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# Dietary seaweeds and obesity

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**Abstract**

Potential therapeutic benefits of seaweed consumption have been reported in the management of body weight and obesity. *In vitro* and *in vivo* animal studies provide the majority of data available at present. The majority of studies assessing the short-term effects of alginate consumption indicate that alginate may increase satiety, reduce energy intake and support weight reduction. Mechanisms suggested for these effects include delayed gastric clearance, stimulation of gastric stretch receptors and attenuated nutrient absorption. Long-term studies in humans are required in order to allow firm conclusions. Animal studies have investigated potential anti-obesity effects of seaweeds on adipogenesis and the inhibition of major lipid hydrolyzing and metabolizing enzymes. The results of these studies suggest beneficial effects of seaweed components such as fucoxanthin on body weight and the percentage of abdominal white adipose tissue. It is premature to extrapolate these findings to humans since consistent findings are still lacking. There is at present no solid evidence indicating that seaweeds are effective in long-term weight management. However, available findings suggest potential benefits of seaweed components on obesity. Future investigations are required to establish the therapeutic efficacy in the management of overweight and obesity in humans and elucidate the underlying mechanisms of actions.


*Keywords:* Seaweed; Fucoxanthin; Functional food; Body weight; Obesity

## 1. Introduction

Obesity is a metabolic disorder and can be defined as increased body weight caused by excessive fat accumulation which presents a risk to health with an increase in health problems and/or reduced life expectancy [1,2]. Obesity is characterized by an increased storage of triglycerides in adipose tissues. In obese individuals, there is an increase in the incidence of various diseases such as cardiovascular disease, type 2 diabetes, certain types of cancer, and osteoarthritis [1]. Obesity has reached epidemic proportions in developed countries and is also increasing in developing countries [3]. The epidemic is a leading preventable cause of death worldwide and has been suggested to be one of the most serious public health problems of the 21st century [4]. In 2008, 35% of adults aged 20 or more were overweight (body mass index $\geq$25 kg/m$^2$) [5]. The worldwide prevalence of obesity has nearly doubled between 1980 and 2008. In 2008, 10% of men and 14% of women in the world were obese (BMI $\geq$30 kg/m$^2$), compared with 5% for men and 8% for women in 1980 [5]. An estimated total of more than half a billion adults over the age of 20 were obese. The prevalence of obesity was highest in the WHO Regions of the Americas (26% in both sexes) and lowest in the WHO Region for South East Asia (3% in both sexes) [5]. Worldwide, at least 2.8 million people die each year as a result of being overweight or obese, and an estimated 35.8 million (2.3%) of global disability-adjusted life years are caused by overweight or obesity [5].

Obesity is most commonly caused by a combination of excessive food energy intake, lack of physical activity, and genetic susceptibility. The epidemic reflects progressive secular and age-related decreases in physical activity, together with substantial dietary changes with passive over-consumption of energy despite the neurobiological processes controlling food intake [1]. The main treatments for obesity are dieting and exercising.

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Effective long-term weight loss depends on permanent changes in dietary quality, energy intake, and physical activity [1]. Diet quality can be improved by reducing the consumption of energy-dense foods and by increasing the intake of dietary fiber. However, behavioral interventions alone have been inconsistent in promoting sufficient and sustained weight loss. The identification of substances that are able to decrease or even prevent obesity has become a major goal of research. Consequently, pharmacological research has focused on the development of anti-obesity medications which may reduce appetite or decrease fat absorption [6]. Due to high costs and potentially hazardous adverse effects of these drugs, researchers have become interested in finding safe and therapeutically effective anti-obesity compounds derived from natural products [7], such as seaweeds.

Seaweeds are marine macroalgae and various seaweed types have traditionally been used as food additives or flavoring materials in many countries. For example, the Japanese use 88 seaweed species in cuisine and as healthcare foods according to the KNApSAcK Lunch Box Database [8–11]. Seaweeds are rich in minerals (e.g. iodine, magnesium, iron, zinc and calcium) and dietary fibers and are consumed mainly in East Asia, e.g., Japan, China, Korea, etc. In Japan, for example, over 20 species of red (Rhodophyta), green (Chlorophyta), and brown (Phaeophyta) algae are popular in meals [12]. The three most common seaweed products in Japan are nori (Porphyra, 33 species), wakame (Undaria, 2 species) and kombu (Laminaria, 12 species).

Seaweed is served in approximately 21% of meals in Japan [13], with 20–38% of the population aged 40–79 years consuming seaweed more than five times per week, 29–35% three to four times per week, 25–35% one to two times per week, 6–13% one to two times per month, and 1–2% rarely consuming seaweed [14]. Estimating the amount of seaweed consumption is difficult due to dietary differences between age groups and geographical regions. Seaweed consumption has been estimated to vary between 4 and 7 g/day dried weight [12,15–17] and 12 g/day using both dry and wet weight [18]. Daily seaweed consumption per person in Japan has been reported to have remained relatively consistent between 1955 (4.3 g/day) and 1995 (5.3 g/day) [15], while the type of seaweed consumed changed over 40 years with an increase in the intake of wakame and nori and a decrease in kombu consumption [19].

