denticulatum* (spinosum)] was shown to be mediated by caspase-3, caspase-9, p53, Bax, and Bcl-2 genes within an MDA-MB-231 metastatic, human, breast cancer cell-line. A review of the harmful, gastro-intestinal effects of carrageenan in animal experiments revealed potentially carcinogenic properties (i.e. colonic ulcerations and gastro-intestinal neoplasms) and cancer-promoting effects of degraded and un-degraded carrageenans in animal and experimental models, respectively (Tobacman, 2001). Therefore, a benefit/risk ratio must be considered in cancer prevention and therapeutic treatments using various carrageenans. A recent study by McKim et al. (2016) on the effects of the three common forms of carrageenan [i.e. lambda (ʎ)-, kappa (k)-, and iota (i)] on cell permeability, cyto-toxicity, and cytokine gene expression in human intestinal and hepatic cell-lines showed that a standard Caco-2 absorption model had no carrageenan permeability and did not cross the membranes of intestinal epithelial cells at different concentrations (100, 500, 1000 μg/mL) and is was also not cyto-toxic to these cells. In addition, carrageenan did not induce IL-8, IL-6, or MCP-1 (CCL2) or cellular toxicity after 24 h in two human intestinal cell-lines (HT-29 and HCT-8). No cellular oxidative stress was observed in HT-29 cells using k-carrageenan at 0.1, 1.0 and 10.0 μg/mL exposure concentrations. ʎ -carrageenan (0.1, 1.0, 10.0 and 100.0 μg/mL) had no effect on the expression of IL-8, IL-6, or MCP-1 (CCL2) in the human (HepG2) liver cell line. FMC Biopolymer (Philadelphia, PA) provided a food-blend carrageenan used for the above study consisting of k- and ʎ-carrageenan, and ι-carrageenan samples were purchased from Sigma-Aldrich (St. Louis, Missouri).

6.3 Anti-viral properties

Seaweeds are known to contain many bioactive compounds, some of which have anti-viral properties which could be used in developing new pharmaceutical agents (Pereira, 2018b; van Hal, Huijgen, & López-Contreras, 2014).

Many preliminary and advanced studies have been made on the anti-viral properties of various macroalgal sources of sulfated polysaccharides (i.e. in particular sulfated galactans and carrageenans) (Pengzhan et al., 2003).

The reported anti-viral compounds from seaweeds include:

(a) carrageenans (such as λ-carrageenan and partially cyclicized μ/ι-carrageenan) against HSV-1 and 2 from *G. skottsbergii* (Carlucci et al., 1997), from *Gymnogongrus griffithsiae* and *Cryptonemia crenulata* (Talarico et al., 2005)

(b) DL-galactan hybrids, against HSV-1 and 2 from *G. griffithsiae* and *C. crenulata* (Talarico et al., 2005), and against HSV-2 and Dengue virus type 2 (DEN-2) from *Gy. torulosus* (Pujol et al., 2002).

(c) fucoidans, against numerous enveloped virii including HSV-1 from *U. pinnatifida* (Hayashi, Nakano, Hashimoto, Kanekiyo, & Hayashi, 2008),

(d) kainic and domoic acids, as anthelmintic agents from *Digenea simplex* and *Chondria armata* (Freile-Pelegrín & Tasdemir, 2019)

(e) major glycolipids: MGDG (from Hydrolithon reinboldii), DGDG (from Sargassum horneri), and SQDG (from Gigartina tenella, Palmaria palmata) as anti-bacterial, anti-tumor, anti-viral and anti-protozoal agents (Plouguerné, da Gama, Pereira, & Barreto-Bergter, 2014),

(f) xylomannan sulfate, against HSV-1 from *Sebdenia polydactyla* (Ghosh, Pujol, Damonte, Sinha, & Ray, 2009), and

(g) galactan sulfate, and sulfated glucurono-galactan (from *Schizymenia binderi*), against HSV-1 & HSV-2, HIV, RSV, HCMV, Dengue virus, Pseudo-rabies virus, and Influenza A and B virii (Pujol et al., 2002; Talarico et al., 2005).

Studies revealed that the above compounds (with particular emphasis on carrageenans) inhibited the cytopathic effect of HIV, and prevented HIV-induced syncytium (giant cell) formation, as well as other sexually transmitted viruses, such as genital warts, human papilloma virus (HPV) and different strains of *Herpes simplex* virus Type 1 and 2 (HSV-1 and 2) (Buck et al., 2006; Mendis & Kim, 2011; Talarico et al., 2005). Reportedly k, ʎ, and ι-carrageenan inhibited the human papilloma virus (HPV) infection process (Buck et al., 2006), and are potential inhibitors of the multiplication of the Dengue virii, Type-2 and Type-3 (DENV-2 & 3) (Talarico et al., 2005). Fucoidans from *Adenocystis utricularis* were also demonstrated to have anti-viral activities against HIV and human cyto-megalovirus (HCMV) (Gupta & Abu-Ghannam, 2011).

Fucoidans extracted from several seaweed species: (i.e. galactofuran and urono-fucoidan) from the alga *A. utricularis* showed that galactofuran had the highest potency against HSV 1 and 2 with no cyto-toxicity, while urono-fucoidan had no anti-viral activity (Ponce, Pujol, Damonte, Flores, & Stortz, 2003); Also fucoidans, inhibited multiple influenza strains such as Mekabu fucoidan from *U. pinnatifida* against (swine flu) H1N1 (Hayashi et al., 2007) and avian influenza A (bird flu) strains H5N1, H5N3, and H7N2 (Synytsya et al., 2014), and fucoidan and L-fucose from *Cladosiphon okamuranus* against para-influenza (Taoda et al., 2008). Similar properties have been observed from polysaccharide fractions of *Sargassum patens* against HSV 1 and 2 (EC_{50} value of 25 mg/mL and 12.5 mg/mL) respectively (Zhu, Ooi, Chan, & Ang, 2003). It is also important to note the presence of the sulfate group and its degree of sulfation, increased potency of the anti-HIV activity. However, the effectiveness of sulfated polysaccharides in the therapy and/or prophylaxis of retro-viral and opportunistic infections must be tested both in animal and human models (Pengzhan et al., 2003). A recent study from the Marinova company showed that their Maritech® fucoidan was a potent inhibitor of HSV-1 and 2 clinical strains and HCMV on human fibroblast cells by strongly inhibiting their activity or preventing entry into cells (Fitton, 2019).

Secondary metabolites (Table 2) from *Ecklonia cava* and *A. utricularis* seaweeds have been reported to have important anti-viral activities, e.g. tannins from *E. cava* showed potency against HIV-1 by inhibiting polymerase and ribo-nuclease activities of reverse transcriptase (RT). Phlorotannin derivatives from *E. cava* (Table 2) were reported to have a high potency against HIV-1 RT, with some inhibition of protease 8,8′-bieckol with (IC50, 0.51 μM) and 8,4‴dieckol (IC50, 5.3 μM) (Ahn et al., 2004). The phloroglucinol derivative 6,6′- bieckol from *E. cava* showed potency against HIV-1 by induced syncytial formation (EC50 1.72 μM), lytic effects (EC50 1.23 μM), and viral p24 antigen production (EC50 1.26 μM). Of these 6,6′- bieckol selectively inhibited HIV-1 RT with an EC50 of 1.07 μM, as well as HIV-1 infection of cells (Artan et al., 2008).

