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Title:

Distinct structural features of seaweed-derived polysaccharides and their differential protective effects on metabolic and multi-organ alterations in diet-induced obesity

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Abstract: (Your abstract must use **Normal style** and must fit in this box. Your abstract should be no longer than 300 words. The box will 'expand' over 2 pages as you add text into it.)

Preparation of Your Abstract

1. The title should be as brief as possible but long enough to indicate clearly the nature of the study. Capitalise the first letter of the first word ONLY (place names excluded). No full stop at the end.
2. Abstracts should state briefly and clearly the purpose, methods, results and conclusions of the work.

Introduction: Clearly state the purpose of the abstract

Methods: Describe your selection of observations or experimental subjects clearly

Results: Present your results in a logical sequence

Discussion: Emphasize new and important aspects of the study and conclusions that are drawn from them

Introduction: Seaweed-derived polysaccharides (SPS) improve obesity-related metabolic disorders, but how structural diversity influences outcomes remains unclear. This study characterized SPS from three edible seaweeds and evaluated their effects in a high-fat diet (HFD)-induced obese mouse model.

Methods: Polysaccharides from *Undaria pinnatifida* sporophyll (UPSPS), *Codium fragile* (CFPS), and *Gracilaria verrucosa* (GVPS) were analyzed using chromatographic and spectroscopic approaches. Male C57BL/6 mice received HFD for 8 weeks, followed by 4 weeks of SPS administration, after which metabolic parameters, tissue pathology, and gut microbiota composition were evaluated.

Results: Structurally, UPSPS was rich in fucose, galactose, and mannuronic acid, typical of fucoidan-type polysaccharides with low molecular weight but large particle size. CFPS, composed mainly of mannose, arabinose, glucose, and galactose, showed higher and heterogeneous molecular weights. GVPS, dominated by galactose, had a broad distribution with ultra-high-molecular-weight fractions, indicating heterogeneity. All SPS significantly ameliorated HFD-induced metabolic impairments, improving body-weight gain, insulin resistance, and lipid profiles, with additional tissue-specific benefits in the colon, liver, and adipose tissue. In the colon, distal mucosal and submucosal inflammation and edema were alleviated, most evident with GVPS. Hepatic steatosis improved in the order GVPS > CFPS > UPSPS, whereas immune-cell infiltration was suppressed in the order UPSPS > CFPS > GVPS. In adipose tissue, CFPS and GVPS reduced adipocyte hypertrophy and crown-like structures, while UPSPS showed limited effects. Gut microbiota profiling demonstrated diet-driven clustering and taxa-specific shifts. GVPS enriched *Clostridium sensu stricto* 1, CFPS increased *Lactobacillus* and *Limosilactobacillus*, and UPSPS promoted *Faecalibaculum* and *Bifidobacterium*.

Conclusions: This study demonstrates that SPS with distinct structural features exert differential protective effects on metabolic and multi-organ alterations in obesity, supporting their potential as dietary interventions for metabolic health and gut microbiota modulation.