Seaweeds contain a variety of potentially bioactive compounds some of which are not present in terrestrial plants. These compounds include, for example, proteins such as lectins or phycobiliproteins, carotenoids, pigments, polyphenols, phlorotannins and certain polysaccharides. They may have health-promoting properties and play a role in modulating chronic disease [20]. Epidemiological studies comparing Southeast Asian and Western-style diets have reported an association between dietary intake of seaweeds and a reduced prevalence of chronic diseases including cardiovascular disease, hyperlipidemia and cancer [21,22]. In Japan, the recent spread of a Western diet including an increase in the consumption of meat and dairy products has coincided with an increase in the incidence of chronic diseases [23,24]. A reduction in regular seaweed consumption and other dietary changes are particularly obvious in young Japanese people [14,25].

## 2. Effects of seaweed fiber on appetite and body weight

A diet rich in fiber has been demonstrated to prolong the gastric emptying rate and thereby increasing satiety and reducing food consumption [26]. Since seaweeds are a good source of dietary fiber [27] several studies have assessed the ability of sodium alginate extracted from brown seaweed to enhance satiety and to decrease energy intake (see Table 1).

Pelkman and her colleagues [28] tested the effects of a novel beverage, consisting of alginate-pectin and calcium components, which forms a stable, fibrous gel in the stomach, on subjective satiety and food intake in overweight and obese women (see Table 1). Twenty-nine individuals drank a 2-part beverage twice per day (once before breakfast and once midafternoon) for 7 days. Three alginate-pectin formulations were tested, i.e. 1.0 g, 2.8 g, and control without fiber. Subjective satiety and ad libitum food intake were measured on days 1 and 7 of each 1-week treatment period with a 1-week washout between testings. A decrease in energy consumption was observed in overweight and obese women with low dietary restraint following a 7-day supplementation with alginate-pectin drinks compared to a control drink. Increased stimulation of endogenous satiety signaling is supposed to be the reason for the decrease in energy intake [28]. Future research needs to assess how dietary restraint affects this observation.

Paxman et al. [29] investigated the effects of alginate on appetite control in free-living healthy normal-weight, overweight and obese adults using a randomized, controlled two-way crossover intervention (see Table 1). They compared the effects of a 7-day daily intake of a strong-gelling sodium alginate formulation with a control group. Daily preprandial ingestion of sodium alginate led to a significant reduction by 7% (134.8 kcal) in mean daily energy intake. In addition, significant reductions in the mean daily ingestion of carbohydrate, fat, saturated fat and protein were found [29]. These results suggest a role for a strong-gelling sodium alginate in the treatment of overweight and obesity. The potential efficacy of this therapeutic approach for individuals in different settings was suggested by the absence of any significant interaction effects between the main effect of preload type and those of gender, classification of body mass index and/or timing of preload delivery.

In a further crossover study performed by Paxman and colleagues [30], the uptake of glucose, cholesterol, and triacylglycerols in humans with normal and high body mass index was investigated (see Table 1). The uptake of these substances increased with increasing body fat. The administration of a beverage containing 1.5 g of strong-gelling alginate restored uptake of glucose and cholesterol in overweight and obese subjects to the levels of healthy participants whose uptake was not affected by the alginate drink. This data also indicates a potential efficacy of gelling fibers.

Jensen and his co-authors [31] studied the effects on postprandial satiety feelings, energy intake, and gastric emptying rate, of two different volumes of an alginate-based preload in normal-weight subjects (see Table 1). Twenty individuals were randomly assigned to receive a 3% preload concentration of either low volume (9.9 g alginate in 330 mL) or high volume (15.0 g alginate

Table 1
Effects of seaweed fiber on body weight, overweight and obesity in humans.