6.4 Anti-thrombotic agents

Thrombosis is a process when a blood clot or thrombus, blocks the normal and smooth flow in the arteries and veins, which culminates in such prevalent diseases including heart attack and strokes. Fibrin and platelets are the most important components. Fibrin is a protein that forms a mesh and traps red blood cells (in veins, causing heart attack). Platelets, are cells within the bloodstream, which form clumps and add to the thrombus mass (causing arterial strokes). Certain marine algal-derived bioactive compounds from *Callophycus serratus* have been reported to have anti-thrombotic effects including: polysaccharides and lipids; small secondary metabolites; such as polyphenols, halogenated phenols, and meroterpenes (Lin et al., 2010). Cardiovascular disease (CVD) is a leading cause of death globally (Cornish, Critchley, & Mouritsen, 2015). An estimated mortality of 17.9 million people or (31%) of all global deaths in 2016 was reportedly due to CVD. Of all of these deaths, 85% were due to heart attack and stroke (Cardiovascular diseases, 2017). Recent studies on human gut microbes or host/microbe inter-dependence (dysbiosis) were reported to be associated with various pathologies, e.g. inflammation, obesity, hypertension, endothelial dysfunction, diabetes, CVD, colitis, and neurological disorders (Cornish, Critchley & Mouritsen, 2019; Mohamed et al., 2012). Since CVD is highly influenced by human food digestion, carbohydrate fermentation, energy harvesting and storage, gene expression, the secondary generation of beneficial compounds (cross-feeding), and the facilitation of metabolic functions, makes applications and utilization of therapeutic dietary impacts of seaweeds to be viable and important for intervention strategies related to food manufacturing and consumption (Cornish et al., 2015, 2019). Judicious consumption of selected seaweeds has been implicated to lower incidence factors involved in CVD occurrence (Mohamed et al., 2012).

A strong-gelling sodium alginate extracted from a particular brown seaweed described in Patent Number WO2007039294 (containing a suggested 1.5 g daily dose) had an indirect, cardiovascular beneficial effect. Sodium alginate was found to limit glucose and cholesterol uptake by reversing the symptoms of hyper-cholesterolemia and diabetes mellitus, thereby reducing CVD risks. Alginates generally are used for tissue engineering and regeneration due to their bio-compatibility and non-thrombogenic nature, also have applications supporting cardiac implants after acute myocardial infarction (Mohamed et al., 2012). Sodium alginate was suggested as a vehicle for the delivery of bioactive molecules, regenerative factors, or even stem-cells into the heart (Paxman, Richardson, Dettmar, & Corfe, 2008).

Another seaweed-derived molecule, i.e. a (400 mg/d) fucoidan fraction from *Laminaria japonica* was administered to nine healthy volunteers for five weeks. This treatment showed an anti-thrombotic effect, as monitored by an *ex vivo* global thrombosis test and measurement of the time required for thrombus lysis (Ren et al., 2013). Dietary fucoidan (derived from

C. okamuranus) stimulated H_2O_2-producing enzymes in intestinal epithelial cells and released H_2O_2 into the blood. This is interpreted as a signaling function which increases prostacyclin (PGI2) production, which in turn shortens the time for thrombolysis. This effect was only found as a result of fucoidan ingestion. No anti-thrombotic effects were observed in the fucoxanthin-treated volunteers. Fucoidan from *C. okamuranus* reportedly provided cardio-protection against isoproterenol-induced myocardial infarction in rats (Thomes, Rajendran, Pasanban, & Rengasamy, 2010) which reduced myocardial damage, oxidative stress, re-equilibrated cholesterol balance (both triglyceride, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and total cholesterol levels) (Huang, Wen, Gao, & Liu, 2010; Thomes et al., 2010). Fucoidan from *L. japonica*, as tested on hyper-lipidemic rats, showed decreased serum levels of (triglyceride, LDL, and total cholesterol), while increasing HDL cholesterol levels and the activities of enzymes linked to the metabolism of lipo-proteins (e.g. lipo-protein lipase, hepatic triglyceride lipase, and lecithin cholesterol acyltransferase) (Huang et al., 2010).

Alpha-linolenic acid (ALA), the precursor to EPA and DHA, inhibits the production of eicosanoids, lowering blood pressure, and blood triglyceride levels (Oomah & Mazza, 1999) while docosapentaenoic acid (DPA) was shown to inhibit platelet aggregation and has strong endothelial cell migration abilities (Kaur, Cameron-Smith, Garg, & Sinclair, 2011). Commercial ALA or hybrid liposomes of ALA ethyl ester (HL-ALAE) seemed to provide benefits against several health problems e.g., decrease in blood cholesterol levels, reduction in the risk of heart attacks, and a growth reduction in breast, colon, and prostate cancer (Tanaka, Goto, Matsumoto, & Ueoka, 2008). Researchers have suggested that elevated blood pressure in adulthood may be associated with peri-natal omega-3 fatty acid deficiency and that early exposure to dietary, long-chain omega-3 played a critical role in supporting heart health and reducing CVD risk in later life (Papanikolaou, Brooks, Reider, & Fulgoni, 2014). Given the situation above, then it is safe to assume that consumption of recommended amounts of omega-3s as ALA in food, or in a supplement, would be generally beneficial to consumers.

6.5 Immune stimulating activities

Beneficial applications of selected seaweed-derived biomolecules is clearly aimed to target nutrition and well-being of humans, whether for nutraceutical, pharmaceutical, or biotechnological applications. Vitamin C is present in all seaweed groups and in relatively large amounts in (green and brown) with substantial levels reportedly in red seaweeds (i.e. from 500 to 3000 mg/kg) (Rajapakse & Kim, 2011). Some seaweeds have larger amounts of vitamin C, i.e. in *Porphyra umbilicalis* (12.88 mg/100 g wet weight) and *P. palmata* (5.5 mg/100 g wet weight) than in some terrestrial foods such as bovine milk (1.7 mg/100 g edible portion) or orange (5 mg/100 g edible portion) (MacArtain et al., 2007; Swarnalatha, 2018).

Consumption of selected seaweeds, as part of the diet and as a source of vitamin C, can strengthen the immune system (Burtin, 2003). Several species of *Eucheuma*, *Ulva*, and *Gracilaria* are reported to have bioactive lectins that interact with specific glycan structures and is also useful in the detection of disease related alterations of glycan synthesis, infectious agents (e.g. virii, bacteria, fungi, parasites), antibiotic, mitogenic, cytotoxic effects, and many others (Holdt & Kraan, 2011; Michalak & Chojnacka, 2015). Peptides from *Porphyra columbina* were reported as immuno-suppressive and anti-hypertensive (Cian, Martinez-Augustin, & Drago, 2012).

