

Proceedings of Women in Academia, Research and Management for Work-life Initiatives for Sustainable Health & Empowering Safety (WARM-WISHES 2026)

Marine-derived Sugars for Cancer Therapy: A New Wave in Natural Drug Discovery

Mohd Jari Hasan Rizvi

Amity Institute of Biotechnology, Amity University Uttar Pradesh, Lucknow Campus,
Gomti Nagar Extension, Lucknow - 226028, India

Aymma Athar

Amity Institute of Biotechnology, Amity University Uttar Pradesh, Lucknow Campus,
Gomti Nagar Extension, Lucknow - 226028, India

 **Aditi Singh**

Amity Institute of Biotechnology, Amity University Uttar Pradesh, Lucknow Campus,
Gomti Nagar Extension, Lucknow - 226028, India

Corresponding Author: asingh3@lko.amity.edu

Received: 10 Apr 2026 | Received Revised Version: 19 Apr 2026 | Accepted: 24 May 2026 | Published: 11 June 2026

DOI: 10.37547/tajas/warm-23

Abstract

Polysaccharides sourced from marine environments (termed “marine sugars”)—notably fucoidan, chitosan, alginate, carrageenan, laminarin, and ulvan—exhibit natural bioactivity and beneficial material properties that make them attractive candidates for oncology drug delivery systems (DDS). Recent developments (2023-2025) indicate that receptor-targeted strategies, like P-selectin–fucoidan interactions, notably enhance transcytosis and promote deeper tumor infiltration. Simultaneously, stimuli-sensitive hydrogels and designed nanoparticles facilitate controlled, localized drug delivery, whereas innovative combined therapies effectively integrate these polysaccharide carriers with leading chemotherapy, radiotherapy, and immunotherapies. This review thoroughly integrates structural–functional relationships, key design strategies, significant preclinical results, production scaling, and vital safety considerations. Additionally, a strategic translational route for progressing marine-sugar DDS to clinical evaluation is outlined. Key translational challenges—including consistent material characterization, strict management of endotoxins and impurities, and clear structure–activity profiles for sulfation and molecular weight—are highlighted, along with suggested steps to connect laboratory findings to clinical applications.

Keywords: marine polysaccharides, fucoidan, chitosan, alginate, drug administration, cancer, selectin targeting, hydrogel.

© 2026 Mohd Jari Hasan Rizvi, Aymma Athar, Aditi Singh. This work is licensed under a Creative Commons Attribution 4.0 International License (CC BY 4.0). The authors retain copyright and allow others to share, adapt, or redistribute the work with proper attribution.

Cite This Article: Rizvi, M. J. H., Athar, A., & Singh, A. (2026). Marine-derived Sugars for Cancer Therapy: A New Wave in Natural Drug Discovery. *The American Journal of Applied Sciences*, 262–271. <https://doi.org/10.37547/tajas/warm-23>

1. Introduction

Cancer remains one of the primary causes of mortality globally (Yao et al., 2022). Despite significant advancements in immunotherapy, radiation, chemotherapy, and targeted medicines, monumental obstacles still exist in clinical oncology. These include inadequate tumor selectivity, off-target toxicity, systemic drug resistance, and the poor solubility or absorption of many potent anticancer medications (Hsu et al., 2024). Traditional drug delivery methods frequently rely on inorganic nanoparticles or synthetic polymers, which introduce long-term safety concerns regarding immunological compatibility, tissue accumulation, and poor biodegradability. Therefore, there is an urgent demand for safe, biocompatible, and multipurpose carriers that can effectively transport therapeutic drugs while exerting inherent biological effects against malignant cells (Lukova et al., 2023).

Comprising over 70% of the Earth's surface, marine ecosystems offer an abundant reservoir of structurally diverse, naturally occurring substances (Yao et al., 2022). In recent years, marine-derived sugars and polysaccharides have garnered increasing interest due to their unique structural characteristics, renewable supply, and diverse range of bioactivities (Cha et al., 2025). These sugars—primarily fucoidan, chitosan, alginate, carrageenan, ulvan, and laminarin—are extracted from marine algae, crustaceans, and specialized microorganisms. They exhibit exceptional biocompatibility alongside inherent pharmacological effects, including anti-inflammatory, anti-cancer, anti-angiogenic, and immunomodulatory qualities. Functional variety not seen in terrestrial polysaccharides is imparted by their chemical structures, which are frequently characterized by sulfation, unique monosaccharide residues, and complex branching configurations (Carrasqueira et al., 2025).

