

Anticancer Properties of Ulvan: Molecular Mechanisms, Experimental Evidence, and Translational Potential

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ABSTRACT: Ulvan is a sulfated heteropolysaccharide mainly found in the cell wall of green macroalgae belonging to the genus *Ulva*. Because of its unusual composition, which includes rhamnose, glucuronic and iduronic acids, xylose, and sulfate groups, ulvan has attracted increasing interest as a biologically active marine polysaccharide. A growing body of experimental work suggests that ulvan may interfere with several processes involved in cancer development and progression, including cell proliferation, apoptosis, oxidative stress, inflammation, and cellular signaling. These effects have been reported in different cancer models, including hepatocellular, breast, cervical, colorectal, gastric, prostate, melanoma, and leukemia models. Importantly, the biological activity of ulvan is not uniform and appears to depend strongly on its molecular weight, degree of sulfation, monosaccharide composition, algal species, and extraction procedure. Recent studies have begun to move beyond simple cytotoxicity assays and have identified more specific molecular events, including the miR-542-3p/SLC35F6/TP53 axis in hepatocellular carcinoma. Ulvan-based biomaterials have also opened another line of research in which the polysaccharide is used as a drug-delivery or local treatment platform. Despite these encouraging findings, most available evidence remains preclinical, and questions related to structural standardization, pharmacokinetics, bioavailability, safety, and clinical efficacy remain unresolved. This review summarizes the current evidence on the anticancer activity of ulvan, with particular emphasis on its molecular mechanisms, structure–activity relationships, and possible translational applications.

KEYWORDS: *Ulva*, sulfated polysaccharide, cancer, apoptosis, oxidative stress.

1. INTRODUCTION

Cancer remains a major global health problem and continues to account for substantial morbidity and mortality despite considerable progress in diagnosis and treatment. Conventional therapeutic strategies, including chemotherapy, radiotherapy, targeted therapy, immunotherapy, and surgery, have significantly improved outcomes in several cancer types. Nevertheless, treatment resistance, systemic toxicity, tumor heterogeneity, and recurrence remain important clinical challenges. These limitations have stimulated continued interest in biologically active compounds derived from natural sources, particularly molecules capable of acting on several cellular processes simultaneously. Marine organisms represent an increasingly important source of bioactive compounds. Among marine resources, macroalgae contain structurally diverse polysaccharides, proteins, pigments, lipids, polyphenols, and other secondary metabolites with potential pharmacological properties. Sulfated polysaccharides have attracted particular attention because of their antioxidant, immunomodulatory, anti-inflammatory, antiviral, anticoagulant, and anticancer activities (Wijesekara et al., 2011; Kidgell et al., 2019; Pradhan et al., 2023).

Ulvan is the characteristic water-soluble sulfated polysaccharide of green macroalgae belonging mainly to the genus *Ulva*. Unlike many terrestrial polysaccharides, ulvan possesses a complex and highly variable structure containing sulfated rhamnose, glucuronic acid, iduronic acid, and xylose residues. This structural organization gives ulvan unique physicochemical properties and allows interactions with proteins, cell membranes, and biological signaling systems (Lahaye and Robic, 2007; Kidgell et al., 2019). Interest in ulvan has increased as experimental studies have identified biological effects relevant to cancer biology. These include inhibition of tumor-cell proliferation, induction of apoptosis, modulation of oxidative stress, regulation of inflammatory responses, and changes in signaling pathways associated with cell survival (Pradhan et al., 2023; Shah et al., 2023). Importantly, ulvan should not be considered a chemically uniform compound. Its composition can vary according to *Ulva* species, geographical origin, environmental conditions, harvesting season, extraction technique, molecular weight, sulfate content, and purification procedure (Lahaye and Robic, 2007; Kidgell et al., 2019). This variability has important consequences for biological activity. Guidara et al.