Metabolism of polyunsaturated fatty acids (PUFAs) causes the production of different eicosanoids, which are known to regulate cellular processes. The roles of eicosapentaenoic acid (EPA), arachidonic acid (AA), and docosahexaenoic acid (DHA) in human health, are to have an effect on immune-regulation (Gillies, Harris, & Kris-Etherton, 2011; Poudyal et al., 2013), cancer prevention (Slagsvold, Pettersen, Follestad, Krokan, & Schønberg, 2009), and pre- and post-natal development of the brain and retina (Guesnet & Alessandri, 2011). Prostaglandins, thromboxane, oxylipins, and other eicosanoids are produced with the aid of its precursors AA and EPA (Qi et al., 2002). These help to regulate inflammation processes and immune reactions (Poudyal et al., 2013) and were evident in the red seaweed *P. umbilicalis*, and also kelp (*Laminaria*) pertaining to important functions in skin growth and protection (Pereira, 2018a). Inhibition of the pro-lipid mediator, leukotriene B4 synthesis (a pro-inflammatory) by stearidonic acid (STA) was tested for use in cystic fibrosis treatments (Primdahl, Tungen, Aursnes, Hansen, & Vik, 2015; Schubert et al., 2007). These studies suggested that STAs found in *Undaria* and *Ulva* spp. affected the immune system in humans (Ishihara et al., 1998). A palmitic acid extract from the calcareous red seaweed *Amphiroa zonata* showed anti-tumor activity by inducing apoptosis in the human leukemic cell line MOLT-4 at 50 μg/mL, and also in an *in vivo* anti-tumor test in mice (Harada et al., 2002).

7. Conclusions

All the red seaweeds described in this chapter, except for A. taxiformis, have a long history of use as a source of sea vegetables, especially in the northern part of Luzon. These are mainly gathered by the locals during the peak months of growth, from November to February, i.e., the colder months of the year.

There is no known cultivation of these seaweeds except for *H. durvillei* which has just been initiated (Trono In Prep). Basic research on the biology and eco-ecophysiology of wild plants leading to their domestication for cultivation is imperative to ensure meeting the anticipated market demands of these seaweeds.

Only a few studies have been reported on the target species presented here for their different biological activities. It will be noteworthy then to explore and pursue further the potential of these emerging red seaweeds with several applications, considering their wide distribution in the country and potential economic value if produced sustainably.

References

Agngarayngay, Z. M. (1984a). Marine macro-algae of Ilocos Norte. II. Phaeophyta and *Rhodopyta. Ilocos Fisheries Journal, 1*, 1—66.

Agngarayngay, Z. M. (1984b). Species of edible seaweeds of Ilocos Norte. *Ilocos Fisheries Journal, 1*, 118—133.

Agngarayngay, Z. M., Llaguno, A. F. C., Aquino, S. G., Taclan, L. B., & Galacgac, E. S. (2005). *Edible seaweeds of Ilocos Norte: Food reparations other local uses and market potentials.*

Ahn, M.-J., Yoon, K.-D., Min, S.-Y., Lee, J. S., Kim, J. H., Kim, T. G., et al. (2004). Inhibition of HIV-1 reverse transcriptase and protease by phlorotannins from the brown alga *Ecklonia cava. Biological & Pharmaceutical Bulletin, 27*(4), 544—547.

Ali, M. M., Yashir, S., Critchley, A. T., & Hurtado, A. Q. (2018). Impacts of *Ascophyllum* marine plant extract powder (AMPEP) on the growth, incidence of the endophyte *Neosiphonia apiculata* and associated carrageenan quality of three, commercial cultivars of *Kappaphycus. Journal of Applied Phycology, 30*, 1185—1196.

Ame, E. C., Ayson, J. P., Okuda, K., & Andres, R. (2010). Porphyra fisheries in the northern Philippines:
Some environmental issues and the socio- economic impact on the ilocano fisherfolk. *Kuroshio Science, 4*, 53—58.

Arao, T., & Yamada, M. (1989). Positional distribution of fatty acids in galactolipids of algae. *Phytochemistry, 28*(3), 805—810. https://doi.org/10.1016/0031-9422(89)80119-0.

Ariffin, S. H. Z., Yeen, W. W., Abidin, I. Z. Z., Abdul Wahab, R. M., Ariffin, Z. Z., & Senafi, S. (2014). Cytotoxicity effect of degraded and undegraded kappa and iota carrageenan in human intestine and liver cell lines. *BMC Complementary and Alternative Medicine, 14*, 508. https://doi.org/10.1186/1472-6882-14-508.

Artan, M., Li, Y., Karadeniz, F., Lee, S.-H., Kim, M.-M., & Kim, S.-K. (2008). Anti-HIV-1 activity of phloroglucinol derivative, 6,6'-bieckol, from *Ecklonia cava. Bioorganic & Medicinal Chemistry, 16*(17), 7921—7926. https://doi.org/10.1016/j.bmc.2008.07.078.

Baweja, P., Kumar, S., Sahoo, D., & Levine, I. (2016). Biology of seaweeds. In J. Fleurence, & I. Levine (Eds.), *Seaweed in health and disease prevention* (pp. 41–106). Amsterdam Boston Heidelberg London: Elsevier, Academic Press.

Buck, C. B., Thompson, C. D., Roberts, J. N., Müller, M., Lowy, D. R., & Schiller, J. T. (2006). Carrageenan is a potent inhibitor of papillomavirus infection. *PLoS Pathogens, 2*(7), e69. https://doi.org/10.1371/journal.ppat.0020069.

Burtin, P. (2003). *Nutritional value of seaweeds*. Retrieved December 6, 2018, from ResearchGate website: https://www.researchgate.net/publication/228554296_Nutritional_value_of_seaweeds.

Buschmann, A. H., Camus, C., Infante, J., Neori, A., Israel, A., Hernández-González, M. C., Pereda, S. V., Pinchetti, J. L., Golberg, A., Tadmor-Shalev, N., & Critchley, A. T. (2017). Seaweed production: Overview of the global state of exploitation, farming and emerging research activity. *European Journal of Phycology, 52*(4), 391–406.

Camara, R. B. G., Costa, L. S., Fidelis, G. P., Nobre, L. T. D. B., Dantas-Santos, N., Cordeiro, S. L., et al. (2011). Heterofucans from the brown seaweed *Canistrocarpus cervicornis* with anticoagulant and antioxidant activities. *Marine Drugs, 9*(1), 124–138. https://doi.org/10.3390/md9010124.

Campo, V., Kawano, D., Braz da Silva, D., & Ivone, C. (2009). Carrageenans: Biological properties, chemical modifications and structural analysis – A review. *Carbohydrate Polymers, 77*, 167–180. https://doi.org/10.1016/j.carbpol.2009.01.020.

Cardiovascular diseases (CVDs), 2017. Retrieved December 6, 2018, from: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds).

Carlucci, M. J., Pujol, C. A., Ciancia, M., Noseda, M. D., Matulewicz, M. C., Damonte, E. B., et al. (1997). Antiherpetic and anticoagulant properties of carrageenans from the red seaweed Gigartina skottsbergii and their cyclized derivatives: Correlation between structure and biological activity. *International Journal of Biological Macromolecules, 20*(2), 97–105. https://doi.org/10.1016/S0141-8130(96)01145-2.

Ciancia, M., Quintana, I., & Cerezo, A. S. (2010). Overview of anticoagulant activity of sulfated polysaccharides from seaweeds in relation to their structures, focusing on those of green seaweeds. *Current Medicinal Chemistry, 17*(23), 2503–2529.

Cian, R. E., Martinez-Augustin, O., & Drago, S. R. (2012). Bioactive properties of peptides obtained by enzymatic hydrolysis from protein byproducts of *Porphyra columbina*. *Food Research International, 49*(1), 364–372.

Codero, P. A., Jr. (1974). Phycological observations I: Genus *Porphyra* of the Philippines, its species and their occurrences. *Bulletin of the Japanese Society of Phycology, 22*, 134–142.

