چهارمین کنگره دانشجویان
کشاورزی، دامپزشکی
محیط‌زیست و منابع طبیعی
4th Congress for
Agriculture, Veterinary
Medicine, Environment and
Natural Resources Students
www.ca.cdsts.ir

A New Review of *Ulva*-Derived Bioactive Compounds, Especially Ulvan, in Improving Metabolic Health and Strengthening the Immune System of Humans and Animals

Zeinab Talebi & Saeed Arab

Email:Zeinabtalebi30@gmail.com

MSc Student in Sports Nutrition, Najafabad Branch, Islamic Azad University, Najafabad, Iran

Email:SaeedArab39@gmail.com

MSc in Agricultural Economics, Marvdasht Branch, Islamic Azad University, Marvdasht, Iran

Abstract

Ulva species are valuable green seaweeds rich in bioactive compounds, particularly the sulfated polysaccharide ulvan, which represents 9–36% of the dry biomass and serves as a major structural and functional component [1–5]. Research has shown that ulvan contains sulfated rhamnose, uronic acids, and xylose, and that its biological activity depends on molecular weight, sulfate content, and extraction conditions [1–6]. Studies consistently report antioxidant, anticancer, immunomodulatory, and prebiotic-like effects of Ulva extracts and ulvan, supporting their relevance to metabolic regulation and immune health in humans and animals [1–5,7–20]. In addition, ulvan has demonstrated promising value in aquaculture, where it improves immune responses, antioxidant defense, and growth performance [14–18]. Overall, Ulva represents a natural marine resource with strong potential for functional food, nutraceutical, and feed applications [1–20].

Key words*: Ulva, Ulvan, green algae, polysaccharides, bioactive compounds, metabolic, human immune system, animal immune system*

Introduction

(Ulva is an abundant edible green seaweed and a promising source of bioactive compounds for food, nutraceutical, and veterinary applications [1–5]. Its main sulfated polysaccharide, ulvan, forms a major fraction of the dry biomass and contains sulfated rhamnose, uronic acids (glucuronic/iduronic), and xylose, which underpin its distinctive biological functions [1–3]. Recent studies report that Ulva extracts and ulvan can support health through antioxidant, anticancer, immunomodulatory, and gut-related (prebiotic-like) effects, including microbial modulation and fermentation to beneficial metabolites in the colon [5,7–20]. Future research should standardize extraction and characterization, clarify structure–activity relationships, and expand well-designed translational studies in humans and animals to enable safe, consistent applications [1–6,14–20].

Materials and Methods

In this review, the Materials and Methods were based on a structured literature-search approach using the keywords seaweed, Ulva, ulvan, anticancer, antioxidant, immunomodulation, cytotoxicity, and pharmacokinetics across Google Scholar, PubMed, Web of Science, ScienceDirect, and Scopus for studies published between 1997 and 2023, yielding a final set of 119 articles searched without language restrictions; only peer-reviewed papers, review articles, and reports focusing on pure or enriched ulvan preparations were retained for the main analysis [1,2]. Because ulvan bioactivity is affected by key structural and processing factors, molecular weight, sulfate content, and extraction method were treated as core variables when interpreting outcomes and comparing evidence across studies [2,3]. Antioxidant activity was reported using standard in-vitro assays including DPPH, FRAP, ORAC, superoxide and hydroxyl radical scavenging, lipid peroxidation inhibition, AAPH-induced oxidation/TBARS, and β-carotene–linoleic acid bleaching assays [4–6], while anticancer and cytotoxic effects were most commonly evaluated using MTT and cell-viability assays, with apoptotic endpoints such as increased caspase-8 and caspase-9 also noted in selected models [7–9]. Immunomodulatory evidence was derived from macrophage-based assays (e.g., nitric oxide and pro-inflammatory cytokine responses) and from aquaculture-relevant in vivo models including Nile tilapia, Labeo rohita, Senegalese sole, and zebrafish [10–14]. Finally, gut-related effects were discussed based on reports that ulvan is not digested in the small intestine, is partly fermented by colonic bacteria into short-chain fatty acids (SCFAs), and can modulate the intestinal microbiota [15].