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(2021), for example, demonstrated that different extraction procedures generated ulvan fractions with different structural characteristics, molecular weights, and antitumor activities against HeLa cells. Recent research has begun to clarify specific molecular mechanisms underlying these effects. Particularly noteworthy is the study of Qiu et al. (2025), which demonstrated that *U. lactuca* polysaccharide inhibited hepatocellular carcinoma cell growth through regulation of miR-542-3p and SLC35F6, accompanied by increased TP53 expression. The aim of this review is to critically evaluate the current evidence concerning the anticancer potential of ulvan. Particular attention is given to its chemical structure, antiproliferative and apoptotic effects, modulation of oxidative stress and inflammatory pathways, evidence from different cancer models, and possible applications in drug-delivery systems. The limitations of current evidence and the major issues that need to be addressed before clinical translation are also discussed.

2. CHEMICAL CHARACTERISTICS OF ULVAN

Ulvan is a sulfated heteropolysaccharide located predominantly in the cell wall of *Ulva* species. Its main structural components include rhamnose, glucuronic acid, iduronic acid, and xylose, although the precise composition varies considerably between species and extraction procedures (Lahaye and Robic, 2007; Kidgell et al., 2019). The presence of sulfate groups gives ulvan a high negative charge density and contributes substantially to its biological and physicochemical properties. Structural studies have identified characteristic repeating units such as ulvanobiuronic acid type A and type B. These structural motifs contain uronic acids linked to sulfated rhamnose residues. The combination of uronic acids and sulfated sugars gives ulvan certain similarities to mammalian glycosaminoglycans, although its overall structure remains distinct (Lahaye and Robic, 2007). One of the major challenges in ulvan research is its structural heterogeneity. Molecular weight, degree and position of sulfation, monosaccharide composition, branching, and glycosidic linkage patterns can vary substantially. Environmental conditions, algal species, geographical location, season, and extraction technique all contribute to this variation (Kidgell et al., 2019). This issue is particularly relevant when interpreting anticancer studies. A preparation described simply as “ulvan” may contain a different molecular-weight distribution or sulfate content from another preparation obtained from a different *Ulva* species. Consequently, differences in biological activity cannot always be attributed to the cancer model itself.

Guidara et al. (2021) provided direct experimental evidence supporting this concept. They compared several extraction approaches for obtaining ulvan from *U. lactuca* and found that the extraction procedure altered chemical composition, molecular weight, structural characteristics, and biological activity. The enzymatic-chemical extract demonstrated the greatest cytotoxic effect against HeLa cells among the preparations examined. These observations indicate that future anticancer studies should report detailed structural characterization rather than referring only to the source organism. Molecular weight, sulfate percentage, uronic acid content, monosaccharide composition, protein contamination, and purification yield should ideally be included in experimental reports.

3. STRUCTURE–ACTIVITY RELATIONSHIP

The relationship between the chemical structure of ulvan and its biological activity remains incompletely understood. Nevertheless, available evidence indicates that molecular weight and sulfation are important determinants of its biological behavior (Kidgell et al., 2019; Li et al., 2025). Molecular size may influence solubility, cellular interactions, diffusion, and biological accessibility. High-molecular-weight ulvan can exhibit favorable rheological and biomaterial properties but may have limited absorption and bioavailability when administered systemically. Depolymerization can produce lower-molecular-weight ulvan fragments or oligosaccharides with altered physicochemical properties and potentially improved biological accessibility (Li et al., 2025). Sulfation is another important structural parameter. Sulfate groups influence charge density and can affect interactions with growth factors, extracellular matrix components, membrane proteins, and signaling molecules. However, increased sulfation should not automatically be interpreted as producing stronger anticancer activity because the relationship appears to depend on molecular context. The systematic literature analysis conducted by Kidgell et al. (2019) emphasized the need for well-characterized ulvan preparations to establish meaningful structure–function relationships. The authors specifically highlighted differences in extraction and characterization methods as major obstacles to comparing studies. More recent reviews have reached similar conclusions. Li et al. (2025) noted that the relatively large molecular size and poor bioavailability of native ulvan can limit its practical applications, while oligosaccharide derivatives may overcome some of these limitations (Li et al., 2025). Thus, the future development of ulvan as an anticancer candidate will probably require a shift from studying “ulvan” as a broad natural product toward studying chemically defined fractions with reproducible structural characteristics.