Colliec, S., Fischer, A. M., Tapon-Bretaudiere, J., Boisson, C., Durand, P., & Jozefonvicz, J. (1991). Anticoagulant properties of a fucoïdan fraction. *Thrombosis Research, 64*(2), 143–154.

Cordero, P. A., Jr. (1976). Phycological observations – II: *Porphyra marcosii*, a new species from the Philippines. *Acta Manilana Research Center, University of Sto Tomas, Series. A, 24*(15), 14–24.

Cordero, P. A., Jr. (1977). Studies of Philippine marine red algae. *Special Publications from the Seto Marine Biological Laboratory, 4*, 1–258.

Cordero, P. A., Jr. (1980). Taxonomy and distribution of Philippine useful seaweeds. *National Research Council of the Philippines Bulletin No, 81*, 36–41.

Cornish, M. L., Critchley, A. T., & Mouritsen, O. G. (2015). A role for dietary macroalgae in the amelioration of certain risk factors associated with cardiovascular disease. *Phycologia, 54*(6), 649–666. https://doi.org/10.2216/15-77.1.

Cornish, M. L., Mouritsen, O. G., & Critchley, A. T. (2019). A mini-review on the microbial continuum: Consideration of a link between judicious consumption of a varied diet of macroalgae and human health and nutrition. *Journal of Oceanology and Limnology*. https://doi.org/10.1007/s00343-019-8104-2.

da Costa, E., Melo, T., Moreira, A. S. P., Bernardo, C., Helguero, L., Ferreira, I., et al. (2017). Valorization of lipids from *Gracilaria* sp. through lipidomics and decoding of antiproliferative and anti-inflammatory activity. *Marine Drugs, 15*(3). https://doi.org/10.3390/md15030062.

Critchley, A. T., Largo, D., Wee, W., Bleicher L'honneur, G., Hurtado, A. Q., & Schubert, J. (2004). A preliminary summary on *Kappaphycus* farming and the impact of epiphytes. *Japanese Journal of Phycology, 52*(Supplement), 231–232.

Cumashi, A., Ushakova, N. A., Preobrazhenskaya, M. E., D'Incecco, A., Piccoli, A., Totani, L., et al. (2007). A comparative study of the anti-inflammatory, anticoagulant, antiangiogenic, and antiadhesive activities of nine different fucoidans from brown seaweeds. *Glycobiology, 17*(5), 541–552. https://doi.org/10.1093/glycob/cwm014.

Dias, P. F., Siqueira, J. M., Vendruscolo, L. F., de Neiva, T. J. C., Gagliardi, A. R., Maraschin, M., et al. (2004). Antiangiogenic and antitumoral properties of a polysaccharide isolated from the seaweed *Sargassum* stenophyllum. *Cancer Chemotherapy and Pharmacology, 56*, 436–446. https://doi.org/10.1007/s00280-004-0995-7.

Doty, M. S. (1995). *Betaphycus philippinensis* gen. et. sp. nov. and related species (Solieriaceae, Gigartinales). In I. A. Abbott (Ed.), *Taxonomy of economic seaweeds with reference to some Pacific species* (Vol. 5, pp. 237–245).

Duarte, M. E. R., Cauduro, J. P., Noseda, D. G., Noseda, M. D., Gonçalves, A. G., Pujol, C. A., et al. (2004). The structure of the agaran sulfate from *Acanthophora* spicifera (Rhodomelaceae, Ceramiales) and its antiviral activity. Relation between structure and antiviral activity in agarans. *Carbohydrate Research, 339*(2), 335–347. https://doi.org/10.1016/j.carres.2003.09.028.

Dumay, J., & Morançais, M. (2016). Proteins and pigments. In J. Fleurence, & I. Levine (Eds.), *Algae: A way of life and health* (pp. 275–318). Amsterdam Boston Heidelberg London: Elsevier, Academic Press.

Dumilag, R. V. (2018). *Betaphycus gelatinus* and *B. philippinensis* (Gigartinales, Rhodophyta) are conspecific. *Phycotaxa, 372*, 022–034.

Dumilag, R. V., Aguinaldo, Z. A., Mintu, C. B., Quinto, M. P., Ame, E. C., Andres, R. C., et al. (2016). Morphological and molecular confirmation of the occurrence of *Pyropia tanegashimensis* (Bangiales, Rhodophyta) from Palaui is., Sta. Ana, Cagayan, Philippines. *Phytotaxa, 255*, 083–090.

Dumilag, R. V., Aguinaldo, Z. A., Mintu, C. B., Quinto, M. P., Ame, E. C., Andres, R. C., et al. (2017). A review of the current taxonomic status of foliose *Bangiales* (Rhodophyta) in the Philippines. *Phytotaxa, 312*, 047–059.

Dumilag, R. V., Liao, L. M., & Lluisma, A. O. (2014). Phylogeny of *Betaphycus* (Gigartinales, Rhodophyta) as inferred from COI sequences and morphological observations on *B. philippinensis*. *Journal of Applied Phycology, 26*, 587–595.

Dumilag, R. V., & Monotilla, W. D. (2018). Molecular diversity and biogeography of Philippine foliose *Bangiales* (Rhodophyta). *Journal of Applied Phycology, 30*, 173–186.

Eitsuka, T., Nakagawa, K., Igarashi, M., & Miyazawa, T. (2004). Telomerase inhibition by sulfoquinovosyldiacylglycerol from edible purple laver (Porphyra yezoensis). *Cancer Letters, 212*(1), 15–20. https://doi.org/10.1016/j.canlet.2004.03.019.

Fitton, H. (2019). *Maritech organic fucoidans: The science* (Vol. 28).

Fleurence, J. (1999). Seaweed proteins: Biochemical, nutritional aspects and potential uses. *Trends in Food Science & Technology, 10*(1), 25–28. https://doi.org/10.1016/S0924-2244(99)00015-1.

Fleurence, J. (2004). Seaweed proteins. In R. Y. Yada (Ed.), *Proteins in food processing* (pp. 197–213). Woodhead Publishing in Food Science and Technology. Google Search. Retrieved January 9, 2019, from https://www.google.com/search?source=hp&ei=r401XPqaDJaBoATA0Ygo&q=Fleurence%2C+J.%2C+2004.+Seaweed+proteins.+In%3A+Yada%2C+R.Y.+%28Ed.%29%2C+Proteins+in+Food+Processing.

+Woodhead+Publishing+in+Food+Science+and+Technology%2C+pp.+197%E2%80%93213.&btnK=Google+Search&oq=Fleurence%2C+J.%2C+2004.+Seaweed+proteins.+In%3A+Yada%2C+R.Y.+%28Ed.%29%2C+Proteins+in+Food+Processing.+Woodhead+Publishing+in+Food+Science+and+Technology%2C+pp.+197%E2%80%93213.&gs_l=psy-ab.3...6472.6472..7373...0.0..0.717.1335.5-1j1......0....1j2..gws-wiz.....0.RYMGm03V_7w.

Food and Agriculture Organization of the United Nations. (2014). *The state of world fisheries and aquaculture* (Rome, Italy).

Food and Agriculture Organization of the United Nations. (2017). *The state of world fisheries and aquaculture* (Rome, Italy).

Freile-Pelegrín, Y., & Tasdemir, D. (2019). Seaweeds to the rescue of forgotten diseases: A review. *Botanica Marina*. https://doi.org/10.1515/bot-2018-0071.