Utilizing these marine polysaccharides in oncology offers two distinct advantages:

1.1 Direct Antitumor Activity: They can directly combat cancer by triggering apoptosis, inhibiting angiogenesis, and stimulating the host immune system (Cha et al., 2025).

1.2 Advanced Delivery Platforms: They serve as versatile biomaterials for drug delivery systems (DDS) because they easily generate hydrogels, micelles, nanoparticles, and polyelectrolyte complexes. This enables the controlled release and targeted delivery of immunotherapeutic medications, chemotherapeutic agents, and nucleic acids (Hsu et al., 2024).

Recent research suggests that by enhancing tumor selectivity, reducing systemic toxicity, and modifying the tumor microenvironment, carriers based on polysaccharides derived from marine sources can help overcome major cancer treatment difficulties (Jia et al., 2025). Fucoidan nanoparticles, for instance, target tumors via natural selectin-targeting mechanisms, whereas the cationic charge of chitosan facilitates the intracellular delivery of therapeutic genes and siRNA (Tamzi et al., 2024). Concurrently, owing to the precise pH-responsive release profiles of alginate and carrageenan, they are ideally suited for the characteristically acidic microenvironment seen in solid tumors (Tripathi et al., 2025).

2. Marine Polysaccharides: Sources, Structures, and Relevance to Oncology Delivery:

Marine ecosystems are a vast reservoir of structurally diverse polysaccharides that are absent in terrestrial organisms (figure 1). Many of these marine sugars possess unusual sulfation patterns, uronic acid residues, and complex branching, which impart distinct physicochemical and biological properties (Carrasqueira et al., 2025). Their biodegradability, biocompatibility, and functional versatility make them highly attractive candidates for drug delivery and cancer therapy.

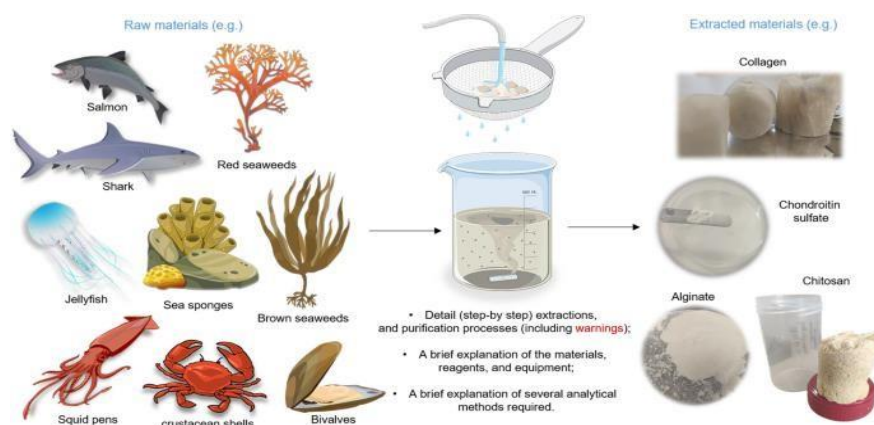


Figure 1: Major marine sources of polysaccharides such as brown (Phaeophyceae), red

(Rhodophyceae), and green (Chlorophyceae) algae, along with crustacean shells and marine microbes.

2.1 Fucoidan

2.1.1 Source & Composition: Obtained mainly from brown algae like *Fucus vesiculosus*, *Laminaria japonica*, and *Undaria pinnatifida*. Fucoidan is a sulfated polysaccharide abundant in alpha(1-3)- and alpha(1-4)-linked L-fucose units, functionalized with sulfate groups and trace monosaccharides like galactose, mannose, and xylose (Jia et al., 2025).

