TPM Vol. 32, No. S5, 2025
ISSN: 1972-6325
https://www.tpmap.org/

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ANTI-CANCER POTENTIAL OF MARINE MICROBES/ MACRO ALGAE DERIVED NATURAL PRODUCTS AS A POTENTIAL THERAPEUTIC AGENT AGAINST ORAL CANCER

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Abstract
Oral cancer, particularly oral squamous cell carcinoma, is a major global health burden with limited treatment options and high recurrence rates. Marine microbes and macroalgae are rich sources of structurally diverse natural products such as polysaccharides, polyketides, alkaloids, and phenolic compounds that exhibit significant anti-cancer activity. These metabolites act through multiple mechanisms including apoptosis induction, inhibition of angiogenesis, and suppression of oncogenic signaling pathways, oxidative stress regulation, and immune modulation. Emerging evidence highlights their potential as novel therapeutic agents against oral cancer, offering opportunities for safer and more effective treatments.
Keywords: Oral cancer, Marine microbes, Macroalgae, Natural products, Apoptosis

INTRODUCTION

Marine microbes, including bacteria, actinomycetes, and fungi, produce a wide array of bioactive secondary metabolites such as polyketides, peptides, lipopeptides, alkaloids, and exopolysaccharides. These compounds have demonstrated cytotoxic, pro-apoptotic, and anti-metastatic activities against oral cancer cell lines [1]. For example, polyketides from marine *Streptomyces* and *Aspergillus* species can inhibit proliferation and induce apoptosis by targeting mitochondrial pathways [2]. Peptides and lipopeptides exert selective cytotoxicity through membrane disruption and modulation of oncogenic signaling, while microbial alkaloids act as topoisomerase inhibitors leading to DNA damage and cell cycle arrest. Additionally, microbial polysaccharides display antioxidant and immunomodulatory effects that may indirectly reduce tumor progression by enhancing host defense mechanisms [3] (Table 1).

Macroalgae, or seaweeds, are equally rich in bioactive molecules, particularly polysaccharides, polyphenols, and terpenoids, which exhibit significant anti-oral cancer potential. *Fucoidan*, a sulfated polysaccharide from brown algae, has been extensively studied for its ability to induce apoptosis in oral cancer cells through caspase activation and suppression of PI3K/Akt signaling [4]. Phlorotannins, polyphenolic compounds from brown algae, are potent antioxidants with anti-proliferative and anti-angiogenic effects that can suppress tumor growth. *Carrageenan* from red algae demonstrates immunomodulatory activity and has the potential to synergize with standard chemotherapeutics, while *ulvan* from green algae shows anti-inflammatory and ROS-regulating properties that can limit oral tumor progression. These algal-derived compounds have shown inhibitory effects on cancer cell proliferation, migration, invasion, and angiogenesis, positioning them as valuable candidates for therapeutic development [5].

The mechanisms underlying the anti-cancer activity of marine-derived compounds are diverse and multi-targeted. They include induction of apoptosis through intrinsic and extrinsic pathways, inhibition of angiogenesis and metastasis via suppression of VEGF and MMP activity, modulation of signaling pathways such as MAPK, NF-κB, and PI3K/Akt, regulation of oxidative stress by enhancing antioxidant defense, and immunomodulation to strengthen anti-tumor immune responses. This multi-pronged action is particularly advantageous for combating oral cancer, which often develops resistance to single-target chemotherapeutic agents [6].

Despite their potential, several challenges hinder the clinical translation of marine-derived compounds. These include scalability of production, limited bioavailability, and insufficient mechanistic understanding *in vivo*. However, advances in biotechnology, synthetic biology, nanotechnology-based drug delivery, and omics-driven approaches are opening new avenues to overcome these barriers. Combination strategies that integrate marine-derived compounds with existing chemotherapeutics also hold promise for overcoming drug resistance and improving treatment efficacy [7, 8]

In conclusion, marine microbes and macroalgae represent an underexplored reservoir of structurally diverse and biologically potent natural products with significant anti-cancer potential against oral cancer. Their ability to target multiple hallmarks of carcinogenesis, combined with emerging advances in biotechnological innovation, makes them promising leads for the development of safer, more effective therapeutic agents. Future research focusing on mechanistic elucidation, *in vivo* validation, and clinical trials will be essential to translate these marine-derived natural products into next-generation therapeutics for oral cancer management.

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Table 1. presents marine microbe- and macroalgae-derived compounds with anti-cancer potential against oral cancer, highlighting their sources, mechanisms of action, and therapeutic significance

Source	Major Compounds	Mechanisms of Action	Notes/Examples	References
Marine microbes	Polyketides (*Streptomyces*, *Aspergillus*)	Inhibit proliferation; induce apoptosis via mitochondrial pathways	Cytotoxic, pro-apoptotic	[1], [2]
	Peptides & Lipopeptides	Membrane disruption; modulation of oncogenic signaling	Selective cytotoxicity	[1], [3]
	Alkaloids	Topoisomerase inhibition , DNA damage & cell cycle arrest	Anti-proliferative	[1]

	Polysaccharides & Exopolysaccharides	Antioxidant, immunomodulatory; enhances host defense	Indirect tumor suppression	[1]
Macroalgae (seaweeds)	Fucoidan (brown algae)	Caspase activation; suppression of PI3K/Akt signaling	Induces apoptosis in oral cancer cells	[4]
	Phlorotannins (brown algae)	Antioxidant, anti-proliferative, anti-angiogenic	Suppresses tumor growth	[5]
	Carrageenan (red algae)	Immunomodulatory; synergistic with chemotherapeutics	Enhances treatment efficacy	[5]
	Ulvan (green algae)	Anti-inflammatory; ROS regulation	Limits tumor progression	[5]