Carrageenans in the Prevention of MetS

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Carrageenans, long-chain polysaccharides extracted from red macroalgae, are present in several foods, such as jelly. Chemically, they present several structures with different applications and purposes in the cosmetic, food, and pharmaceutical industries. The bioactive potential of carrageenans has demonstrated potential in the reduction of the levels of parameters of the lipid profile, being able to be an alternative in the reversion of MetS （Metabolic Syndrome） and, consequently, in the prevention and treatment of CVD (Cardiovascular Diseases).

carrageenan dyslipidemia TC HDL-C LDL-C

1. Introduction

Technological evolution has led to efficient and qualified progress, with a strong impact on the institutional and social environments [1], promoting a change in life and time management. The lack of time for meals is reflected in the proliferation of fast food [2]. Professional evolution, on the other hand, favors a sedentary lifestyle. The social pressure related to the prestige of the worker led to increased productivity but also to the detriment of health [3]. As a result, pathologies such as alterations in the lipid profile, metabolic syndrome (MS), and cardiovascular diseases (CVD) arise [4].

The balance of the lipid profile is sensitive to dietary and behavioral changes and is easily modified. Lipid profile variations are characterized by the deregulation of one or more parameters: total cholesterol (TC); high-density lipoprotein cholesterol (HDL-C); low-density lipoprotein cholesterol (LDL-C); or triglycerides (TG). The most common alteration is an increase in TC, called hypercholesterolemia. Two of the main factors in the high number of variations in the lipid profile are sedentary habits and the abandonment of healthier and nutritionally balanced diets [4][5][6]. About 38% of American adults have high cholesterol (total blood cholesterol ≥ 200 mg/dL). Too much cholesterol increases the risk of heart disease and stroke, two of the leading causes of death in the United States. Based on this value, researchers can evaluate that 22.7% of the population has one of the main risk factors for the development of MetS and CVD [7][8][9]. A sedentary lifestyle and a poor diet favor changes in the lipid profile, the development of hypertension, weight gain and increase in abdominal circumference, as well as insulin resistance, characteristic factors of MetS [6]. Due to the complexity of MetS, different criteria allow its diagnosis, such as those defined by the World Health Organization (WHO), the National Cholesterol Education Program (NCEP), and the International Diabetes Federation (IDF). The multiplicity of criteria makes it difficult to uniformly characterize, monitor, and unify the information [8]. Considering the limitations, calculating a worldwide incidence rate has become a complex task. However, according to US statistics, it was possible to relate the incidence rate of diabetes to the incidence rate of MetS, revealing that the incidence of MetS is approximately three times higher than that presented by diabetes [7][9]. Thus, it is estimated that about a quarter of the world population is affected by MetS [7]. Given that MetS is closely related to an increased risk of developing type 2 diabetes mellitus and cardiovascular events, reversing this condition is essential [10]. The increased prevalence of changes in lipid profile and MetS, coupled with risk behaviors such as smoking and sedentary lifestyle, promote an increase in the incidence rate of CVD to levels of concern [10]. A high percentage (31%) of the number of deaths worldwide is caused by cardiovascular events, which have become a serious epidemiological problem, and the need to promote preventive habits is emerging [11]. In this group of pathologies, researchers can find stroke and myocardial infarction, which represent 85% of the total events [8][12]. The very high impact that these pathologies represent on society and the health of the populations, favors the investment of researchers in the problem [12][13][14]. The inefficiency of pharmacological treatment and of awareness/promotion campaigns leads to the search for more appealing and effective alternatives. The need for more appealing treatments and prevention that can be easily integrated into everyday life has led to the emergence of the concept of Functional Foods, which is based on combining food with direct benefits to the individual's health [15][16].

The bioactivity of several polysaccharides which can be found in macroalgae is known and the ease of their integration in food reinforces the action in the prevention and treatment of various pathologies [17][18][19]. It should be noted that carrageenans, linear sulfated polysaccharides present in red algae, are already approved by the European Union as a food additive and described in the literature as having multiple benefits for human health. The need to objectively assess the potential of carrageenans in the prevention and rebalance of lipid profile and body mass index parameters constitutes a research target [17].

2. The Potential of Carrageenans in the Prevention of CVD

An extension of MetS may be CVD, and the consumption of carrageenans may be a preventive factor. The relationship between the alteration of the lipid profile and the development of CVD has led to the investigation of alternative ways of regulating the lipid profile. The hypothesis of the biopotential of carrageenans emerged as a possibility in the promotion and development of studies to evaluate the impact of carrageenan ingestion on the lipid profile of patients with CVD, carrying out studies in animal models and even in humans.