Fujiwara-Arasakil, T., Minol, N., & Kuroda, M. (1984). The protein value in human nutrition of edible marine algae in Japan. *Hydrobiologia, 116*, 513–516.

Ganesan, P., Matsubara, K., Sugawara, T., & Hirata, T. (2013). Marine algal carotenoids inhibit angiogenesis by down-regulating FGF-2-mediated intracellular signals in vascular endothelial cells. *Molecular and Cellular Biochemistry, 380*, 1–9. https://doi.org/10.1007/s11010-013-1651-5.

Ganzon-Fortrs, E. T. (2012). A historical account of biodiversity studies on Philippine seaweeds (1800–1999). *Coastal Marine Science, 35*(1), 182–201.

Ghosh, T., Pujol, C. A., Damonte, E. B., Sinha, S., & Ray, B. (2009). Sulfated xylomannans from the red seaweed *Sebdenia polydactyla* : Structural features, chemical modification and antiviral activity. *Antiviral Chemistry and Chemotherapy, 19*(6), 235–242. https://doi.org/10.1177/095632020901900603.

Gillies, P. J., Harris, W. S., & Kris-Etherton, P. M. (2011). Omega-3 fatty acids in food and pharma: The enabling role of biotechnology. *Current Atherosclerosis Reports, 13*(6), 467–473. https://doi.org/10.1007/s11883-011-0206-z.

Guesnet, P., & Alessandri, J. M. (2011). Docosahexaenoic acid (DHA) and the developing central nervous system (CNS) – implications for dietary recommendations. *Biochimie, 93*(1), 7–12. https://doi.org/10.1016/j.biochi.2010.05.005.

Gupta, S., & Abu-Ghannam, N. (2011). Bioactive potential and possible health effects of edible brown seaweeds. *Trends in Food Science & Technology, 22*(6), 315–326. https://doi.org/10.1016/j.tifs.2011.03.011.

van Hal, J. W., Huijgen, W. J. J., & López-Contreras, A. M. (2014). Opportunities and challenges for seaweed in the biobased economy. *Trends in Biotechnology, 32*(5), 231–233. https://doi.org/10.1016/j.tibtech.2014.02.007.

Hamed, I., Özogul, F., Özogul, Y., & Regenstein, J. M. (2015). Marine bioactive compounds and their health benefits: A review: Importance of functional seafood. *Comprehensive Reviews in Food Science and Food Safety, 14*(4), 446–465. https://doi.org/10.1111/1541-4337.12136.

Harada, H., Yamashita, U., Kurihara, H., Fukushi, E., Kawabata, J., & Kamei, Y. (2002). Antitumor activity of palmitic acid found as a selective cytotoxic substance in a marine red alga. *Anticancer Research, 22*(5), 2587–2590.

Hayashi, T., Hayashi, K., Kanekiyo, K., Ohta, Y., Lee, J.-B., Hashimoto, M., et al. (2007). *Promising antiviral glyco-molecules from an edible alga*. Hoboken, NJ, USA: John Wiley & Sons.

Hayashi, K., Nakano, T., Hashimoto, M., Kanekiyo, K., & Hayashi, T. (2008). Defensive effects of a fucoidan from brown alga *Undaria pinnatifida* against herpes simplex virus infection. *International Immunopharmacology, 8*(1), 109–116. https://doi.org/10.1016/j.intimp.2007.10.017.

Hayashi, L., Reis, R. P., Alves dos Santos, A. A., Castelar, B., Robledo, D., de Vega, G. B., et al. (2017). The cultivation of *Kappaphycus* and *Eucheuma* in tropical and sub-tropical waters. In A. Q. Hurtado, A. T. Critchley, & I. C. Neish (Eds.), *Tropical seaweed farming trends, problems and opportunities: Focus on spinosum and cottonii of commerce* (pp. 55—90). Netherlands: Springer.

Holdt, S. L., & Kraan, S. (2011). Bioactive compounds in seaweed: Functional food applications and legislation. *Journal of Applied Phycology, 23*(3), 543—597. https://doi.org/10.1007/s10811-010-9632-5.

Hotimchenko, S. V. (2002). Fatty acid composition of algae from habitats with varying amounts of illumination. *Russian Journal of Marine Biology, 28*(3), 218—220. https://doi.org/10.1023/A:1016861807103.

Huang, L., Wen, K., Gao, X., & Liu, Y. (2010). Hypolipidemic effect of fucoidan from *Laminaria* japonica in hyperlipidemic rats. *Pharmaceutical Biology, 48*(4), 422—426. https://doi.org/10.3109/13880200903150435.

Hurtado, A. Q. (2018). Seaweed-carrageenan industry of the Philippines: Quo vadis?. In *Paper presented at the 2018 national seaweed congress, Cebu city, Philippines, 10—12 October 2018*.

Hurtado-Ponce, A. Q. (1983). Marine macrobenthic algae of Currimao, Ilocos Norte. *Ilocos Fisheries Journal, 1*, 104—149.

Hurtado-Ponce, A. Q. (1984). List of edible seaweeds of Currimao, Ilocos Norte. *Ilocos Fisheries Journal, 1*, 179—181.

Hurtado, A. Q., & Critchley, A. T. (2006). Seaweed industry of the Philippines and the problem of epiphytism in *Kappaphycus* farming. In S. M. Phang, A. T. Critchley, & P. Ang, Jr. (Eds.), *Advances in seaweed cultivation and utilization in Asia* (pp. 21—28). Kuala Lumpur: University of Malaya Maritime Research Centre, University of Malaya.

Hurtado, A. Q., Gerung, G. S., Yasir, S., & Critchley, A. T. (2014). Cultivation of tropical red seaweeds in the BIMP-EAGA region. *Journal of Applied Phycology, 26*, 702—718.

Hurtado, A. Q., Joe, M., Sanares, R. C., Fan, D., Prithiviraj, B., & Critchley, A. T. (2012). Investigation of the application of Acadian Marine plant extract powder (AMPEP) to enhance the growth, phenolic content, free radical scavenging, and iron chelating activities of *Kappaphycus* Doty (Solieriaceae, Gigartinales, Rhodophyta). *Journal of Applied Phycology, 24*, 601—611.

Hurtado, A. Q., Luhan, M. R. J., & Guanzon, N. G., Jr. (2006). *Seaweeds of panay*. Tigbauan, Iloilo: SEAFDEC Aquaculture Department (Monograph). 50pp.

Hurtado, A. Q., Neish, I. C., & Critchley, A. T. (2019). Phyconomy: The extensive cultivation of seaweeds, sustainability and economic value — with reference from experiences in eucheumatoid farming. *Phycologia*. https://doi.org/10.1080/00318884.2019.1625632.

Ishihara, K., Murata, M., Kaneniwa, M., Saito, H., Shinohara, K., & Maeda-Yamamoto, M. (1998). Inhibition of icosanoid production in MC/9 mouse mast cells by n-3 polyunsaturated fatty acids isolated from edible marine algae. *Bioscience, Biotechnology, and Biochemistry, 62*(7), 1412—1415. https://doi.org/10.1271/bbb.62.1412.

Ito, K., Tsuchiya, Y., & Tohoku, U. (1977). Differential fatty acid composition of some marine algae associated with their habitat depths. *Tohoku Journal of Agricultural Research*. Retrieved from http://agris.fao.org/agris-search/search.do?recordID=JP7806824.