Discussion and conclusion

In this study, the discussion of results shows that Ulva and its major sulfated polysaccharide ulvan are biologically active marine compounds with notable antioxidant, anticancer, immunomodulatory, and prebiotic-related potential, and the novelty of the reviewed evidence lies in the clearer link between structure–activity relationships and function, especially the roles of molecular weight, sulfate content, and extraction method in determining bioactivity [1,2]. The antioxidant findings were supported by standard in vitro assays such as DPPH, FRAP, ORAC, TBARS, and β-carotene bleaching, while anticancer activity was evaluated through cell viability and MTT-based tests and, in some studies, apoptosis-related markers such as p53, Bcl-2, and caspase-8/9, showing that ulvan can suppress proliferation while preserving normal cells in several models [3–7]. Compared with authoritative studies in the background, the newer literature provides stronger evidence that ulvan is not only a general antioxidant but also a structurally tunable bioactive polysaccharide with promising chemopreventive and immune-regulating effects, including activity in macrophage systems and aquaculture species such as Nile tilapia, Senegalese sole, Labeo rohita, and zebrafish [8–12]. In addition, ulvan's non-digestibility in the small intestine, partial fermentation into short-chain fatty acids, and positive influence on gut microbiota suggest practical value as a functional food ingredient and prebiotic candidate [13–15]. Overall, these findings are important because they support the development of natural antioxidants, nutraceuticals, cancer-related supportive agents, and aquaculture feed additives, while also indicating that future work should focus on standardized extraction, purification, in vivo validation, and safety testing to improve real-world application and production potential [1,2,6,12,15].

a) References

2) *Kidgell JT, Magnusson M, de Nys R, Glasson CR. Ulvan: A systematic review of extraction, composition and function. Algal Res. 2019;39:101422.*

3) *Lahaye M, Robic A. Structure and functional properties of ulvan, a polysaccharide from green seaweeds. Biomacromolecules. 2007;8:1765-1774.*

4) *Hassan S, Abd El-Twab S, Hetta M, Mahmoud B. Improvement of lipid profile and antioxidant of hypercholesterolemic albino rats by polysaccharides extracted from the green alga Ulva lactuca Linnaeus. Saudi J Biol Sci. 2011;18:333-340.*

5) *Li W, Jiang N, Li B, Wan M, Chang X, Liu H, Zhang L, Yin S, Qi H, Liu S. Antioxidant activity of purified ulvan in hyperlipidemic mice. Int J Biol Macromol. 2018;113:971-975.*

6) *Yaich H, Amira AB, Abbes F, Bouaziz M, Besbes S, Richel A, Blecker C, Attia H, Garna H. Effect of extraction procedures on structural, thermal and antioxidant properties of ulvan from Ulva lactuca collected in Monastir coast. Int J Biol Macromol. 2017;105:1430-1439.*

7) *Wang R, Paul VJ, Luesch H. Seaweed extracts and unsaturated fatty acid constituents from the green alga Ulva lactuca as activators of the cytoprotective Nrf2-ARE pathway. Free Radic Biol Med. 2013;57:141-153.*

8) *Thanh TTT, Quach TMT, Nguyen TN, Luong DV, Bui ML, Van Tran TT. Structure and cytotoxic activity of ulvan extracted from green seaweed Ulva lactuca. Int J Biol Macromol. 2016;93:695-702.*

9) *Ahmed O, Ahmed R. Anti-proliferative and apoptotic efficacies of ulvan polysaccharides against different types of carcinoma cells in vitro and in vivo. J Cancer Sci Ther. 2014;6:202-208.*

10) *Alves A, Sousa RA, Reis RL. In vitro cytotoxicity assessment of ulvan, a polysaccharide extracted from green algae. Phytother Res. 2013;27:1143-1148.*

11) *Hussein UK, Mahmoud HM, Farrag AG, Bishayee A. Chemoprevention of diethylnitrosamine-initiated and phenobarbital-promoted hepatocarcinogenesis by ulvan in rats. Food Chem Toxicol. 2015;76:1-10.*

12) *Kaeffer B, Bottex C, Chancerelle Y, Mace K, Lahaye M. A polysaccharide from the marine alga Ulva lactuca as a potent in vitro and ex vivo stimulator of rat intestinal immunity. J Nutr. 1999;129:1984-1991.*

13) *Jose S, Shah NJ, Kumar MS. Immunostimulant activity of ulvan on macrophage cell line (RAW264.7). Int J Biol Macromol. 2007;40:247-250.*

14) *Ponce NMA, Pujol CA, Damonte EB, Flores ML, Stortz CA. Sulfated polysaccharides from Ulva species have protective effects against HSV-1 infection. Virus Res. 2003;95:1-8.*

15) *Quezada-Rodríguez FR, Fajer-Ávila EJ. Ulvan as a prebiotic for marine fish: Effects on gut microbiota and immunity in Nile tilapia. Aquaculture. 2017;479:412-420.*

16) *Lahaye M, Kaeffer B. Digestion of Ulva polysaccharides by human colonic bacteria: Fermentation and short-chain fatty acid production. J Agric Food Chem. 1997;45:2876-2882.*