



Kappaphycus Alvarezii Compound Powder Prevents Chemotherapy-Induced Intestinal Mucositis in BALB/c Mice

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ABSTRACT

This study aimed to formulate *Kappaphycus alvarezii* compound powder containing *Kappaphycus alvarezii* powder (KP), cooked sorghum powder (SP), and longan powder (LP); which was evaluated for its therapeutic effects against chemotherapy-induced intestinal mucosal injury (CIMI). Based on rheological properties, sensory evaluation, and antioxidant activity and using single factor and response surface methodology, the optimal formula to develop the compound powder was determined to be 35% KP, 30% SP, 5% LP, and 30% xylitol. Thereafter, the efficacy of the compound powder was tested by feeding BALB/c mice with diets supplemented with the *Kappaphycus alvarezii* compound powder (3% and 5%) for 14 consecutive days. The chemotherapeutic drug 5-fluorouracil was intraperitoneally injected (50 mg/kg) in the mice to induce CIMI for the last three consecutive days. Compared to the CIMI mice, those fed 5% *Kappaphycus alvarezii* compound powder (HC) showed significantly improved the intestinal injury, increased mucin-2 secretion, and reduced TNF- α , IL-1 β , IL-6, LT, and COX-2 levels. Furthermore, HC intake significantly reduced the Firmicutes-to-Bacteroidetes ratio, promoted the growth of beneficial bacteria, such as *Alloprevotella*, and inhibited the growth of harmful bacteria, such as *Clostridium*. In conclusion, HC has a protective effect against CIMI and provides a novel dietary strategy for patients undergoing chemotherapy.

ARTICLE HISTORY


Received 26 August 2021
Accepted 9 June 2022

Introduction

Chemotherapeutic drugs are commonly used to treat various types of malignant tumors; however, they can damage the structure and function of the gastrointestinal tract, a condition known as chemotherapy-induced intestinal mucosal injury (CIMI). Approximately two million patients with cancer are treated annually with chemotherapy drugs worldwide (1). The widely used chemotherapy agent 5-fluorouracil (5-FU) is the most effective chemotherapeutic agent for the clinical treatment of malignant tumors. However, 5-FU also adversely affects the gastrointestinal mucosal cells and normal cells with the potential to rapidly proliferate, leading to intestinal inflammation and intestinal flora dysbiosis (2). Therefore, strategies are being explored to treat CIMI, including products from plant natural sources, which have been reported to possess a remarkable ability to protect the intestine (3–5).

Kappaphycus alvarezii is an important commercial red seaweed, known as the “sea-bird nest”. It contains many bioactive compounds, such as polysaccharides, polyphenols, flavonoids, and anthocyanins, which have been documented to exert pharmacological activities, including anti-tumor, antioxidant, anti-bacterial, and anti-inflammatory activities (6, 7). Moreover, studies have reported that extracts produced from *Kappaphycus alvarezii* can slow tumor cell growth rate to prevent colon carcinogenesis and be used for colitis treatment (8, 9). Our previous study also reported that *Kappaphycus alvarezii* can be used to treat CIMI, modulate the gut microbiota and promote human intestinal health (10, 11). Thus, *Kappaphycus alvarezii* with its various biological activities is an important preventive agent against CIMI, and its dietary intake would be suitable for patients with CIMI.

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 Supplemental data for this article can be accessed <https://doi.org/10.1080/01635581.2022.2089699>

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