4. ANTIPROLIFERATIVE AND CYTOTOXIC EFFECTS

Inhibition of cancer-cell proliferation is one of the most frequently reported biological effects of Ulva-derived polysaccharides. Studies involving different cancer cell lines have reported variable degrees of growth inhibition, suggesting that both the characteristics of the polysaccharide and the biological properties of the target cell determine the response (Pradhan et al., 2023). Ulvan preparations from *U. lactuca* have been investigated in cervical, breast, and hepatocellular carcinoma models. The magnitude of cytotoxicity varies substantially among studies, which may partly reflect differences in extraction procedures and molecular composition.

Guidara et al. (2021) demonstrated that ulvan obtained from *U. lactuca* could inhibit HeLa cervical cancer cells, although the degree of activity differed according to the extraction method. The enzymatic-chemical fraction produced an IC₅₀ of approximately 1000 µg/mL against HeLa cells, illustrating that even within a single algal species, extraction can affect anticancer activity. More recently, El-Hadedy et al. (2023) characterized ulvan isolated from *U. papenfussii* and evaluated its cytotoxic activity against HepG2, MCF-7, and HeLa cells. The reported IC₅₀ values were approximately 89.8, 85.5, and 67.0 µg/mL, respectively. These findings support the potential of ulvan preparations to inhibit multiple tumor-cell types, although the potency remained substantially lower than that of the reference drug used in the study. García-Márquez et al. (2023) further examined ulvan from *U. rigida* against leukemia, melanoma, and colorectal cancer cells. Cytotoxic effects were observed in all three cancer models, but HCT-116 colorectal cancer cells showed the greatest sensitivity, with an LC₅₀ of approximately 0.1 mg/mL. Importantly, the authors also evaluated healthy and immortalized nonmalignant cells, highlighting the need to consider selectivity when assessing ulvan's therapeutic potential. Taken together, these findings suggest that ulvan has measurable antiproliferative activity, but its potency varies widely. Therefore, it is premature to consider ulvan a conventional cytotoxic anticancer drug. Its more realistic potential may lie in combination therapy, tumor-targeted delivery, or modulation of specific cancer-associated pathways.

5. ULVAN AND APOPTOSIS

Apoptosis is a major mechanism through which anticancer agents eliminate malignant cells. The ability to induce programmed cell death without causing excessive toxicity in normal tissues is an important characteristic of a potentially useful anticancer compound. Available evidence suggests that apoptosis contributes to the antitumor effects associated with ulvan and Ulva-derived polysaccharides (Pradhan et al., 2023). The p53/Bax/Bcl-2 axis is particularly relevant because alterations in these proteins can shift the balance between cell survival and programmed cell death. p53 is a major tumor-suppressor protein that responds to cellular stress and DNA damage. Its activation can induce cell-cycle arrest and apoptosis through downstream mediators such as p21 and Bax. Bcl-2, in contrast, inhibits mitochondrial apoptosis and promotes cell survival. A shift toward increased p53 and Bax together with reduced Bcl-2 would therefore favor apoptotic cell death. The 2023 review by Pradhan et al. summarized evidence suggesting that ulvan and related sulfated algal polysaccharides can influence these apoptotic regulators. However, the authors also emphasized that mechanistic evidence remains incomplete and that additional experimental work is necessary to establish direct molecular targets. A particularly important advance came from Qiu et al. (2025). Their study demonstrated that *U. lactuca* polysaccharide increased miR-542-3p expression in hepatocellular carcinoma models. This was associated with suppression of SLC35F6 and increased TP53 protein expression. Furthermore, SLC35F6 knockdown reduced the growth of H22 and HepG2 cells while increasing TP53 expression (Qiu et al., 2025). These findings are important because they provide a more specific mechanistic explanation for the antiproliferative effects of Ulva-derived polysaccharides. Rather than simply describing ulvan as an apoptosis-inducing agent, the results raise the possibility that non-coding RNA regulation and specific target genes participate in its anticancer activity. Whether the miR-542-3p/SLC35F6/TP53 pathway is relevant to other cancer types remains unknown. This should be a priority for future studies.