Jin, D.-Q., Lim, C. S., Sung, J.-Y., Choi, H. G., Ha, I., & Han, J.-S. (2006). *Ulva conglobata*, a marine algae, has neuroprotective and anti-inflammatory effects in murine hippocampal and microglial cells. *Neuroscience Letters, 402*, 154—158.

Kaur, G., Cameron-Smith, D., Garg, M., & Sinclair, A. J. (2011). Docosapentaenoic acid (22:5n-3): A review of its biological effects. *Progress in Lipid Research, 50*(1), 28—34. https://doi.org/10.1016/j.plipres.2010.07.004.

Kawasaki, A., Ono, A., Mizuta, S., Kamiya, M., Takenaga, T., & Murakami, S. (2017). The taurine content of Japanese seaweed. In *Advances in experimental medicine and biology* (Vol. 975, pp. 1105—1112). https://doi.org/10.1007/978-94-024-1079-2_88.

Kendel, M., Barnathan, G., Fleurence, J., Rabesaotra, V., & Wielgosz-Collin, G. (2013). Non-methylene interrupted and hydroxy fatty acids in polar lipids of the alga Grateloupia turuturu over the four seasons. *Lipids, 48*(5), 535—545. https://doi.org/10.1007/s11745-013-3783-5.

Kho, F. B., Orbita, M. L. S., & Manting, M. M. E. (2016). Mindanao, Philippines. *Carrageenan and biochemical composition of three species of Halymenia (Halymenia durvillaea bory de Saint-Vincent, Halymenia maculata J. Agardh and Halymenia dilatata zanardini) in initao, misamis oriental* (Vol. 8).

Kim, J. K., Yarish, C., Hwang, E. K., Park, M., & Kim, Y. (2017). Seaweed aquaculture: Cultivation technologies, challenges and its ecosystem services. *Algae, 32*, 1—13.

Kinley, R. D., de Nys, R., Vucko, M. J., Machado, L., & Tomkins, N. W. (2016). The red macroalgae *Asparagopsis* taxiformis is a potent natural anti-methanogenic that reduces methane production during in vitro fermentation with rumen fluid. *Animal Production Science, 256*, 282—289.

Koch, K., Hagen, W., Graeve, M., & Bischof, K. (2017). Fatty acid compositions associated with high-light tolerance in the intertidal rhodophytes *Mastocarpus stellatus* and *Chondrus crispus*. *Helgoland Marine Research, 71*(1), 15. https://doi.org/10.1186/s10152-017-0495-x.

Largo, D. B. (2002). Recent development in seaweed diseases. In A. Q. Hurtado, N. G. Guanzon, Jr., T. R. de Castro-Mallare, & M. R. J. Luhan (Eds.), *Proc nat seaweed planning workshop. Tigbauan, Iloilo* (pp. 35—42).

Lin, A.-S., Stout, E. P., Prudhomme, J., Roch, K. L., Fairchild, C. R., Franzblau, S. G., et al. (2010). Bioactive bromophycolides R—U from the Fijian red alga Callophycus serratus. *Journal of Natural Products, 73*(2), 275—278. https://doi.org/10.1021/np900686w.

Liu, J., Kandasamy, S., Zhang, J., Kirby, C. W., Karakach, T., Hafting, J., et al. (2015). Prebiotic effects of diet supplemented with the cultivated red seaweed *Chondrus crispus* or with fructo-oligo-saccharide on host immunity, colonic microbiota and gut microbial metabolites. *BMC Complementary and Alternative Medicine, 15*, 279. https://doi.org/10.1186/s12906-015-0802-5.

Liu, Z., Gao, T., Yang, Y., Meng, F., Zhan, F., Jiang, Q., & Sun, X. (2019). Anti-cancer activity of porphyran and carrageenan from red seaweeds. *Molecules, 24*, 4286. https://doi.org/10.3390/molecules24234286.

Lordan, S., Ross, R. P., & Stanton, C. (2011). Marine bioactives as functional food ingredients: Potential to reduce the incidence of chronic diseases. *Marine Drugs, 9*(6), 1056—1100. https://doi.org/10.3390/md9061056.

Lourenço, S. O., Barbarino, E., De-Paula, J. C., Pereira, L. O. da S., & Marquez, U. M. L. (2002). Amino acid composition, protein content and calculation of nitrogen-to-protein conversion factors for 19 tropical seaweeds. *Phycological Research, 50*(3), 233—241. https://doi.org/10.1046/j.1440-1835.2002.00278.x.

MacArtain, P., Gill, C. I. R., Brooks, M., Campbell, R., & Rowland, I. R. (2007). Nutritional value of edible seaweeds. *Nutrition Reviews, 65*(12), 535—543. https://doi.org/10.1111/j.1753-4887.2007.tb00278.x.

Machado, L. (2015). *Tropical macroalgae as a natural alternative for the mitigation of methane emissions in ruminant livestock systems*. PhD thesis. Australia: James Cook University http://researchonline.jcu.edu.au/46419/.

Magalhaes, K. D., Costa, L. S., Fidelis, G. P., Oliveira, R. M., Nobre, L. T. D. B., Dantas-Santos, N., et al. (2011). Anticoagulant, antioxidant and antitumor activities of heterofucans from the seaweed Dictyopteris delicatula. *International Journal of Molecular Sciences, 12*(5), 3352—3365. https://doi.org/10.3390/ijms12053352.

Marcos-Agngarayngay, Z. D. (1984). Marine macro-algae of Ilocos Norte, II: Phaeophyta and Rhodophyta. *Ilocos Fisheries Journal, 1*(2), 1—66.

McDermid, K. J., & Stuercke, B. (2003). Nutritional composition of edible Hawaiian seaweeds. *Journal of Applied Phycology, 15*(6), 513–524. https://doi.org/10.1023/B:JAPH.0000004345.31686.7f.

McKim, J. M., Baas, H., Rice, G. P., Willoughby, J. A., Weiner, M. L., & Blakemore, W. (2016). Effects of carrageenan on cell permeability, cytotoxicity, and cytokine gene expression in human intestinal and hepatic cell lines. *Food and Chemical Toxicology, 96*, 1–10. https://doi.org/10.1016/j.fct.2016.07.006.

Melo, T., Alves, E., Azevedo, V., Martins, A. S., Neves, B., Domingues, P., et al. (2015). Lipidomics as a new approach for the bioprospecting of marine macroalgae — unraveling the polar lipid and fatty acid composition of *Chondrus crispus*. *Algal Research, 8*, 181–191. https://doi.org/10.1016/j.algal.2015.02.016.

Mendis, E., & Kim, S.-K. (2011). Present and future prospects of seaweeds in developing functional foods. *Advances in Food & Nutrition Research, 64*, 1–15. https://doi.org/10.1016/B978-0-12-387669-0.00001-6.

Michalak, I., & Chojnacka, K. (2015). Algae as production systems of bioactive compounds. *Engineering in Life Science, 15*(2), 160–176. https://doi.org/10.1002/elsc.201400191.

Milstein, D., Madeiros, A. S., Oliveira, E. C., & Oliveira, M. C. (2015). Native or introduced? A re-evaluation of *pyropia* species (*Bangiales*, Rhodophyta) from Brazil based on molecular analysis. *European Journal of Phycology, 50*, 37–45. https://doi.org/10.1080/09670262.2014.982202.