3. Studies Carried Out in Animal Models

After analysis of the studies carried out on a non-human animal model, it was found that all of them recorded a significant reduction in the serum concentration of TC [20][21][22]. Most studies have selected the male Wistar rats as a model (8-week-old male C57BL/6J mice [23]; 8-week-old male Wistar rats [20]; 9-week-old male Wistar rats [24]; 8-week-old male C57BL/6J mice [25]; two of the works developed in Wistar rats did not provide the age and sex of the rats [21][26]; male Sprague Dawley rats [27]). In addition, a study was conducted on chicks [22]. The work developed with chicks, with one day of life, had as objective to verify the effect of the ingestion of fermented carrageenans [22] [28], described by Hasanuddin et al. [22], in different concentrations (2.5, 5, 7.5 and 10%) during 5 weeks. At the end of the experimental period, they found that the higher the concentration of carrageenans ingested, the greater the reduction in TC, LDL-C, TG and increase in HDL-C levels, with statistically significant results [22].

Other researchers have tested the action of carrageenans when introduced in association with carbohydrate and/or lipid-enriched diets. In these works, the results presented some dichotomy observed in the two analyzed articles [24][26]. According to Wanyonyi and collaborators, the ingestion of a diet enriched in carbohydrates, lipids and with the introduction of about 5% of algae *K. alvarezii*, in a period of 8 weeks, showed a tendency for the increase of the TC concentration and a reduction of TG; however, neither alteration was significant [24]. In relation to the study of Xia et al., there was a reduction in the concentration of TC and TG, when, for 30 days, Wistar rats were supplied with 1% of carrageenans (CC), 1% (1% LC) and 3% (3% LC) of low-density carrageenans, obtained through the red alga *Eucheuma denticulatum* (formerly *Eucheuma spinosum,* Rhodophyta), along with a high-fat feeding (HC: 3.5% cholesterol, 10% lard, 0.2% propylthiouracil, 0.5% sodium cholate and 5% refined sugar) and also a group with normal powder (NC: 19% fats, 55%, carbohydrates, 22% proteins, 7% ash, and 5% cellulose) [26]. There was, however, greater efficiency in reducing serum concentrations with the ingestion of low molecular weight carrageenans; all results were obtained through comparison with the HC group.

In Du Preez' and co-authors' works, the action of carrageenans on the lipid profile was beneficial both when introduced in a diet enriched with carbohydrates and fats, and in a diet with corn starch. It was demonstrated that in both diets there was a statistically significant decrease in the concentrations of TC and TG [20].

Bhattacharyya et al. [23] evaluated the action of carrageenans introduced in water, in male C57BL/6J mice at 8 weeks of age. For this, 1% of non-degraded carrageenans (carrageenan λ and κ; Sigma Chemical Co., St Louis, MO, USA) was added to water for 44 weeks and the mice were divided into two groups (with and without carrageenans). The total sample was subdivided into four groups, control group (standard feeding), CGN group (standard feeding and 1% carrageenans in water), HDF group (high fat feeding) and HDF+CGN group (high fat feeding and 1% carrageenans in water). At the end of the experimental period, the results did not correspond to the expected, with an increase in the concentration of TC, TG and LDL-C [23]. The team of Chin et al. [25] sought to estimate how best to reduce lipid profile levels, with a diet enriched in carbohydrates and supplemented with 5% *K. alvarezii* (T), 5% native κ-carrageenan (CGN), and the 5% leftover sans-carrageenan fraction (SCGN). The three groups with supplemented diet were analyzed before and after 6 weeks. After the beginning of the diet it was verified, comparatively to the model (carbohydrate enriched diet), a tendency in the decrease of TC, LDL-C, TG, and an increase of HDL-C concentrations. There were only significant results in the HDL-C concentration in the SCGN group [25].

In the study developed by Tsai and collaborators, it was recorded that the time of ingestion of carrageenans can influence the results. This team of researchers observed an increase in TC levels after 32 days of diet enriched with 7% carrageenans and a decrease of the same parameter after 42 days of intake [27]. The work done by Gómez-Ordóñez et al. evaluated the effect of the introduction on the feeding of Wistar rats of 10% of *Mastocarpus stellatus* (Rhodophyta). After 4 weeks of ingestion, the results were analyzed, comparing the experimental group (feeding with carrageenans) with the control group. A statistically significant decrease in TC and TG concentrations was observed [21]. The results of the studies are compiled in (**Table 1**).