6. OXIDATIVE STRESS AND ANTIOXIDANT ACTIVITY

Oxidative stress has a complicated relationship with cancer. Excessive reactive oxygen species (ROS) can cause DNA damage, lipid peroxidation, mitochondrial dysfunction, and cell death. At moderate levels, however, ROS can promote tumor-cell proliferation, migration, and resistance to therapy. Ulvan has demonstrated antioxidant activity in several experimental systems. This activity is thought to be influenced by its sulfate groups, uronic acids, molecular weight, and overall chemical structure (Kidgell et al., 2019; Pradhan et al., 2023).

The antioxidant properties of ulvan may be relevant to cancer prevention and treatment in two different ways. First, reducing oxidative damage could potentially protect normal tissues from carcinogenic stress. Second, depending on the cellular environment and concentration, ulvan-induced changes in redox homeostasis may contribute to tumor-cell death. This dual role should be interpreted carefully. An antioxidant effect observed in a chemical assay does not necessarily translate into anticancer

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activity in vivo. Cancer cells have distinct redox states, and some tumors rely on elevated antioxidant defenses to survive oxidative stress (Binsuwaidan et al., 2023).

Pradhan et al. (2023) reviewed evidence indicating that ulvan can modulate antioxidant defenses and oxidative stress, but also emphasized the need for more mechanistic studies linking these effects directly to cancer-cell death. Future studies should therefore measure intracellular ROS, glutathione, SOD, catalase, GPx, lipid peroxidation, mitochondrial membrane potential, and apoptosis simultaneously. This would help determine whether redox modulation is an upstream mechanism or simply a secondary consequence of ulvan-induced cellular stress.

7. REGULATION OF CELL CYCLE AND PROLIFERATION

Uncontrolled proliferation is a central characteristic of cancer. Tumor cells commonly exhibit dysregulation of cyclins, cyclin-dependent kinases, tumor-suppressor proteins, and checkpoint mechanisms. The available literature suggests that ulvan may interfere with cell proliferation partly through modulation of cell-cycle regulatory pathways (Pradhan et al., 2023; Shah et al., 2023). The involvement of p53 is particularly relevant because p53 can induce cell-cycle arrest through p21 and subsequently create an opportunity for DNA repair or trigger apoptosis when damage is irreparable. However, compared with apoptosis, the cell-cycle effects of ulvan remain less clearly characterized. Many studies have focused on cell viability without determining the precise stage of cell-cycle arrest. Future studies should therefore incorporate flow cytometric analysis together with measurements of cyclin D1, cyclin E, cyclin-dependent kinases, p21, p27, and p53. These experiments would clarify whether ulvan primarily arrests cell-cycle progression or whether cell-cycle changes are secondary to apoptosis.