Mišurcová, L., Kráčmar, S., Klejdus, B., & Vacek, J. (2010). Nitrogen content, dietary fiber, and digestibility in algal food products. *Czech Journal of Food Sciences*. https://doi.org/10.17221/111/2009-CJFS.

Mohamed, S., Hashim, S. N., & Rahman, H. A. (2012). Seaweeds: A sustainable functional food for complementary and alternative therapy. *Trends in Food Science & Technology, 23*(2), 83–96. https://doi.org/10.1016/j.tifs.2011.09.001.

Monotilla, W. D., & Notoya, M. (2004). Morphological and physiological responses of *Porphyra suborbiculata* Kjellman (*Bangiales*, Rhodophyta) blades from five localities. *Botanica Marina, 47*, 323–334.

Monotilla, W. D., & Notoya, M. (2010). Growth and development of *Porphyra marcosii* (*Bangiales*, Rhodophyta) under different temperatures and photoperiod. *Philippine Journal of Science, 139*, 197–206.

Murad, H., Ghannam, A., Al-Ktaifani, M., Abbas, A., & Hawat, M. (2015). Algal sulfated carrageenan inhibits proliferation of MDA-MB-231 cells via apoptosis regulatory genes. *Molecular Medicine Reports, 11*(3), 2153–2158. https://doi.org/10.3892/mmr.2014.2915.

Okolie, C., Mason, B., & Critchley, A. T. (2018). Seaweeds as a source of proteins for use in pharmaceuticals and high-value applications. In M. Hayes (Ed.), *Novel Proteins for Food, Pharmaceuticals and Agriculture: Sources, Applications and Advances*. Wiley. Chapter: 11 (Edition: 1). https://onlinelibrary.wiley.com/doi/abs/10.1002/9781119385332.ch11.

Oomah, B., & Mazza, G. (1999). Health benefits of phytochemicals from selected Canadian crops. *Trends in Food Science & Technology, 10*(6–7), 193–198. https://doi.org/10.1016/S0924-2244(99)00055-2.

Pangestuti, R., & Kim, S. K. (2011). Neuroprotective effects of marine algae. *Marine Drugs, 9*, 803–818.

Papanikolaou, Y., Brooks, J., Reider, C., & Fulgoni, V. L. (2014). U.S. Adults are not meeting recommended levels for fish and omega-3 fatty acid intake: Results of an analysis using observational data from NHANES 2003–2008. *Nutrition Journal, 13*, 31. https://doi.org/10.1186/1475-2891-13-31.

Paxman, J. R., Richardson, J. C., Dettmar, P. W., & Corfe, B. M. (2008). Daily ingestion of alginate reduces energy intake in free-living subjects. *Appetite, 51*(3), 713–719. https://doi.org/10.1016/j.appet.2008.06.013.

Pengzhan, Y., Quanbin, Z., Ning, L., Zuhong, X., Yanmei, W., & Zhi'en, L. (2003). Polysaccharides from Ulva pertusa (*Chlorophyta*) and preliminary studies on their antihyperlipidemia activity. *Journal of Applied Phycology, 15*(1), 21–27. https://doi.org/10.1023/A:1022997622334.

Pereira, L. (2016). *Edible Seaweeds of the World*. CRC Press. https://doi.org/10.1201/b19970.

Pereira, L. (2018a). Seaweeds as source of bioactive substances and skin care therapy—cosmeceuticals, algotheraphy, and thalassotherapy. *Cosmetics, 5*(4), 68. https://doi.org/10.3390/cosmetics5040068.

Pereira, L. (2018b). Biological and therapeutic properties of seaweed polysaccharides. *International Biology Review, 2*, 1–50.

Pereira, L., & Ribeiro-Claro, P. J. A. (2014). Analysis by vibrational spectroscopy of seaweed polysaccharides with potential use in food, pharmaceutical and cosmetic industries. In L. Pereira, & M. N. Joao (Eds.), *Marine algae: Biodiversity, taxonomy, environmental assessment and biotechnology* (pp. 225–247). CRC Press. Taylor & Francis Group.

Plouguerné, E., da Gama, B. A. P., Pereira, R. C., & Barreto-Bergter, E. (2014). Glycolipids from seaweeds and their potential biotechnological applications. *Frontiers in Cellular and Infection Microbiology, 4*. https://doi.org/10.3389/fcimb.2014.00174.

Ponce, N. M. A., Pujol, C. A., Damonte, E. B., Flores, M. L., & Stortz, C. A. (2003). Fucoidans from the brown seaweed *Adenocystis utricularis*: Extraction methods, antiviral activity and structural studies. *Carbohydrate Research, 338*(2), 153–165.

Poudyal, H., Panchal, S. K., Ward, L. C., & Brown, L. (2013). Effects of ALA, EPA and DHA in high-carbohydrate, high-fat diet-induced metabolic syndrome in rats. *The Journal of Nutritional Biochemistry, 24*(6), 1041–1052. https://doi.org/10.1016/j.jnutbio.2012.07.014.

Primdahl, K. G., Tungen, J. E., Aursnes, M., Hansen, T. V., & Vik, A. (2015). An efficient total synthesis of leukotriene B4. *Organic and Biomolecular Chemistry, 13*(19), 5412–5417. https://doi.org/10.1039/C5OB00473J.

Pujol, C. A., Estevez, J. M., Carlucci, M. J., Ciancia, M., Cerezo, A. S., & Damonte, E. B. (2002). Novel DL-galactan hybrids from the red seaweed Gymnogongrus torulosus are potent inhibitors of herpes simplex virus and dengue virus. *Antiviral Chemistry & Chemotherapy, 13*(2), 83–89. https://doi.org/10.1177/095632020201300202.

Qi, B., Beaudoin, F., Fraser, T., Stobart, A. K., Napier, J. A., & Lazarus, C. M. (2002). Identification of a cDNA encoding a novel C18-Delta(9) polyunsaturated fatty acid-specific elongating activity from the docosahexaenoic acid (DHA)-producing microalga, Isochrysis galbana. *FEBS Letters, 510*(3), 159–165.

Ragonese, C., Tedone, L., Beccaria, M., Torre, G., Cichello, F., Cacciola, F., et al. (2014). Characterisation of lipid fraction of marine macroalgae by means of chromatography techniques coupled to mass spectrometry. *Food Chemistry, 145*, 932–940. https://doi.org/10.1016/j.foodchem.2013.08.130.

Rajapakse, N., & Kim, S.-K. (2011). Nutritional and digestive health benefits of seaweed. In *Advances in food and nutrition research* (Vol. 64, pp. 17–28). https://doi.org/10.1016/B978-0-12-387669-0.00002-8.

Ren, R., Azuma, Y., Ojima, T., Hashimoto, T., Mizuno, M., Nishitani, Y., et al. (2013). Modulation of platelet aggregation-related eicosanoid production by dietary F-fucoidan from brown alga *Laminaria* japonica in human subjects. *British Journal of Nutrition, 110*(5), 880–890. https://doi.org/10.1017/S000711451200606X.

Rodrigues, D., Freitas, A. C., Pereira, L., Rocha-Santos, T. A. P., Vasconcelos, M. W., Roriz, M., et al. (2015). Chemical composition of red, brown and green macroalgae from Buarcos bay in central west coast of Portugal. *Food Chemistry, 183*, 197–207. https://doi.org/10.1016/j.foodchem.2015.03.057.