2.1.2 Oncological Relevance: Demonstrates anti-angiogenic, pro-apoptotic, and immunomodulatory properties. Its negative charge facilitates electrostatic interaction with cationic polymers, leading to stable nanoparticle creation (Jia et al., 2025). Nanoparticles coated with fucoidan utilize selectin-mediated targeting of tumors, as P- and L-selectins are found in high amounts on the membranes of cancer cells and tumor blood vessels (Tylawsky et al., 2023). Clinical data show that fucoidan has progressed into nutraceuticals and initial pilot trials, underscoring its translational promise (Liu et al., 2024).

Recent investigation has advanced the concept of fucoidan-mediated delivery by engineering of a dual-targeted nanodelivery vehicle that chemically conjugates a fucoidan outer shell with triphenylphosphine (TPP) to deliver encapsulated pterostilbene and coordinated manganese ions (Mn^{2+}). In this system, the native carbohydrate shell governs initial macro-level homing by binding directly to overexpressed P-selectin receptors on

the tumor endothelium and malignant cell membranes. Following receptor-mediated endocytosis, the appended TPP residues make a second-tier, nano-level navigation that collapses polymeric matrix directly into the mitochondrial network. Once inside, the platform induces severe mitochondrial dysfunction and triggers the cGAS-STING (cyclic GMP-AMP synthase-stimulator of interferon genes) pathway. (Xue et al., 2026).

2.2 Chitosan

2.2.1 Source & Structure: Acquired by deacetylating chitin, a structural polymer found in fungi, marine insects, and crustacean shells (crab, shrimp). Structurally, beta-(1-4)-linked D-glucosamine and N-acetyl-D-glucosamine units combine to form a linear cationic polymer, whose properties are governed by its degree of deacetylation (DD) and molecular weight (Tamzi et al., 2024).

2.2.2 Oncological Relevance: Promotes immune cell activation and triggers apoptosis through reactive oxygen species (ROS) mechanisms (Yao et al., 2022). It is a promising gene delivery vector because of its cationic structure, which allows for robust electrostatic contact with negatively charged DNA, RNA, and proteins. Better drug absorption across mucosal barriers is made possible by its mucoadhesive qualities. It readily creates films, hydrogels, and nanoparticles that encapsulate chemotherapeutics and nucleic acids (e.g., siRNA, doxorubicin, and paclitaxel) for targeted delivery (Hsu et al., 2024).

2.3 Alginate

2.3.1 Source & Composition: Obtained from brown algae (*Macrocystis pyrifera*, *Laminaria spp.*) and certain marine bacteria like *Pseudomonas* and *Azotobacter*. It is a linear anionic copolymer made up of beta-D-mannuronic acid (M) and alpha-L-guluronic acid (G) units organized in homopolymeric M-segments, G-segments, or interspersed MG-segments (Tripathi et al., 2025).

2.3.2 Oncological Relevance: Demonstrates slight antitumor properties by boosting immune responses and decreasing oxidative stress (Yao et al., 2022). In drug delivery, it is recognized for creating hydrogels via divalent ionic crosslinking (Ca^{2+} -facilitated gelation), allowing for controlled and pH-sensitive release of drugs. It is widely employed as a tumor-targeted injectable hydrogel reservoir for the prolonged delivery of chemotherapeutics and immunomodulators. Alginate nanoparticles exhibit pH-sensitive release within the acidic tumor microenvironment, enhancing targeted drug delivery (Tripathi et al., 2025).

2.4 Carrageenan

2.4.1 Origin & structure: Derived from red seaweeds, including *Eucheuma denticulatum* and *Kappaphycus alvarezii*. Depending on the degree and location of sulfation, this family of sulfated galactans is divided into κ -, ι -, and λ -types (Silva et al., 2024).

2.4.2 Oncological Relevance: Shows synergistic cytotoxicity with chemotherapeutic medicines, induces apoptosis, and modifies immunological function. Complexation with cationic medicines or polymers is made possible by the negative charge provided by the sulfate groups. In acidic tumor tissues, carrageenan hydrogels and nanoparticles can release medications selectively by acting as stimuli-responsive carriers. Additionally, it prolongs the half-life of systemic circulation by giving liposomes and micelles enhanced structural stability (Hsu et al., 2024).

2.5 Ulvan

2.5.1 Origin & Structure: Extracted specifically from *Ulva* species of green algae. It is a branched sulfated heteropolysaccharide containing high concentrations of rhamnose, xylose, iduronic acid, and glucuronic acid.