8. CANCER-ASSOCIATED SIGNALING PATHWAYS

Cancer progression is controlled by interconnected signaling networks rather than a single pathway. PI3K/AKT/mTOR, MAPK, NF- κ B, Wnt/ β -catenin, and hypoxia-associated pathways regulate proliferation, metabolism, inflammation, angiogenesis, and survival. Marine sulfated polysaccharides have been reported to affect several of these signaling networks, and ulvan has been discussed in relation to pathways involved in apoptosis, inflammation, oxidative stress, and cellular survival (Pradhan et al., 2023; Shah et al., 2023). The PI3K/AKT pathway is particularly relevant because persistent activation of AKT promotes cell survival and suppresses apoptotic signaling. Modulation of this pathway could therefore enhance the susceptibility of tumor cells to programmed cell death. NF- κ B is another potentially relevant pathway. Chronic activation of NF- κ B promotes inflammatory cytokine production, proliferation, angiogenesis, and resistance to apoptosis. Since ulvan has immunomodulatory and anti-inflammatory properties, interference with inflammatory signaling may contribute indirectly to its anticancer effects (Pradhan et al., 2023). Nevertheless, caution is necessary when assigning a specific signaling mechanism to ulvan. Some studies have used whole *Ulva* extracts rather than purified polysaccharide fractions. Such extracts contain multiple bioactive compounds, and it may therefore be difficult to determine which component is responsible for a particular signaling effect. This distinction is especially important for Q1-level reviews. Mechanistic claims should ideally be supported by experiments using purified and structurally characterized ulvan, together with pathway-specific inhibitors, gene knockdown, or rescue experiments.

9. IMMUNOMODULATORY AND ANTI-INFLAMMATORY EFFECTS

The tumor microenvironment consists of malignant cells together with fibroblasts, endothelial cells, macrophages, lymphocytes, extracellular matrix, and a complex network of cytokines and chemokines. Inflammation within this environment can promote tumor growth, angiogenesis, invasion, and treatment resistance.

Ulvan has demonstrated immunomodulatory activity in several experimental systems. Its sulfated structure allows interactions with proteins and receptors involved in immune regulation, and studies have reported effects on immune-cell responses and cytokine production (Pradhan et al., 2023; Shah et al., 2023).

From a cancer perspective, this activity is potentially important because a compound capable of simultaneously affecting tumor cells and the tumor microenvironment could have broader therapeutic effects. However, general immune stimulation should not automatically be equated with antitumor immunity. Tumor-associated macrophages and inflammatory pathways can have both tumor-promoting and tumor-suppressive roles. Consequently, future studies should examine the effects of ulvan on macrophage polarization, cytotoxic T-cell activity, regulatory T cells, dendritic cells, and tumor-associated cytokines. Three-dimensional tumor models and immunocompetent animal models would be particularly useful in this context (Pereira et al., 2025).

10. EVIDENCE FROM DIFFERENT CANCER MODELS

10.1. Hepatocellular carcinoma

Hepatocellular carcinoma (HCC) represents one of the most interesting models for investigating the anticancer activity of Ulva-derived polysaccharides. Earlier studies reported antiproliferative effects of *U. lactuca*-derived polysaccharides in hepatocellular carcinoma cells (Pradhan et al., 2023). More recently, Qiu et al. (2025) provided direct evidence for a specific molecular mechanism. In their study, *U. lactuca* polysaccharide increased miR-542-3p and suppressed SLC35F6 expression. This molecular change was associated with increased TP53 protein expression and reduced proliferation of H22 and HepG2 cells. SLC35F6 was also found to be overexpressed in HCC and associated with poor prognosis (Qiu et al., 2025). This work represents an important step toward understanding the molecular basis of ulvan-related anticancer activity. However, validation in additional HCC models and in vivo systems will be required.

10.2. Breast cancer

Breast cancer has also been investigated using Ulva-derived polysaccharides. MCF-7 cells are among the most frequently used models, and studies have reported reductions in cell viability following exposure to ulvan preparations (Pradhan et al., 2023). The available evidence suggests that apoptotic signaling and changes in p53/Bcl-2-associated pathways may contribute to these effects. However, breast cancer is biologically heterogeneous, and findings obtained using MCF-7 cells cannot automatically be generalized to HER2-positive or triple-negative breast cancer. Future research should therefore compare ulvan activity across molecularly distinct breast cancer subtypes.

