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# A Pilot Study on Anti-Obesity Mechanisms of *Kappaphycus Alvarezii*: The Role of Native $\kappa$ -Carrageenan and the Leftover Sans-Carrageenan Fraction

Yao Xian Chin <sup>1</sup>, Ye Mi <sup>1</sup>, Wan Xiu Cao <sup>1</sup>, Phaik Eem Lim <sup>2</sup>, Chang Hu Xue <sup>1,\*</sup> and Qing Juan Tang <sup>1,\*</sup>

<sup>1</sup> Human Health Research Laboratory, College of Food Science and Engineering, University of China, Qingdao 266003, Shandong, China; chinyx1@gmail.com (Y.X.C.); MYmy824@163.com (Y.M.); caowanxiu2014@sina.com (W.X.C.)

<sup>2</sup> Institute of Ocean and Earth Sciences, University of Malaya, Kuala Lumpur 50603, Malaysia; phaikem@um.edu.my

\* Correspondence: xuech@ouc.edu.cn (C.H.X.); tangqingjuan@ouc.edu.cn (Q.J.T.); Tel.: +86-0532-82032468 (C.H.X.); +86-0532-82032597 (Q.J.T.)

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**Abstract:** *Kappaphycus* is a commercially important edible red alga widely cultivated for carrageenan production. Here, we aimed to investigate the anti-obesity mechanism of *Kappaphycus alvarezii* by comparing the effects of whole seaweed (T), extracted native  $\kappa$ -carrageenan (CGN), and the leftover fraction sans-carrageenan (SCGN) supplementations (5%, *w/w*) on diet-induced obese C57BL/6J mice. A high-fat diet induced both a raised body fat percentage and serum cholesterol level, increased adipocytes size, abnormal levels of adipocytokines, and promoted gut dysbiosis. Our results showed that, overall, both CGN and SCGN were more effective in reversing obesity and related metabolic syndromes to normal levels than T. Furthermore, these findings suggested that CGN- and SCGN-modulated gut dysbiosis induced by a high-fat diet, which may play an influencing role in adiponectin dysregulation. Our data also showed some evidence that CGN and SCGN have distinct effects on selected genes involved in lipid metabolism. In conclusion, both  $\kappa$ -carrageenan and SCGN have novel anti-obesity potential with possible different mechanisms of action.

**Keywords:** *Kappaphycus*; obesity; metabolic syndrome; carrageenan; food additive; zero-waste; functional food; precision nutrition; gut microbiota

## 1. Introduction

The global prevalence of overweight and obesity has become a major concern for societies around the world and places a great burden on governments and individuals alike, both medically and financially. Even greater, concerted efforts from health authorities in promoting health awareness are not enough to prevent the growth of overweight and obese populations, regardless of the economic status of the society [1]. While exercise and healthy living habits are vital for any weight management regime, diet undeniably plays a large part in sustaining its success. Dietary interventions such as a balanced diet coupled with calorie restriction have been proven to be effective in reversing metabolic complications linked to obesity such as diabetes [2]. However, the reality is that implementing and maintaining calorie restriction in daily life is both challenging and ineffective for many people, as it is susceptible to many disruptive factors including both behavioral and physiological vulnerabilities [3–6]. Hence, there is a need for daily diets to incorporate food that promotes weight loss. While terrestrial plants