2.5.2 Oncological Relevance: Exhibits immune-stimulating and antioxidant qualities for chemoprevention and cancer treatment. Ulvan's

sulfated polysaccharide backbone can encapsulate drug cargo to form stable polyelectrolyte complexes or nanoparticles. Furthermore, ulvan's structural similarities to mammalian glycosaminoglycans may allow it to interact selectively with cellular receptors throughout the carcinogenesis process (Carrasqueira et al., 2025).

2.6 Laminarin

2.6.1 Source: Found in brown algae, such as *Laminaria digitata*. Compared to other algal polysaccharides, it possesses a low molecular weight and is soluble in water, featuring a β -(1 \rightarrow 3)-glucan backbone and β -(1 \rightarrow 6)-connected side chains.

2.6.2 Oncological Relevance: Stimulates the immune system by binding to dectin-1 and toll-like receptors (TLRs) on dendritic cells, NK cells, and macrophages. Although it is not as extensively studied for drug delivery systems as chitosan or fucoidan, laminarin is under active investigation as a co-carrier for immune checkpoint therapy and as an immunological adjuvant in cancer vaccines (Pramanik et al., 2024).

3. Mechanisms of anticancer action

3.1 Initiation of Apoptosis and Cell Cycle Halt

Fucoidan (a polysaccharide rich in sulfated fucose from brown algae) stimulates caspase-3 and caspase-9, resulting in mitochondrial apoptosis. It reduces the levels of anti-apoptotic proteins Bcl-2 and Bcl-xL, while increasing the levels of pro-apoptotic Bax. Chitosan oligosaccharides trigger ROS-induced apoptosis, affecting mitochondrial membrane potential. Cell cycle blockage at G0/G1 or G2/M stages has been documented for alginate and carrageenan derivatives, preventing tumor growth.

3.2 Inhibition of Angiogenesis and Metastasis

Fucoidan inhibits VEGF/VEGFR2 signaling, reducing endothelial cell growth and angiogenesis. Carrageenan blocks matrix metalloproteinases (MMP-2 and MMP-9), stopping the degradation of the extracellular matrix and tumor invasion. Laminarin boosts immune monitoring, reducing metastasis via macrophage stimulation.

3.3 Tumor Immunity Modification

Chitosan nanoparticles improve antigen presentation by stimulating macrophages and dendritic cells. By acting as a β -glucan immunomodulator, laminarin triggers antitumor immune responses by activating pattern recognition receptors like TLR-2 and dectin-Fucoidan promotes an anti-tumor immune milieu by increasing NK cell cytotoxicity and secreting more IL-2, IFN- γ , and TNF- α (Cha et al., 2025).

3.4 Tumor Microenvironment (TME) Regulation

When employed in hydrogel scaffolds, marine polysaccharides can improve vascular perfusion and lessen hypoxia in solid tumors. They encourage the infiltration of cytotoxic T cells and decrease levels of immunosuppressive cytokines (IL-10, TGF- β). Their antioxidant qualities prevent the growth of tumors caused by ROS.

3.5 Chemosensitization in Synergy

Fucoidan modifies efflux pumps (e.g., P-glycoprotein) to increase the cytotoxicity of doxorubicin, paclitaxel, and cisplatin. Chitosan-siRNA complexes restore tumor suppressor expression. These marine polysaccharides exert distinct anticancer actions by simultaneously modulating tumor immunity, halting the cell cycle, and disrupting angiogenesis (figure 2). To maximize the clinical impact of RNA interference (RNAi) therapies, synthesis of Chitosan-Hyaluronic Acid Dialdehyde (CS-HAD) nanoparticles is tried. By subjecting hyaluronic acid to controlled periodate oxidation, they successfully conjugated its dialdehyde groups covalently with the primary amines of chitosan, creating a highly stable, non-toxic delivery matrix. When deployed in aggressive bladder cancer models, these hybrid nanoparticles use the CD44-receptor-targeting capacity of the hyaluronic acid shell to achieve highly efficient cellular uptake and subsequent intracellular delivery of Bcl-2 siRNA, restoring apoptotic sensitivity to resistant cells (Liang et al., 2026).