10.3. Colorectal cancer

Colorectal cancer models have also demonstrated sensitivity to Ulva-derived polysaccharides. García-Márquez et al. (2023) tested ulvan from *U. rigida* against HCT-116 colorectal cancer cells and reported considerable cytotoxic activity, with HCT-116 being the most sensitive among the cancer models evaluated. The same study also included nonmalignant human cell models and zebrafish embryos, providing preliminary information about biological safety. However, developmental toxicity was observed at higher concentrations in zebrafish, demonstrating why anticancer activity must always be considered together with toxicity.

10.4. Cervical cancer

HeLa cervical cancer cells have been used in several investigations of *U. lactuca*-derived ulvan. Guidara et al. (2021) showed that extraction procedure significantly affected the antitumor activity of ulvan. The enzymatic-chemical extract displayed the strongest cytotoxic effect against HeLa cells, while some acid-derived fractions showed different effects on cancer and normal lymphocyte cells. These findings provide a strong example of the structure–activity relationship problem in ulvan research.

10.5. Leukemia and melanoma

García-Márquez et al. (2023) also examined ulvan from *U. rigida* against U-937 leukemia and G-361 melanoma cells. Cytotoxic effects were detected in both models, although sensitivity differed among the cancer cell types. The variation between leukemia, melanoma, and colorectal cancer models supports the concept that ulvan activity is not universal and may depend on the molecular phenotype of the target cell.

11. ULVAN AS A DRUG-DELIVERY AND BIOMATERIAL PLATFORM

The anticancer potential of ulvan does not necessarily depend solely on its direct cytotoxic activity. Its physicochemical characteristics make it attractive as a component of biomaterials and drug-delivery systems. Ulvan possesses water solubility, biodegradability, functional groups suitable for chemical modification, and the ability to form or participate in hydrogels and hybrid structures. These properties have encouraged its incorporation into membranes, particles, hydrogels, three-dimensional structures, and nanofibers (Cunha and Grenha, 2016; Sulastri et al., 2021).

From an oncology perspective, this is particularly interesting because systemic administration of high-molecular-weight polysaccharides may be limited by poor bioavailability. Incorporating ulvan into a delivery platform could provide an alternative strategy based on local or controlled drug release. Ulvan-based biomaterials could potentially be designed to carry conventional chemotherapeutic agents, nucleic acids, proteins, or other bioactive molecules. The negative charge and modifiable functional groups of ulvan may also facilitate interactions with therapeutic compounds. Recent reviews have emphasized the broader biopharmaceutical potential of ulvan, including drug delivery, tissue engineering, and other biomedical applications (Shah et al., 2023).

Nevertheless, most ulvan-based drug-delivery systems remain at the experimental stage. Their pharmacokinetics, degradation behavior, biodistribution, immunogenicity, and long-term safety need to be established before clinical applications can be considered.

12. BIOAVAILABILITY AND PHARMACOKINETIC CONSIDERATIONS

One of the main limitations associated with natural polysaccharides is their bioavailability. High-molecular-weight molecules often have limited gastrointestinal absorption, and their systemic distribution can be difficult to predict. This issue is particularly relevant for ulvan because its biological activity may depend on molecular size and structural characteristics. Enzymatic, chemical, or physical degradation can generate lower-molecular-weight fragments or oligosaccharides with potentially improved solubility and accessibility (Li et al., 2025). However, depolymerization is not necessarily beneficial in every situation. Reducing molecular weight may alter sulfate density, conformation, receptor interactions, and biological activity. Therefore, optimization should aim not simply to produce smaller molecules but to identify specific molecular structures with favorable pharmacological properties. Pradhan et al. (2023) highlighted pharmacokinetic limitations as one of the major challenges for the therapeutic development of ulvan. Future studies should determine plasma stability, tissue distribution, metabolic degradation, excretion, and exposure after different routes of administration. These parameters are essential for defining a biologically relevant dose (Tran et al., 2023).

