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Tropical Seaweeds Improve Cardiovascular and Metabolic Health of Diet-Induced Obese and Hypertensive Rats †

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Abstract: Seaweeds have been an important part of the diet of coastal populations in Asia possibly for millennia but only a few scattered coastal communities in Europe and the Americas have maintained these traditions. Our studies have investigated the potential of two tropical seaweeds grown commercially in Asia, *Sarconema* and *Caulerpa* spp., as functional foods for the reversal of metabolic syndrome and possible mechanisms. *Sarconema* spp. are a source of carrageenans used as thickening and gelling agents in foods while *Caulerpa* spp. are consumed in South-East Asia as low-energy foods with high contents of vitamins and minerals. For our studies, male Wistar rats were divided into groups in a 16-week protocol: corn starch diet-fed rats (C); C rats supplemented with 5% dried seaweed for the last 8 weeks; high-carbohydrate, high-fat diet-fed rats (H); and H rats supplemented with 5% dried seaweed for the last 8 weeks. H rats developed obesity, hypertension, dyslipidaemia, glucose intolerance, fatty liver and increased left ventricular collagen deposition, infiltration of inflammatory cells and plasma liver enzyme activities. Seaweed supplementation decreased body weight, abdominal and liver fat, systolic blood pressure, plasma lipid concentrations, plasma activities of liver enzymes and collagen deposition. Further, seaweed supplementation modulated gut microbiota. Possible mechanisms for improved cardiovascular and metabolic health include a reduced infiltration of inflammatory cells into organs as well as an increased intake of fibre modulating gut microbiota composition.

Keywords: metabolic syndrome; seaweeds; *Sarconema*; *Caulerpa*; gut microbiota; inflammation

1. Introduction

Seaweeds have generated extensive mythology, folklore and poetry around the world [1]. In ancient Japan and China, seaweeds were valued, even revered, and used to pay taxes or presented as a delicacy to honoured guests. However, they were not appreciated by the ancient Romans or Greeks and their consumption was a sign of penury or frugality in much of the Western world [1]. Globally, seaweeds are still under-utilised but the interest in seaweeds as foods or phycogastronomy is increasing [2].

Tropical fruits such as mangosteens, coffee and seaweeds have been evaluated as functional foods, defined as foods that provide nutrition as well as therapeutic benefits [3]. Seaweeds are an important part of traditional diets in many Asian countries such as Japan, Korea, China, Vietnam and the Philippines. Seaweeds are also an important product of aquaculture; the Food and Agriculture

Organization of the United Nations reported in 2020 that total production of aquatic plants, mainly seaweeds and mainly by aquaculture, reached 32.4 million tonnes world-wide in 2018, with the three major species being the brown seaweed, Japanese kelp (*Laminaria japonica*; 11.5 million tonnes), the red seaweed, *Eucheuma* spp. (9.2 million tonnes) and the red seaweed, *Gracilaria* spp. (3.5 million tonnes) [4]. The related *Kappaphycus* and *Eucheuma* are the major red seaweeds commercially grown in the tropical waters of South-East Asia, especially Indonesia, the Philippines and Malaysia. This large-scale production has raised many issues including lack of seaweed biodiversity, lack of commercialisation of indigenous cultivars, failure to implement new farming techniques and environmental issues such as invasive organisms and plastics [5].

The use of seaweeds as raw materials for agriculture and industry is widespread. Waste algae have been successfully composted although there are many challenges to produce an effective product [6]. Biochar produced from seaweed biomass is high yield with nutrients including N, P, K, Ca, Mg and Mo, leading to reduced soil emissions of greenhouse gases, reduced nutrient leaching, reduced soil acidity, and reduced irrigation and fertiliser requirements [7] as well as 35–40% increased growth of radishes [8]. Seaweeds are effective in removing pollutants such as dyes, nitrogen, phosphorus and heavy metals from wastewater [9]. Freshwater macroalgae were used to recover N and P from municipal wastewater to then increase agricultural productivity in low fertility soil [10]; this action also decreases the access of these pollutants from coastal cities to the surrounding ocean. Freshwater macroalgae can effectively bioremediate effluents from coal-fired power stations [11]. Further, the use of seaweed biomass to produce biofuels is now being intensively researched to decrease concerns about the depletion of fossil fuels [12]. Macroalgal polysaccharides such as alginates and carrageenans are potential sources of bio-based plastics as an alternative to fossil fuel [13]. In the oceans, physiological buffering by a marine alga since photosynthetic activity increases pH in the microenvironment which may ameliorate the negative effects of changing ocean conditions such as increased temperatures and carbon dioxide concentrations [14].