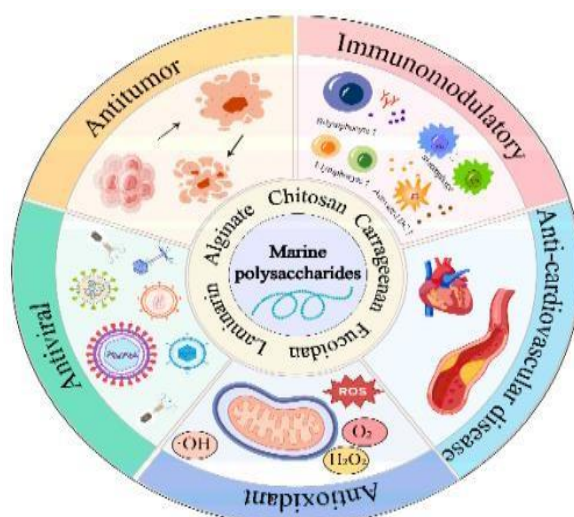


Figure 2: Schematic representation of marine polysaccharide-based drug delivery systems in cancer therapy

4. Delivery Platforms and Representative Recent Studies (2023–2025)

4.1 Nanocups and Nanoparticles Decorated with Fucoidan: A landmark study by Tylawsky et al. (2023) employed fucoidan-coated nanoparticles to target P-selectin, initiating caveolin-1-dependent transcytosis into brain tumors. This targeted mechanism notably enhanced the delivery of vismodegib and therapeutic results in medulloblastoma models, establishing a structural standard for glycan approaches aimed at selectins (Tylawsky et al., 2023). Follow-up research in 2024

explored fucoidan nanoparticles for triple-negative breast cancer (TNBC) and integrated fucoidan carriers with chemotherapy agents or radiosensitizers to enhance tumor cell destruction (Jia et al., 2025).

4.2 Chitosan Nanoparticles for Nucleic Acid and Chemotherapy Delivery: Advanced formulations encapsulate chitosan nanoparticles for targeted cancer treatment, encompassing stimuli-responsive, ligand-targeted, and PEG-shielded systems designed for siRNA and mRNA transport. Structural benefits include easy ionic interaction with nucleic acids and

adjustable surface chemistry for targeted action (Hsu et al., 2024).

4.3 Localized Reservoirs Using Alginate Hydrogels:

It has been shown that alginate hydrogels can serve as local reservoirs for the administration of immunomodulators, chemotherapeutics, and photosensitizers. This allows for responsive release that is triggered by light, redox, or pH, which is highly advantageous for intratumoral injection or implantation after surgical tumor resection (Tripathi et al., 2025).

4.4 Hybrid and Composite Systems: Targeting, photothermal conversion, immunostimulation, and controlled release are all made possible by hybrid carriers, such as fucoidan-gold and fucoidan-chitosan polyelectrolyte complexes. In preclinical research, these composites have demonstrated improved pharmacokinetics and cooperative anticancer activities (Hsu et al., 2024).

4.5 Overcoming Anatomical Barriers Via Stimuli-Primed Transcytosis: Overcoming tight physiological barriers—most notably the blood-brain barrier (BBB)—remains a historical bottleneck for macromolecular drug delivery. However, 2026 investigations have demonstrated that combining marine sugar architectures with low-dose non-destructive radiotherapy can effectively unlock these restricted anatomical spaces. This approach was successfully validated using clinically compatible fucoidan nanoparticles (Fi-NPs) designed to treat H3K27-altered diffuse midline glioma (DMG), a highly lethal pediatric brain malignancy (Li et al., 2025)

5. Safety, Immunogenicity, and Regulatory Considerations

When developing marine-derived sugars as cancer therapies or drug delivery systems, their safety profile and immune responses are just as important as their anticancer efficacy. Since these biomolecules are natural and sourced from marine environments, they may have fewer adverse side effects than manufactured synthetic polymers; however, extensive toxicological validation remains mandatory (Jeong et al., 2024).