| Authors | Subjects | Substance | Study design | Study duration | Dependent variables | Results | Major limitations |
|---|---|---|---|---|---|---|---|
| Pelkman et al. [28] | Overweight and obese women ($n = 29$) | Alginate | Within-subjects, double-blind, placebo-controlled crossover trial. 3 conditions: 1.0 g/drink, 2.8 g/drink or no alginate (control). 2 test drinks daily for 7 days. 1 week washout. | 5 weeks | Energy intake on days 1 and 7 | Decrease in energy intake for both active formulations compared to control group. | Short study duration, only 1 dependent variable assessed |
| Paxman et al. [29] | Healthy men and women ($n = 68$) | Sodium alginate from brown algae | Randomized, controlled two-way crossover study. Preprandial 1.5 sodium alginate beverage or control drink for 7 days. 2-Week washout phase. Crossover | 4 weeks | Energy intake | Decrease in daily energy intake in sodium alginate group. | Short study duration, only 1 dependent variable assessed |
| Paxman et al. [30] | Healthy men ($n = 14$) | Sodium alginate from brown algae | Crossover study. 1.5 g sodium alginate beverage or control drink 3 hours after set breakfast before test lunch. 7 days washout. Crossover | 1 day measurement | Pre- and postprandial plasma levels of glucose, triacylglycerols and cholesterol | Decrease in glucose and cholesterol uptake in participants of sodium alginate group with higher body mass index. | Small sample size, only 1 timepoint measured |
| Odunsi et al. [34] | Overweight and obese male and female subjects ($n = 48$) | Alginate (brown seaweed *Laminaria digitata*) | Randomized, parallel, placebo-controlled, allocation-concealed study. 3 alginate or control capsules per day before meals for 7 days. 6 capsules on days 8–10. | 10 days | Gastric emptying, gastric volume, satiation, calorie intake, gut hormones | No group effect of treatment on any dependent variable. | |
| Georg Jensen et al. [32] | Obese subjects ($n = 24$) | Alginate | Randomized, controlled intervention study. 3% alginate 500 mL drink or placebo 500 mL drink. 3 times preload drink per day before meals as an adjuvant to a calorie-restricted diet. | 2 weeks | Weight loss | Weight loss in both groups due to calorie restriction but not enhanced by alginate supplementation. | Short study duration, small sample size |
| Georg Jensen et al. [31] | Normal-weight men ($n = 10$) and women ($n = 10$) | Alginate | Randomized placebo-controlled, double-blind, four-way crossover trial. 4 conditions: Low volume alginate (9.9 g) 330 mL drink, high volume alginate (15 g) 500 mL drink, 330 mL control drink or 500 mL control drink. | 1 day each on four occasions | Energy intake, satiety feelings, hunger | Low volume-alginate drink reduced energy intake, high volume alginate drink increased satiety and reduced hunger. | Short study duration |

Table 1 (*Continued*)

| Authors | Subjects | Substance | Study design | Study duration | Dependent variables | Results | Major limitations |
|---|---|---|---|---|---|---|---|
| Georg Jensen et al. [33] | Obese men and women ($n = 96$) | Alginate | Randomized, double-blind, placebo-controlled study. 3% alginate 500 mL drink or placebo 500 mL drink. 3 times preload drink per day before meals as an adjuvant to a calorie-restricted diet. | 12 weeks | Weight loss and metabolic risk markers (plasma glucose, insulin, C-reactive protein, ghrelin, HOMA-IR, lipid metabolism) | Weight loss in alginate group greater than in placebo group mainly due to reduced body fat. No change in metabolic risk markers. | |
| Hall et al. [39] | Healthy overweight men ($n = 12$) | *Ascophyllum nodosum* | Single blind crossover study. 100 g of bread containing *Ascophyllum nodosum* (4%) or no seaweed | 1 day measurement | Energy intake, plasma glucose and cholesterol | Decrease in energy intake at meal 4 hours following administration of *Ascophyllum nodosum* bread. No changes in plasma glucose and cholesterol levels | Measurement at one time point only |
| El Khoury et al. [38] | Healthy men ($n = 24$) | Alginate | Randomized crossover study. 325 mL drinks of chocolate milk, 1.25% alginate chocolate milk, 2.5% alginate chocolate milk or 2.5% alginate solution 2 hours before an ad libitum meal | 1 day measurement | Energy intake, appetite, plasma glucose and insulin | No group differences in energy intake. 2.5% alginate chocolate milk reduced peak glucose levels compared to 1.25% alginate chocolate milk and chocolate milk alone. Insulin peaks reduced after 2.5% alginate chocolate milk compared to chocolate milk. Alginate chocolate milk reduced pre-meal appetite. 2.5% alginate chocolate milk reduced appetite compared to chocolate milk alone. | |

in 500 mL) alginate-based beverage, or an iso-volume placebo drink. The preloads were consumed 30 min before a fixed breakfast and again before an ad libitum lunch. The ingestion of low volume-alginate preload induced a significant decrease (8.0%) in energy intake compared to the placebo drink at the following lunch meal, while differences in satiety feelings were not observed. The high volume-alginate induced a non-significant reduction in energy consumption by only 5.5% although a significant increase in satiety feelings, reduced hunger and the feeling of prospective food consumption was reported [31]. These findings suggest that alginate consumption can affect satiety feelings and energy intake.

In a pilot study, Jensen et al. [32] investigated in obese participants the effects on body weight loss and gastrointestinal tolerance of consuming low viscous alginate fiber-based preloads of 3% concentration (500 mL volume) three times a day as an adjuvant to a calorie-restricted diet (see Table 1). The intake of the alginate preloads was moderately acceptable to the majority of subjects but did not produce additional body weight loss beyond calorie restriction in comparison to the control group. These findings do not suggest that alginate supplementation can enhance the weight loss following a hypo-caloric diet [32].