Seaweeds also have important roles in the food industry and health. Seaweeds added to foods such as meat, fish and bakery can improve shelf-life and overall quality of these foods [15]. There are extensive reviews on the potential usefulness of seaweeds in health [16,17], especially concerning the roles of polysaccharides as prebiotics [18]. One particular emphasis is the role of seaweeds to attenuate the signs of metabolic syndrome, especially obesity and hypertension [19–21]. While seaweeds can provide a sustainable source of nutrients as well as many health interventions, there are potential risks in seaweed consumption, such as excess intake of iodine and heavy metals such as arsenic [22].

This project has investigated the effectiveness of two tropical seaweeds, *Sarconema filiforme* and *Caulerpa lentillifera*, to attenuate the signs of metabolic syndrome in rats following a diet high in simple sugars such as fructose and sucrose as well as saturated fats. We have determined the changes in cardiovascular, liver and metabolic parameters.

2. Methods

Source of seaweeds: *S. filiforme* was cultured at the University of the Sunshine Coast seaweed aquaculture facility at the Bribie Island Research Centre, Woorim, QLD, Australia (27°04′10″ S; 153°12′15″ E) from January to March 2018. *C. lentillifera* was purchased from Viet Delta Corporation (http://vdelta.com.vn/c/3/seaweed?pagenumber=2#), Ho Chi Minh City, Vietnam.

Rats and diets: Male Wistar rats (8–9 weeks old; 330–340 g) were obtained from the Animal Resource Centre, Murdoch, WA, Australia. Rats were randomly allocated to four groups for each intervention, each of 12 rats. Two groups were fed either corn starch or high-carbohydrate, high-fat diets (C and H, respectively) [23] for the full 16 weeks. The other two groups received C and H diets for eight weeks and then received either 5% *S. filiforme* or *C. lentillifera* mixed in the food for the final eight weeks. Rat measurements of body weights, food and water intakes, abdominal circumference, systolic blood pressure, body composition by dual energy X-ray absorptiometry, oral glucose and insulin tolerance, indirect calorimetry, plasma measurements, isolated Langendorff heart preparation, organ weights, plasma measurements, histological analyses and gut microbiota, together with statistical analyses, have been previously described [23,24].

3. Results and Discussion

Rats fed for 16 weeks with a diet high in simple sugars and saturated fats developed the signs of metabolic syndrome, including obesity, hypertension, dyslipidaemia, glucose intolerance, fatty liver and increased left ventricular collagen deposition. We then used a reversal protocol to determine whether intervention with either *S. filiforme* or *C. lentillifera* attenuated these physiological changes. Both interventions decreased body weight, systolic blood pressure, left ventricular stiffness, visceral adiposity, plasma cholesterol concentrations and infiltration of inflammatory cells into the heart and liver [24,25]. These results are consistent with our previous study on the red seaweed, *Kappaphycus alvarezii* [26]. These changes show that both seaweeds can be described as functional foods to improve diet-induced metabolic syndrome. Since obesity is described as a low-grade chronic inflammation, the anti-inflammatory responses to both seaweed interventions are likely to be the mechanism for the observed changes.

Further, for both seaweeds, the alterations in the bacterial community structure correlated with the physiological data [24,25], suggesting that the changes in the gut microbiota produced the changes in the physiological parameters in the rats with diet-induced metabolic syndrome. Since both seaweeds are important sources of dietary fibre, this indicates that the seaweed polysaccharides are acting as prebiotics to change bacterial composition in the colon. Prebiotics have been proposed as effective treatments for obesity and NAFLD with plausible mechanisms of action [27,28]. Thus, our results support the concept that these seaweeds improve cardiovascular, liver and metabolic health by prebiotic actions in the colon.

4. Conclusions

Rats fed a diet with increased simple carbohydrates and saturated fatty acids developed the cardiovascular, liver and metabolic signs of metabolic syndrome. Addition of either *S. filiforme* or *C. lentillifera* to the diet reversed these diet-induced changes. Likely mechanisms of actions include markedly decreased infiltration of inflammatory cells into the organs of the body together with prebiotic actions in the gastrointestinal tract. These studies then define both seaweeds as functional foods. Large-scale cultivation of these seaweeds in tropical waters can support the production of high-value health products as additional uses for the seaweeds including as animal food, as broad-spectrum crop fertilisers, to remediate agricultural and industrial waste-water and to store energy as biofuels [29].

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