5.1 Critical Risk Factors vs. Intrinsic Safety Profile

In animal models and preliminary clinical pilot studies,

many marine polysaccharides have demonstrated high tolerance and have a long history of safe use in foods, nutraceuticals, and topical wound dressings. Significant risk factors that must be managed to satisfy regulatory requirements include:

Batch and Source Variability: Influenced heavily by species, harvest season, and geographic extraction site (Lukova et al., 2023).

5.1.2 Impurities: Endotoxins, residual proteins, polyphenols, organic solvents, and heavy metals.

5.1.3 Chemical Modifications: Degree and position of sulfation, and depolymerization techniques.

5.1.4 Administration Route: Topical versus intravenous (IV) or intratumoral (IT) routes demand drastically different safety thresholds.

5.2 Specific Safety Concerns

5.2.1 Endotoxins and Microbiological Contaminants: Gram-negative bacteria generate endotoxins (lipopolysaccharides; LPS), potent pyrogens that can disrupt immunomodulatory assessments or trigger systemic inflammation when given parenterally. Regulatory agencies mandate validated control and testing of endotoxins for parenteral and implantable products. Developers must follow regulatory guidelines and pharmacopeial sections (like USP <85>), modifying protocols to account for polysaccharide interference during Limulus Amebocyte Lysate (LAL) testing. For complex polysaccharide matrices, Monocyte Activation Tests (MAT) or recombinant factor C (rFC) assays serve as vital complementary tests (Jeong et al., 2024).

5.2.2 Heavy Metals, Phenolics, and Residual Proteins: Toxic metal ions (As, Cd, Pb) and proteinaceous contaminants are often present in raw extractions from natural sources (Jeong et al., 2024). These must be rigorously quantified since they directly impact long-term immunogenicity and systemic toxicity. Inductively Coupled Plasma Mass Spectrometry (ICP-MS) should be utilized for metals, and BCA or Kjeldahl assays for protein quantification.

5.2.3 Hypersensitivity and Complement Activation:

Certain sulfated polysaccharides can bind pre-existing anti-glycan antibodies in human serum or trigger complement pathways via the innate immune system. This can induce infusion reactions or alter biodistribution through rapid clearance by Kupffer cells. Translational risk assessment requires checking for anti-glycan antibody binding and evaluating complement activation (CH50, C3a, C5a) using Complement Activation-Related Pseudoallergy (CARPA) models.

5.2.4 Hemocompatibility and Anticoagulant Effects:

Carrageenans and highly sulfated fucoidan fractions can exert anticoagulant properties and affect clinical coagulation assays, such as activated partial thromboplastin time (aPTT) and prothrombin time (PT) (Silva et al., 2024). Hemocompatibility evaluations—including thromboelastography and platelet activation studies—are vital for any IV or intratumoral applications requiring vascular exposure.

5.2.5 Gastrointestinal Safety and Localized Inflammation:

An important toxicological distinction must be made between food-grade carrageenan and poligeenan (degraded carrageenan produced by extreme heat or acid). Poligeenan is a known inflammatory agent; regulatory investigations verify that raw materials must be of pharmaceutical quality and free of degraded fractions to prevent localized gastrointestinal inflammation in oral or colorectal applications (Silva et al., 2024).

5.2.6 Immunostimulation vs. Unintended Inflammation:

Various marine sugars possess potent immunostimulatory properties, making them beneficial as adjuvants but hazardous if unregulated (potentially inducing cytokine storms or persistent systemic inflammation) (Cha et al., 2025). It is critical to precisely adjust dosages, monitor cytokine panels (IL-6, TNF- α , IFN- γ), and incorporate comprehensive immunotoxicology assessments in Good Laboratory Practice (GLP) toxicology packages (Jeong et al., 2024).

5.3 Regulatory Guidelines

FDA-approved topical medications and wound dressings contain alginate and chitosan, establishing precedents for manufacturing controls and biocompatibility for non-parenteral applications (FDA Access Information, 2024). While these precedents are helpful, drug or biologic regulatory routes will be mandatory for cancer DDS with systemic delivery.

Similarly, although fucoidan and its products are available in the nutraceutical market with Generally Recognized as Safe (GRAS) status, parenteral oncology indications cannot be supported by nutraceutical status alone. Pilot clinical data show excellent oral tolerability, but they are not a replacement for Investigational New Drug (IND)-enabling packages and GLP toxicology studies (Liu et al., 2024).