Table 1. Summary of studies carried out in animal and human models.

Authors	Model	Period	Carrageenans %	Mode	MetS	Lipid Profile
Hasanuddin et al. [22]	chicks	5 weeks	2.5 fermented CC	Diet	-	↓TC *; ↓LDL-C *; ↑HDL-C *; ↓TG *
			5 fermented CC		-	↓TC *; ↓LDL-C *; ↑HDL-C *; ↓TG *
			7.5 fermented CC		-	↓TC *; ↓LDL-C *; ↑HDL-C *; ↓TG *
			10 fermented CC		-	↓TC *; ↓LDL-C *; ↑HDL-C *; ↓TG *
Wanyonyi et al. [24]	rats	8 weeks	HFD + 5 *K. alvarezii*	Diet	↓BW; ↓F; ↓AC; ↓SBP	↑TC; ↓TG
Xia et al. [26]	rats	30 days	HC + 1 CC	Diet	↓BW	↓TC; ↓LDL-C; ↑HDL-C; ↓TG
			HC + 1 LC		↓BW	↓TC *; ↓LDL-C; ↑HDL-C; ↓TG *
			HC + 3 LC		↓BW	↓TC *; ↓LDL-C *; ↑HDL-C; ↓TG *
Du Preez et al. [20]	rats	16 weeks	HFD + 5 *S. filiforme*	Diet	↓BW; ↓F; ↓AC; ↓SBP	↓TC *; ↓TG *
			Corn Starch + 5 *S. filiforme*		↓BW; ↓F; ↓AC; ↓SBP	↓TC *; ↓TG *
Bhattacharyya et al. [23]	mice	44 weeks	CGN	Water	↑BW;	↑TC; ↑LDL-C; ↓HDL-C; ↑TG
			HFD + CGN		↑BW;	↑TC *; ↑LDL-C *; ↑HDL-C *; ↑TG *
Chin et al. [25]	mice	16 weeks	HFD + 5 *K. alvarezii*	Diet	↓BW; ↓F	↓TC; ↓LDL-C; ↑HDL-C; ↓TG
			HFD + 5 k-CGN		↓BW *; ↓F	↓TC; ↓LDL-C; ↑HDL-C; ↓TG
			HFD + 5 SCCGN		↓BW *; ↓F *	↓TC; ↓LDL-C;

Authors	Model	Period	Carrageenans %	Mode	MetS	Lipid Profile
						↑HDL-C *; ↓TG
Tsai et al. [27]	rats	32 days	7 CC	Diet	-	↑TC
		42 days			-	↓TC
Gómez-Ordóñez et al. [21]	rats	4 weeks	10 *Mastocarpus stellatus*	Diet	-	↓TC *; ↓TG *
Panlasigui et al. [29]	humans	8 weeks	40 g/day, in food	Diet	-	↓TC *; ↓TG *; ↑LDL-C; ↑HDL-C *
Sokolova et al. [30]	humans	20 weeks	Capsules 250 mg	Capsule	-	↓TC *; ↑TG *; ↓LDL-C *; ↑HDL-C
Valado et al. [31]	humans	30 days	100 mL/day of vegetable jelly	Diet	-	↓TC *; ↑TG *; ↓LDL-C; ↓HDL-C *
		60 days			-	↓TC *; ↑TG *; ↓LDL-C; ↓HDL-C *

↓: decrease; ↑: increase; AC: abdominal circumference; BW: body weight; CC: carrageenan; CGN: water with 1% carrageenans; F: total fat mass; HC: high-carrageenan; HDL-C: high-density lipoprotein cholesterol; HFD: high fat diet; LC: low-carrageenan; LDL-C: low-density lipoprotein cholesterol; MetS: metabolic syndrome; SBP: systolic blood pressure; SCCGN: sans-carrageenan fraction; T: total; TC: total cholesterol; TG: triglycerides. * $p < 0.05$.