Jensen et al. [33] repeated the study using a larger sample (see Table 1) and investigated the effects of alginate supplementation in conjunction with energy restriction (−300 kcal/day) on loss of body weight and on several metabolic risk markers. In conjunction with an energy-restricted diet either an alginate-based preload supplement (15 g fiber) or a placebo preload supplement were administered. The preload drinks were given 3 times a day before main meals for 12 weeks. At completion of trial, a greater weight loss was observed with alginate than with placebo. This was mainly attributed to a reduction in the percentage of body fat. Differences in plasma concentrations of glucose, insulin, C-reactive protein, ghrelin, HOMA-IR, and lipid metabolism were not found [33]. These results suggest that alginate administration as an adjunct to energy restriction may improve weight loss due to alterations in body fat mass in obese subjects who complete a 12-week dietary alginate intervention as an adjuvant to a calorie-controlled diet.

The positive effects of alginate supplementation on weight management reported previously have been challenged by findings of Odunsi et al. [34]. These authors analyzed the effects of a 10-day treatment with alginate or placebo on gastric functions, satiation, appetite and gut hormones associated with satiety in overweight or obese adults without psychiatric co-morbidity or binge eating disorder (see Table 1). In all participants, gastric emptying, fasting and postprandial gastric volumes, postprandial satiation, calorie intake at a free choice meal and gut hormones (ghrelin, CCK, GLP-1, PYY) were measured after 1 week of alginate (3 capsules versus placebo per day, ingested 30 min before the main meal). Six capsules were ingested with 30 min before the gastric emptying and the gastric volume and satiation tests on days 8–10. Group effects of treatment were not found in regard to gastric emptying or volumes, gut hormones, satiation, total and macronutrient calorie intake at a free choice meal. No differences were observed between obese and overweight participants [34]. Alginate treatment over 10 days did not appear to affect gastric motor functions, satiation, appetite or gut hormones. However, other authors [35] urge caution in extrapolating results from the specific commercially available product used by Odunsi et al. [34] to alginates in general since both chemical structure and concentration of the specific alginate source material can have effects on the gel strength [36,37].

The conflicting findings of Jensen et al. [31,33] and Odunsi et al. [34] may be the result of different modes of alginate delivery. The greater volume of drinks compared to the volume of capsules may stimulate gastric stretch receptors, increase satiety and therefore reduce energy consumption.

El Khoury et al. [38] investigated the effect of adding strong-gelling sodium alginate to chocolate milk on glycemia, insulinemia, appetite and food intake. In this randomized crossover study (see Table 1), 24 healthy men were provided with isovolumetric (325 mL) beverages of chocolate milk, 1.25% alginate chocolate milk, 2.5% alginate chocolate milk or 2.5% alginate solution. The drinks were standardized for lactose, sucrose and calcium content, and administered 120 min before an ad libitum pizza meal during which food intake was measured. Appetite as well as plasma glucose and insulin were measured at baseline and at intervals pre- and post-meal. Addition of 2.5% alginate to chocolate milk led to a decrease in peak glucose concentrations, at 30 min, by an average of 6% and 13% compared with 1.25% alginate chocolate milk and chocolate milk alone, respectively. Insulin peaks at 30 min were lower by 46% after 2.5% alginate chocolate milk compared to chocolate milk. Pre-meal appetite was reduced dose-dependently by alginate chocolate milk. Chocolate milk with 2.5% alginate reduced mean appetite by an average of 134% in comparison with chocolate milk alone. However, there were no differences regarding total caloric intake at the pizza meal [38].

Some of the studies presented above suggest that energy consumption can be reduced by the dietary intake of seaweed isolates such as alginate. Hall and her colleagues [39] investigated the effect of adding whole seaweed to bread on energy intake. They studied the acceptability of *Ascophyllum nodosum* enriched bread as part of a meal, and measured its effect on energy consumption and nutrient absorption in overweight healthy men. The acceptability study including 79 untrained sensory panelists indicated that it is acceptable to add seaweed (*Ascophyllum nodosum*) to bread at concentrations of up to 4% per 400 g wholemeal loaf. In a single blind cross over trial (see Table 1), the authors compared both energy intake and nutrient uptake following a breakfast meal using the enriched bread (4% *A. nodosum*) or control bread (no *A. nodosum*). Consumption of the enriched bread at breakfast significantly reduced (16.4%) energy intake, but not nutrient uptake at a test meal consumed 4 h later [39]. Plasma blood glucose and cholesterol levels did not differ between groups. The alginate in the seaweed enriched bread may have caused gastric stretching due to bulking.