Schmid, M., Guihéneuf, F., & Stengel, D. B. (2014). Fatty acid contents and profiles of 16 macroalgae collected from the Irish coast at two seasons. *Journal of Applied Phycology, 26*(1), 451–463. https://doi.org/10.1007/s10811-013-0132-2.

Schubert, R., Kitz, R., Beermann, C., Rose, M. A., Baer, P. C., Zielen, S., et al. (2007). Influence of low-dose polyunsaturated fatty acids supplementation on the inflammatory response of healthy adults. *Nutrition, 23*(10), 724–730. https://doi.org/10.1016/j.nut.2007.06.012.

Silva, P. C., Menez, E. G., & Moe, R. L. (1987). Catalog of the benthic marine algae of the Philippines. *Smithsonian Contributions to the Marine Sciences,* 27, 190pp.

Slagsvold, J. E., Pettersen, C. H. H., Follestad, T., Krokan, H. E., & Schønberg, S. A. (2009). The antiproliferative effect of EPA in HL60 cells is mediated by alterations in calcium homeostasis. *Lipids, 44*(2), 103–113. https://doi.org/10.1007/s11745-008-3263-5.

Stengel, D. B., Connan, S., & Popper, Z. A. (2011). Algal chemodiversity and bioactivity: Sources of natural variability and implications for commercial application. *Biotechnology Advances, 29*(5), 483–501. https://doi.org/10.1016/j.biotechadv.2011.05.016.

Stiger-Pouvreau, V., Bourgougnon, N., & Deslandes, E. (2016). Carbohydrates from seaweeds. In J. Fleurence, & I. Levine (Eds.), *Algae: A way of life and health* (pp. 223–274). Amsterdam Boston Heidelberg London: Elsevier, Academic Press.

Sugawara, T., Matsubara, K., Akagi, R., Mori, M., & Hirata, T. (2006). Antiangiogenic activity of brown algae fucoxanthin and its deacetylated product, fucoxanthinol. *Journal of Agricultural and Food Chemistry, 54*(26), 9805–9810. https://doi.org/10.1021/jf062204q.

Swarnalatha, G. (2018). *Comparison of nutritive values of seaweed with other terrestrial foods – A review*. Retrieved April 11, 2019, from https://www.ijfans.com/ijfansadmin/upload/ijfans_5a7935678f6ed.pdf.

Synytsya, A., Bleha, R., Synytsya, A., Pohl, R., Hayashi, K., Yoshinaga, K., et al. (2014). Mekabu fucoidan: Structural complexity and defensive effects against avian influenza a viruses. *Carbohydrate Polymers, 111*, 633–644. https://doi.org/10.1016/j.carbpol.2014.05.032.

Talarico, L. B., Pujol, C. A., Zibetti, R. G. M., Faría, P. C. S., Noseda, M. D., Duarte, M. E. R., et al. (2005). The antiviral activity of sulfated polysaccharides against dengue virus is dependent on virus serotype and host cell. *Antiviral Research, 66*(2–3), 103–110. https://doi.org/10.1016/j.antiviral.2005.02.001.

Tanaka, Y., Goto, K., Matsumoto, Y., & Ueoka, R. (2008). Remarkably high inhibitory effects of docosahexaenoic acid incorporated into hybrid liposomes on the growth of tumor cells along with apoptosis. *International Journal of Pharmaceutics, 359*(1–2), 264–271. https://doi.org/10.1016/j.ijpharm.2008.03.045.

Taoda, N., Shinji, E., Nishii, K., Nishioka, S., Yonezawa, Y., Uematsu, J., et al. (2008). Fucoidan inhibits parainfluenza virus type 2 infection to LLCMK2 cells. *Biomedical Research, 29*(6), 331–334.

Thomes, P., Rajendran, M., Pasanban, B., & Rengasamy, R. (2010). Cardioprotective activity of *Cladosiphon* okamuranus fucoidan against isoproterenol induced myocardial infarction in rats. *Phytomedicine, 18*(1), 52–57. https://doi.org/10.1016/j.phymed.2010.06.006.

Tobacman, J. K. (2001). Review of harmful gastrointestinal effects of carrageenan in animal experiments. *Environmental Health Perspectives, 109*(10), 983–994. https://doi.org/10.1289/ehp.01109983.

Torres, M. D., Flórez-Fernández, N., & Domínguez, H. (2019). Integral Utilization of Red Seaweed for Bioactive Production. *Marine Drugs, 17*(6), 314. https://doi.org/10.3390/md17060314.

Trono, G. C., Jr. (1977). *Field guide and atlas of the seaweed resources of the Philippines*. Bookmark, Makati City, 306 pp.

Trono, G. C., Jr. (2010). *A primer on the land-based culture of* Halymenia *durvillaei bory de Saint-Vincent (Rhodophyta)*. Quezon City: Marine Science Institute, University of the Philippines Diliman.

Tsai, C.-J., & Sun Pan, B. (2012). Identification of sulfoglycolipid bioactivities and characteristic fatty acids of marine macroalgae. *Journal of Agricultural and Food Chemistry, 60*(34), 8404–8410. https://doi.org/10.1021/jf302241d.

Tungpalan, A. Y. (1984). Ethnobotanical study of the seaweeds of Ilocos Norte. *Ilocos Fisheries Journal, 1*, 134–146.

Vairappan, C. S., Chung, C. S., Hurtado, A. Q., Msuya, F. E., Bleicher L'honneur, G., & Critchley, A. T. (2008). Distribution and symptoms of epiphyte infection in major carrageenophyte-producing farms. *Journal of Applied Phycology, 20*, 477–483.

Wang, J., Chen, S., Xu, S., Yu, X., Ma, D., Hu, X., et al. (2012). In vivo induction of apoptosis by fucoxanthin, a marine carotenoid, associated with down-regulating STAT3/EGFR signaling in sarcoma 180 (S180) xenografts-bearing mice. *Marine Drugs, 10*(9), 2055–2068. https://doi.org/10.3390/md10092055.

Wielgosz-Collin, G., Kendel, M., & Couzinet-Mossion, A. (2016). Lipids, fatty acids, glycolipids, and phospholipids. In J. Fleurence, & I. Levine (Eds.), *Algae: A way of life and health* (pp. 185–222). Amsterdam Boston Heidelberg London: Elsevier, Academic Press.

Wijesinghe, W. A. J. P., & Jeon, Y. J. (2011). Biological activities and potential cosmeceutical applications of bioactive components from brown seaweeds: A review. *Phytochemistry Reviews, 10*(3), 431–443. https://doi.org/10.1007/s11101-011-9214-4. Request PDF.

Ye, J., Li, Y., Teruya, K., Katakura, Y., Ichikawa, A., Eto, H., et al. (2005). Enzyme-digested fucoidan extracts derived from seaweed mozuku of *Cladosiphon* novae-caledoniae kylin inhibit invasion and angiogenesis of tumor cells. *Cytotechnology, 47*(1–3), 117–126. https://doi.org/10.1007/s10616-005-3761-8.

Zhu, W., Ooi, V. E., Chan, P. K. S., & Ang, P. O., Jr. (2003). *Inhibitory effect of extracts of marine algae from Hong Kong against herpes simplex viruses*. Request PDF. Retrieved December 6, 2018, from ResearchGate website: https://www.researchgate.net/publication/291158077_Inhibitory_effect_of_extracts_of_marine_algae_from_Hong_Kong_against_Herpes_simplex_viruses.