... Western ... btained in ... [29][30][31]. In the study of Panlasigui et al. [29], a portion of carrageenans was added to the food prepared and normally eaten by a group of volunteers for 8 weeks. The experimental group ingested 40 g of carrageenans daily. At the end of the experimental period, there was a significant decrease in TC and TG concentrations and an increase, also significant, in HDL-C [29]. Afterwards, Sokolova et al. [30] showed that taking a supplement in the form of capsules containing carrageenans and administered for 20 days to a group of hospitalized patients with cardiovascular events presents benefits in their recovery. After 20 days, a significant decrease in TC and LDL-C concentration was observed; however, a significant increase in TG levels was registered [30]. Most recently, Valado et al. [31] revealed that the daily intake of 100 mL of vegetable jelly, which has carrageenans in its constitution, presents benefits to the regulation of the lipid profile. In the study, two periods of time, 30 and 60 days, were tested. In both it was observed a significant decrease in the concentrations of TC and an increase of TG, without, however, exceeding the reference levels defined [31]. The results are compiled in (**Table 1**).

References

1. Sakurai, R.; Zuchi, J.D. Industrial revolutions to industry 4.0. Interface Tecnol. 2018, 15, 480–491.
2. Li, C.; Mirosa, M.; Bremer, P. Review of Online Food Delivery Platforms and their Impacts on Sustainability. Sustainability 2020, 12, 5528.

3. Park, J.H.; Moon, J.H.; Kim, H.J.; Kong, M.H.; Oh, Y.H. Sedentary Lifestyle: Overview of Updated Evidence of Potential Health Risks. Korean J. Fam. Med. 2020, 41, 365–373.
4. Kassi, E.; Pervanidou, P.; Kaltsas, G.; Chrousos, G. Metabolic syndrome: Definitions and controversies. BMC Med. 2011, 9, 48.
5. Kopčeková, J.; Holovičová, M.; Gažarová, M.; Mrázová, J.; Habánová, M.; Mečiarová, L.; Bronkowska, M. Association between Selected Dietary Habits and Lipid Profiles of Patients with Cardiovascular Disease. Int. J. Environ. Res. Public Health 2020, 17, 7605.
6. Cortez-Dias, N.; Robalo Martins, S.; Belo, A.; Fiúza, M. Characterization of lipid profile in primary health care users in Portugal. Rev. Port. Cardiol. 2013, 32, 987–996.
7. Saklayen, M.G. The Global Epidemic of the Metabolic Syndrome. Curr. Hypertens. Rep. 2018, 20, 12.
8. Tsao, C.W.; Aday, A.W.; Almarzooq, Z.I.; Alonso, A.; Beaton, A.Z.; Bittencourt, M.S.; Boehme, A.K.; Buxton, A.E.; Carson, A.P.; Commodore-Mensah, Y.; et al. Heart Disease and Stroke Statistics—2022 Update: A Report From the American Heart Association. Circulation 2022, 145, e153–e639.
9. Guembe, M.J.; Fernandez-Lazaro, C.I.; Sayon-Orea, C.; Toledo, E.; Moreno-Iribas, C.; Investigators, R.S. Risk for cardiovascular disease associated with metabolic syndrome and its components: A 13-year prospective study in the RIVANA cohort. Cardiovasc. Diabetol. 2020, 19, 195.
10. Li, X.; Zhai, Y.; Zhao, J.; He, H.; Li, Y.; Liu, Y.; Feng, A.; Li, L.; Huang, T.; Xu, A.; et al. Impact of Metabolic Syndrome and It’s Components on Prognosis in Patients With Cardiovascular Diseases: A Meta-Analysis. Front. Cardiovasc. Med. 2021, 8, 704145.
11. Roth, G.A.; Mensah, G.A.; Johnson, C.O.; Addolorato, G.; Ammirati, E.; Baddour, L.M.; Barengo, N.C.; Beaton, A.Z.; Benjamin, E.J.; Benziger, C.P.; et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019. J. Am. Coll. Cardiol. 2020, 76, 2982–3021.
12. WHO—World Health Organization. Cardiovascular Diseases (CVDs). Available online: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds) (accessed on 25 October 2022).
13. Kruk, M.E.; Gage, A.D.; Arsenault, C.; Jordan, K.; Leslie, H.H.; Roder-DeWan, S.; Adeyi, O.; Barker, P.; Daelmans, B.; Doubova, S.V.; et al. High-quality health systems in the Sustainable Development Goals era: Time for a revolution. Lancet Glob. Health 2018, 6, e1196–e1252.
14. Stuckler, D. Population causes and consequences of leading chronic diseases: A comparative analysis of prevailing explanations. Milbank Q. 2008, 86, 273–326.