## 3. Anti-obesity activity of seaweed components in animals and humans

Recent studies in animals have demonstrated that fucoxanthin from brown seaweed, for example, can reduce both body weight

and the percentage of white adipose tissue, suggesting that other seaweed components besides alginate may have potential in weight management.

Mitochondrial uncoupling protein-1 is usually expressed only in brown adipose tissue and a key molecule for metabolic thermogenesis to avoid an excess of fat accumulation [40]. Adaptive thermogenesis by uncoupling protein-1 may be a physiological defense mechanism against obesity [41] and the dysfunctioning of uncoupling protein-1 has been shown to be involved in the development of obesity [42]. Little brown adipose tissue is found in adult humans. The expression of mitochondrial uncoupling protein-1 in tissues other than brown adipose tissue is therefore expected to reduce abdominal fat. Maeda et al. [40] investigated the effect of feeding mice *Undaria pinnatifida* lipids (mainly glycolipids and seaweed carotenoid, fucoxanthin). While there was little expression of uncoupling protein-1 in white adipose tissue of mice fed control diet, clear signals of uncoupling protein-1 and its mRNA were observed in white adipose tissue of mice fed Undaria lipids. In mice receiving fucoxanthin, white adipose tissue was markedly reduced and uncoupling protein-1 clearly expressed. No difference in white adipose tissue weight was observed in mice fed glycolipids.

In another publication, Maeda and his colleagues [43] reported that abdominal white adipose tissue weights of rats and mice fed fucoxanthin were markedly reduced compared to those fed a control diet. The daily consumption of fucoxanthin in mice also significantly decreased body weight. Again clear signals of uncoupling protein-1 and its mRNA were found in abdominal white adipose tissue in mice fed fucoxanthin, although there is little expression of uncoupling protein-1 in white adipose tissue in mice fed a control diet. These findings suggest that the seaweed carotenoid, fucoxanthin, upregulates the expression of uncoupling protein-1 in white adipose tissue and is an active component for the anti-obesity effect of Undaria lipids [40,43].

Maeda et al. [44] also investigated the anti-obesity effects of fucoxanthin-rich wakame lipids on high fat diet-induced obesity in mice. A diet of both high fat and wakame lipids rich in fucoxanthin markedly suppressed body weight and white adipose tissue weight gain induced by a high fat diet. These results suggest that dietary wakame lipids may ameliorate changes in lipid metabolism induced by a high fat diet. The administration of fucoxanthin-rich wakame lipids as a functional food may therefore provide a biochemical and nutritional basis for the prevention of obesity.

In order to understand the mechanisms underlying the anti-obesity effects of fucoxanthin and its metabolite fucoxanthinol, Matsumoto and her colleagues [45] investigated the effects of these carotenoids on the absorption of triglycerides in conscious rats implanted with cannulae into a lymph duct and the portal or jugular vein. A duodenal infusion of test oil emulsion with or without 2 mg of fucoxanthin or fucoxanthinol was administered in the lymph duct and the portal or the jugular vein. The inhibitory activities of fucoxanthin and fucoxanthinol on pancreatic lipase activity were assessed *in vitro*. Increases in lymphatic and blood triglyceride levels were much lower in the two carotenoid-treated groups than in the carotenoid-free group, indicating that these marine carotenoids inhibit both lipase activity in the gastrointestinal lumen and triglyceride absorption [45].

Jeon et al. [46] assessed an ethanol extract of fucoxanthin-rich seaweed in mice in regard to potential anti-obesity effects. Groups of mice received a high-fat diet supplemented with 0.2% conjugated linoleic acid as the positive control or 1.43% or 5.72% fucoxanthin-rich seaweed ethanol extract for six weeks. The study showed that supplementation with two doses of fucoxanthin-rich seaweed reduced body and abdominal white adipose tissue weights, plasma and hepatic triglyceride, and/or cholesterol concentrations compared to a high-fat control group. Activities of adipocytic fatty acid synthesis, hepatic fatty acid and triglyceride synthesis, and cholesterol-regulating enzyme were also reduced by fucoxanthin-rich seaweed ethanol extract. These results indicate that fucoxanthin affects the plasma and hepatic lipid profile and body fat mass [46].

Maeda et al. [47] showed that both fucoxanthin and fucoxanthinol inhibited intercellular lipid accumulation during adipocyte differentiation of 3T3-L1 cells. The suppressive effect of fucoxanthinol on the differentiation in mice of preadipocytes to adipocytes was stronger than that of fucoxanthin [47], and the suppressive effect of amarouciaxanthin A, a dominant metabolite of fucoxanthin in white adipose tissue, was stronger than that of fucoxanthinol [48]. Kang et al. [49] reported that fucoxanthin inhibited 3T3-L1 adipocyte differentiation at intermediate and late stages, while it enhanced adipocyte differentiation at an early stage by affecting the expression of key adipogenic transcriptional regulators and inhibited glucose uptake. These findings suggest that fucoxanthin exerts anti-obesity effects by inhibiting the expression of key transcriptional regulators and glucose uptake in mature adipocytes.