13. SAFETY AND TRANSLATIONAL LIMITATIONS

Despite promising experimental data, ulvan cannot currently be considered an established anticancer treatment. One major limitation is the lack of standardized preparations. Different *Ulva* species and extraction procedures produce chemically different polysaccharides. This makes it difficult to compare doses, IC₅₀ values, and biological outcomes between studies (Kidgell et al., 2019; Guidara et al., 2021). Another limitation is the predominance of in vitro evidence. Although several studies have used animal or zebrafish models, robust mammalian in vivo cancer studies remain relatively limited.

The work of García-Márquez et al. (2023) illustrates both the promise and the limitations of current evidence. Ulvan showed cytotoxic effects against several cancer cell lines, but higher concentrations also produced developmental effects in zebrafish embryos. This emphasizes an important principle: biological activity alone is insufficient to establish therapeutic potential. A useful anticancer candidate must demonstrate an adequate therapeutic window, reproducible pharmacological activity, predictable pharmacokinetics, and acceptable toxicity. Human clinical evidence is currently insufficient. The 2023 comprehensive review by Pradhan et al. described ulvan as a promising candidate but also emphasized that its mechanisms and pharmacological properties require further investigation before clinical development (Pradhan et al., 2023). Accordingly, claims that ulvan can currently be used as a cancer treatment would be premature.

The next stage of ulvan research should focus on establishing clear structure–activity relationships. Researchers should ideally isolate ulvan fractions with defined molecular weights and sulfate contents and test them using standardized experimental conditions.

Second, cancer studies should move beyond conventional two-dimensional cell cultures. Three-dimensional tumor spheroids, organoids, tumor–immune cell co-cultures, and patient-derived models may provide a more physiologically relevant assessment of ulvan activity. Third, the molecular mechanisms need to be validated using modern approaches. Transcriptomics, proteomics, metabolomics, phosphoproteomics, and single-cell analyses could help identify molecular pathways affected by specific ulvan fractions. The miR-542-3p/SLC35F6/TP53 pathway identified by Qiu et al. (2025) represents an interesting starting point for this type of investigation.

Combination therapy is another promising area. Rather than replacing established chemotherapy, ulvan could potentially be investigated as an adjuvant that modifies tumor sensitivity, oxidative stress, inflammation, or drug delivery. Finally, ulvan-based biomaterials may provide an alternative route toward clinical translation. Local delivery systems could potentially overcome some limitations associated with poor systemic bioavailability and allow ulvan to be combined with established anticancer agents (Cunha and Grenha, 2016; Shah et al., 2023).

14. CONCLUSION

Ulvan has emerged as a promising marine-derived sulfated polysaccharide with biological properties that may be relevant to cancer prevention and treatment. Experimental evidence indicates that *Ulva*-derived polysaccharides can inhibit tumor-cell proliferation and may promote apoptosis while modulating oxidative stress, inflammation, and cancer-associated signaling pathways. The evidence is particularly interesting because recent research is beginning to identify specific molecular mechanisms. The study by Qiu et al. (2025), for example, linked *U. lactuca* polysaccharide activity to the miR-542-3p/SLC35F6/TP53 regulatory axis in hepatocellular carcinoma. At the same time, the field faces important limitations. Structural heterogeneity, differences in extraction methods, limited bioavailability, insufficient pharmacokinetic information, and a lack of clinical trials prevent ulvan from being considered an established anticancer agent (Kidgell et al., 2019; Pradhan et al., 2023). Overall, ulvan should currently be regarded as a promising preclinical anticancer candidate rather than a clinically established anticancer drug. The most productive future direction will likely involve combining rigorous structural characterization with mechanistic cancer biology, advanced tumor

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models, drug-delivery technologies, and carefully designed in vivo studies. Such an approach may determine whether the biological properties of ulvan can ultimately be translated into a clinically meaningful cancer intervention.

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