15. Granato, D.; Barba, F.J.; Bursać Kovačević, D.; Lorenzo, J.M.; Cruz, A.G.; Putnik, P. Functional foods: Product development, technological trends, efficacy testing, and safety. Annu. Rev. Food Sci. Technol. 2020, 11, 93–118.
16. Nystrand, B.T.; Olsen, S.O. Consumers’ attitudes and intentions toward consuming functional foods in Norway. Food Qual. Prefer. 2020, 80, 103827.
17. Cardoso, S.M.; Pereira, O.R.; Seca, A.M.; Pinto, D.C.; Silva, A.M. Seaweeds as Preventive Agents for Cardiovascular Diseases: From Nutrients to Functional Foods. Mar. Drugs 2015, 13, 6838.
18. Pereira, L. Biological and therapeutic properties of the seaweed polysaccharides. Int. Biol. Rev. 2018, 2, 1762.
19. Prajapati, V.D.; Maheriya, P.M.; Jani, G.K.; Solanki, H.K. Carrageenan: A natural seaweed polysaccharide and its applications. Carbohydr. Polym. 2014, 105, 97–112.
20. du Preez, R.; Paul, N.; Mouatt, P.; Majzoub, M.E.; Thomas, T.; Panchal, S.K.; Brown, L. Carrageenans from the red seaweed Sarconema filiforme attenuate symptoms of diet-Induced metabolic syndrome in rats. Mar. Drugs 2020, 18, 97.
21. Gomez-Ordonez, E.; Jimenez-Escrig, A.; Ruperez, P. Effect of the red seaweed Mastocarpus stellatus intake on lipid metabolism and antioxidant status in healthy Wistar rats. Food Chem. 2012, 135, 806–811.
22. Hasanuddin, A.; Rusdi; Arief, R. Effects of inclusion of fermented carrageenan by-products in the basal diet of broiler chickens on growth performance, blood profiles and meat composition. Int. J. Poult. Sci. 2017, 16, 209–214.
23. Bhattacharyya, S.; Feferman, L.; Unterman, T.; Tobacman, J.K. Exposure to Common Food Additive Carrageenan Alone Leads to Fasting Hyperglycemia and in Combination with High Fat Diet Exacerbates Glucose Intolerance and Hyperlipidemia without Effect on Weight. J. Diabetes Res. 2015, 2015, 513429.
24. Wanyonyi, S.; du Preez, R.; Brown, L.; Paul, N.A.; Panchal, S.K. Kappaphycus alvarezii as a Food Supplement Prevents Diet-Induced Metabolic Syndrome in Rats. Nutrients 2017, 9, 1261.
25. Chin, Y.X.; Mi, Y.; Cao, W.X.; Lim, P.E.; Xue, C.H.; Tang, Q.J. A pilot study on anti-obesity mechanisms of Kappaphycus alvarezii: The role of native kappa-carrageenan and the leftover sans-carrageenan Fraction. Nutrients 2019, 11, 1133.
26. Qiu, X.; Zhong, W. Antihyperglycemic and antihyperlipidemic effects of low-molecular-weight carrageenan in rats. Open Life Sci. 2018, 13, 379–384.
27. Tsai, A.C.; Elias, J.; Kelley, J.J.; Lin, R.S.; Robson, J.R. Influence of certain dietary fibers on serum and tissue cholesterol levels in rats. J. Nutr. 1976, 106, 118–123.

28. Hasanuddinrusdi, A. Evaluation of nutritional values of fermented carrageenan by-product of seaweed (Eucheuma cottonii) raw materials. Agrisains 2012, 13, 159–166.

29. Panlasigui, L.N.; Baello, O.Q.; Dimatangal, J.M.; Dumelod, B.D. Blood cholesterol and lipid-lowering effects of carrageenan on human volunteers. Asia Pac. J. Clin. Nutr. 2003, 12, 209–214.

30. Sokolova, E.V.; Bogdanovich, L.N.; Ivanova, T.B.; Byankina, A.O.; Kryzhanovskiy, S.P.; Yermak, I.M. Effect of carrageenan food supplement on patients with cardiovascular disease results in normalization of lipid profile and moderate modulation of immunity system markers. PharmaNutrition 2014, 2, 33–37.

31. Valado, A.; Pereira, M.; Caseiro, A.; Figueiredo, J.P.; Loureiro, H.; Almeida, C.; Cotas, J.; Pereira, L. Effect of Carrageenans on Vegetable Jelly in Humans with Hypercholesterolemia. Mar. Drugs 2019, 18, 19.