The unique suppressive effect of fucoxanthin on adipocyte differentiation appears to be linked to its structural properties, since an allenic bond is essential for the expression of this activity, and carotenoids without this bond show no activity [50]. A more detailed account of anti-obesity effects of fucoxanthin and its metabolites has been provided by Peng and co-authors [51].

Lai et al. [52] investigated the inhibitory effects of xanthigen, fucoxanthin, and punicic acid (70% in pomegranate seed oil) on the differentiation of 3T3-L1 preadipocytes. Xanthigen potently and dose-dependently suppressed accumulation of lipid droplets in adipocytes compared to its individual components, fucoxanthin and pomegranate seed oil. Xanthigen down-regulated the protein levels of key adipogenesis transcription factors and up-regulated various enzymes signaling in differentiated 3T3-L1 adipocytes. These findings indicate that xanthigen suppresses adipocyte differentiation and lipid accumulation through multiple mechanisms and may have therapeutical benefits in obesity [52].

Administration of alginic acids from the brown macroalgae *Sargassum wightii* was shown to prevent the inflammatory cell infiltration in arthritic rats by reducing the expression of C-reactive protein kinase and the corresponding increase in enzymes linked to inflammation (e.g. cyclooxygenase, lipooxygenase and myeloperoxidase) [53]. This mechanism could be useful in the treatment of obesity which appears to be associated with chronic low-grade inflammation [54].

In order to investigate a beneficial role of fucoidan, extracted from the sporophyll of *U. pinnatifida*, in adipogenesis by inhibiting inflammatory-related cytokines, Kim and Lee [55] assessed the obesity-specific therapeutic action of fucoidan adipocytes. The authors found that mRNA gene expression of key adipogenic markers (adipocyte protein 2, etc.) was down-regulated by fucoidan, and the expression of inflammation-related genes in adipocytes during adipogenesis was reduced. In addition, fucoidan also decreased the accumulation of lipids and reactive oxygen species in adipocytes. These findings show that fucoidan suppresses adipogenesis by inhibiting major markers and inflammation-related cytokines in adipocytes, suggesting that fucoidan may have anti-obesity effects [55].

In a study by Park et al. [56], the inhibitory effect of fucoidan on the lipid accumulation in differentiated adipocytes was examined. Fucoidan showed high lipid inhibition activity at 200 μg/mL concentration. Lipolytic activity in adipocytes is highly dependent on hormone sensitive lipase, which is one of the most important targets of lipolytic regulation. Fucoidan increased hormone-sensitive lipase expression indicating stimulation of lipolysis [56]. These findings suggest that fucoidan reduces lipid accumulation by stimulating lipolysis and may be useful in the management of obesity.

Kim et al. [57] investigated the antiobesity effects of fucoidan in an animal model of diet-induced obesity. Mice were fed a standard diet or high-fat diet for five weeks. The animals were then divided into four groups, i.e. a standard diet group, a high-fat diet group, and two high-fat diet groups containing 1% or 2% fucoidan. The fucoidan supplementation group showed a decrease in body-weight gain, food efficiency ratio and relative liver and epididymal fat mass compared with the high-fat diet group. The mice supplemented with fucoidan showed reduced plasma levels of triglyceride, total cholesterol and low-density lipoprotein levels. In addition, fucoidan affected the down-regulation expression patterns of epididymal adipose tissue genes [57]. These results suggest that fucoidan may inhibit adipogenesis and have a role in the control or prevention of obesity.

Stearoyl-coenzyme A desaturase-1 is a rate-limiting enzyme which catalyzes the biosynthesis of monounsaturated fatty acids from saturated fatty acids. The down-regulation of stearoyl-coenzyme A desaturase-1 has been implicated in the prevention of obesity and also in the improvement of insulin and leptin sensitivity. Beppu et al. [58] investigated the effect of the marine caretenoid, fucoxanthin, on hepatic stearoyl-coenzyme A desaturase-1 in obese mouse models of hyperleptinemia KK-A(y) and leptin-deficiency ob/ob. In KK-A(y) mice, a two-week diet containing 0.2% fucoxanthin for 2 weeks significantly suppressed stearoyl-coenzyme A desaturase-1 mRNA and protein expression in the liver. The fatty acid composition of liver lipids was also affected, i.e. the ratio of oleic acid to stearic acid was reduced. Furthermore, serum leptin levels were significantly decreased in hyperleptinemia KK-A(y) mice after 2 weeks of fucoxanthin administration. The suppressive effects of fucoxanthin on hepatic stearoyl-coenzyme A desaturase-1 and body weight gain were not observed in ob/ob mice [58]. These findings indicate that fucoxanthin down-regulates the expression of stearoyl-coenzyme A desaturase-1 and changes the fatty acid composition of the liver via regulation of leptin signaling in hyperleptinemia KK-A(y) mice but not in leptin-deficient ob/ob mice. Since a large proportion of obesity in humans is characterized by leptin resistance and not leptin deficiency, fucoxanthin may be useful in the therapy of obese individuals by maintaining adequate homeostatic mechanisms [58].

A study by Hu et al. [59] examined the effects of combined fucoxanthin and conjugated linoleic acid on high-fat diet-induced obesity in rats. The animals were fed a high-fat diet (control), supplemented with two doses of fucoxanthin or low-dose fucoxanthin plus conjugated linoleic acid for 52 days. In comparison to the control group, body weight and white adipose tissue weight were reduced in the combined group, white adipose tissue weight was decreased in the two fucoxanthin groups. Serum total cholesterol level, triacylglycerol and leptin levels were reduced in the fucoxanthin groups. Furthermore, the mRNA expression of adiponectin, adipose triacylglycerol lipase, carnitine palmitoyltransferase 1A was up-regulated in all fucoxanthin groups. These findings indicate that fucoxanthin administered alone or in combination with conjugated linoleic acid decreases serum levels of triacylglycerol and leptin, and fucoxanthin may exert anti-obesity effects by regulating mRNA expression of enzymes related to lipid metabolism in white adipose tissue weight of rats with diet-induced obesity [59].

Wu et al. [60] attempted to elucidate the mechanism of how fucoxanthin reduces adipose accumulation and studied the effects of fucoxanthin on metabolic rate and expressions of genes related to thermogenesis, mitochondria biogenesis and homeostasis. Mice were fed high sucrose or high-fat diets supplemented with or without 0.2% fucoxanthin. Fucoxanthin increased oxygen consumption and carbon dioxide production and reduced white adipose tissue mass. Dietary fucoxanthin enhanced the metabolic rate and lowered adipose mass irrespective of the diet. These effects were associated with upregulated genes of, among others, mitochondrial fusion in inguinal and epididymal white adipose tissue [60].

Ha and Kim [61] investigated the effects of fucoxanthin on gene expressions related to lipid metabolism in rats on a high-fat diet. The findings of this study indicate that fucoxanthin consumption decreases lipid accumulation in the liver of rats fed a high fat diet. A fucoxanthin-enriched diet also suppressed mRNA expression of transcription factors and enzymes involved in hepatic lipogenesis. In addition, fucoxanthin consumption increased expression of enzymes that stimulate fatty acid oxidation and decreased expression of cholesterol synthesizing enzyme [61]. Fucoxanthin appears therefore to be effective in improving lipid metabolism in rats with a high fat diet.

The peptidyl prolyl cis/trans isomerase Pin1 has been shown to increase the uptake of triglycerides and the differentiation of fibroblasts into adipose cells in response to insulin stimulation. A down-regulation of Pin1 may therefore be a novel approach to prevent and treat obesity-related disorders [62]. The Pin1 inhibitor 974-B, a phlorotannin isolated from the seaweed *Ecklonia kurome*, was able to inhibit the differentiation of mouse embryonic fibroblasts into adipose cells, suggesting that this

compound could be a potential drug for obesity-related disorders [62].

The promising findings of animal experiments need to be confirmed in humans. Abidov et al. [63] have assessed the effectiveness of dietary fucoxanthin supplementation for weight loss in humans. These authors investigated the effects of xanthigen (brown marine algae fucoxanthin plus pomegranate seed oil) on body weight, body fat, liver lipids, and blood biochemistry in the weight management of 151 non-diabetic, obese premenopausal women (113 with non-alcoholic fatty liver disease and 38 with normal liver fat) in a 16-week, double-blind, randomized, placebo-controlled study. The administration of xanthigen-600/2.4 mg (300 mg pomegranate seed oil + 300 mg brown seaweed extract containing 2.4 mg fucoxanthin) resulted in a statistically significant reduction of body weight, waist circumference, body and liver fat content, liver enzymes, serum triglycerides and C-reactive protein. Fucoxanthin (>2.4 mg) and xanthigen-400/1.6 mg (200 mg pomegranate seed oil + 200 mg brown seaweed extract containing 1.6 mg fucoxanthin) significantly increased resting energy expenditure in participants with non-alcoholic fatty liver disease compared to placebo [63]. The decrease in body weight following the administration of xanthigen may be caused by the stimulation of resting energy expenditure and by anti-inflammatory and metabolism normalizing mechanisms.

## 4. Limitations of existing studies and suggestions for future research

The incidence of the metabolic disorders including obesity is increasing worldwide and has reached epidemic proportions in developed countries, with notable exceptions of some Southeast Asian countries where seaweeds are part of the staple diet. However, basing the utility of seaweeds in the prevention and control of obesity on epidemiological evidence is problematic due to general differences in dietary habits and since a wide range of herbal plants associated with anti-obesity effects (e.g. black tea, catechin-enriched green tea, oolong tea) are also commonly consumed in Southeast Asia [64,65].

Medicinal plants and plant metabolites are thought to harbor potential anti-obesity compounds which may be able to prevent weight gain or promote weight loss [66]. Dietary seaweed fibers are of particular interest in the management of obesity and a proposed mechanism of action is the modulation of nutrient uptake from the small intestine. Most published studies available suggest that alginate consumption affects satiety feelings and energy intake. However, studies investigating the effects of alginate preparations in animals and humans have been of short duration. This means that long-term effects on appetite and energy intake cannot be assessed. In addition, further assessment in regard to the volume of alginate administered is needed.

A major drawback in regard to the evaluation of anti-obesity effects of seaweeds is the fact that most experiments were performed *in vitro* or *in vivo* using animal models. The results of these studies cannot be extrapolated to humans and may therefore have no therapeutic consequences. A sufficient number of well-controlled studies in human subjects are still lacking. A first study by Abidov et al. [63] assessed the effects of a 16-week administration of xanthigen on body weight, body fat and other parameters in the weight management of obese female participants. The design and methodology of this double-blind, randomized, placebo-controlled study were sound. However, sufficiently powered long-term studies including both sexes and various age groups are needed in order to evaluate the efficacy of seaweed compounds in the prevention and control of obesity in human participants.

Several problems in regard to the use of seaweeds in the treatment of obesity need to be addressed by future research. These problems include the description of the underlying bioactive principles, the definition of oral bioavailability of the active compounds and the assessment of therapeutic doses. Various findings suggest that fucoxanthin might act as a regulator of lipid metabolism in fat tissues [67]. However, the bioavailability of fucoxanthin in brown seaweeds was shown to be low in human subjects [51]. Orally administered fucoxanthin is metabolized into fucoxanthinol and amarouciaxanthin A in mice and these and other metabolites in humans should be investigated in regard to the bioactivity of fucoxanthin. Different concentrations and compositions of bioactive compounds present in different seaweed species may contribute to potential anti-obesity effects. The role of these parameters needs therefore to be evaluated in more extensive animal experiments and well-controlled clinical trials.

Seaweeds are mixtures of partly defined complex chemicals and this complexity makes the discovery of novel therapeutic substances difficult. Well defined and standardized mixtures of bioactive ingredients from seaweeds (nutraceuticals) should be investigated *in vitro*, in animal models of obesity and in overweight and obese human subjects.

Solid evidence indicating that seaweeds are effective in long-term weight management is still lacking. The effective non-toxic doses of seaweed preparations need to be defined by future investigations. A particular problem is bioavailability since sufficient amounts of orally administered nutraceuticals are required for adequate efficacy. Large-scale, sufficiently powered, well-designed, randomized controlled trials in clinical and home settings are required to investigate the putative effects of seaweed components. Improvements in future study designs regarding sample size, duration, parameters measured and full reporting will allow more definitive conclusions concerning the therapeutic value of seaweed in the management of obesity.

## 5. Conclusion

The therapeutic utilization of marine bioactive substances including seaweeds is common in Asia. Potential benefits of seaweed consumption have been reported, among others, in the management of body weight and obesity.

The majority of acute studies assessing the short-term effects of dietary alginate supplementation indicate that alginate may increase satiety, reduce energy intake and support weight reduction. Mechanisms proposed for these effects include delayed gastric clearance, stimulation of gastric stretch receptors, increased viscosity of digesta and attenuated nutrient absorption.

However, long-term studies in humans are required in order to allow firm conclusions to be drawn in regard to anti-obesity effects of alginate intake and their underlying mechanisms.

Numerous studies in animals have investigated the potential anti-obesity effects of seaweed on a wide range of parameters including the reduction of adipogenesis and the inhibition of major lipid and carbohydrate hydrolyzing and metabolizing enzymes. In addition, anti-inflammatory properties of seaweed compounds such as alginic acids may support the therapy of obesity which seems to be associated with chronic inflammation [54]. The results of the available studies suggest beneficial effects of seaweed components such as fucoxanthin. However, it is premature to extrapolate these findings to humans. Human data suggest that xanthigen may be a promising food supplement in regard to the treatment of obesity [63]. Future studies are required in order to confirm the importance of this finding in the long-term weight management in humans. In addition, it needs to be established whether seaweed consumption exerts anti-obesity effects in different populations. For example, the genes encoding enzymes that are able to digest seaweed are present in the microbiota of the Japanese endogenous population and absent in North American individuals. These genes originate from marine microbes present on seaweed consumed [68].

In summary, the data available at present suggest potential benefits on obesity of seaweed and seaweed components. Future investigations are required to establish the therapeutic efficacy in humans and elucidate the mechanisms of actions.

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