6. Characterization, Manufacturing, and Quality Control (QC) Framework

Clinical translation of marine-derived polysaccharides depends heavily on developing robust production processes and strict Quality Control (QC) procedures to manage natural heterogeneity (Lukova et al., 2023).

6.1 Extraction, Purification, and Modification Workflow

6.1.1 Sourcing and Tracking: Species, geographic origin, and harvest season must be documented, as they directly influence polymer structure and bioactivity. Aquaculture and microbial fermentation should be utilized where possible to enhance batch sustainability and regulatory tracking.

6.1.2 Extraction and Purification: Traditional methods rely on heated water, acid/base extractions, and ethanol sedimentation. Advanced workflows utilize microwave- or ultrasound-assisted extraction and pressurized techniques. Purification must actively remove endotoxins, heavy metals, and residual proteins using size-exclusion, ion-exchange chromatography, and ultrafiltration (Lukova et al., 2023).

6.1.3 Chemical Modification & Nanoscale Structuring: Polysaccharides are modified via sulfation, carboxymethylation, phosphorylation, or hydrophobic drug grafting to improve encapsulation stability (Hsu et al., 2024). Manufacturing platforms include ionic

gelation, polyelectrolyte complexation, spray-drying, and hydrogel crosslinking. The overriding challenge is ensuring consistency in molecular weight (M_w), degree of substitution, and polydispersity index (PDI) (Lukova et al., 2023).

A comprehensive Chemistry, Manufacturing, and Controls (CMC) package for clinical submission requires a suite of orthogonal analytical assays to establish batch consistency, as detailed in Table 1.

Table 1: Comprehensive Analytical Characterization and Quality Control Toolkit for Marine Polysaccharide-Based Drug Delivery Systems.

Characterization Category	Analytical Targets & Methods
Structural Metrics	<ul style="list-style-type: none"> • Monosaccharide composition (HPAEC-PAD) • Linkage analysis (GC-MS) • Functional groups (FTIR, $^{13}\text{C}/^1\text{H}$ NMR) • Molecular weight distribution (SEC-MALS)
Physicochemical Properties	<ul style="list-style-type: none"> • Nanoparticle size and polydispersity (DLS) • Surface charge (Zeta potential) • Morphology (TEM/SEM) • Stability and drug release profiles
Biological & Safety QC	<ul style="list-style-type: none"> • Cytotoxicity assays • Apoptosis/angiogenesis markers • Hemocompatibility panels • Endotoxin thresholds (USP <85>, <5 EU/kg/hr>) • Sterility (USP <71>) • Residual solvents (USP <467>)

7. Conclusion

Marine-derived polysaccharides represent one of the most promising categories of natural biomaterials for oncology applications. Their unique structural diversity—including varied sulfation patterns, precise molecular weights, and complex branching configurations, provides a rich chemical landscape for designing drug carriers with inherent biological activity. Unlike inert synthetic polymers, these natural sugars function as dual-purpose platforms, simultaneously driving therapeutic action (inducing apoptosis, blocking angiogenesis, and modulating the immune microenvironment) while systematically delivering delicate therapeutic cargo.

Recent innovations in advanced extraction technologies, chemical modifications, and nanoscale engineering have significantly enhanced the stability, functionality, and reproducibility of these biomaterials. Preclinical models have highlighted their immense potential to work synergistically with frontline chemotherapeutics, nucleic acids, and immunotherapies.

Nevertheless, critical translational hurdles remain. Future progress requires strict standardization of quality control parameters, the mitigation of batch-to-batch source variability, and the optimization of extraction yields under strict GMP guidelines. Comprehensive safety and immunogenicity screenings—specifically regarding complement activation and endotoxin contamination—must be executed early in the

development cycle for any systemic applications. By combining strategic design principles with a clearly defined translational roadmap, interdisciplinary collaboration among marine biologists, chemists, bioengineers, oncologists, and regulatory bodies will effectively transition marine-derived sugars from the laboratory bench to the patient's bedside, establishing a safer and more effective standard for natural drug delivery in oncology.

Author's contribution: MJHR: Data curation, Literature study, Analysis, Writing original draft, Illustrations. AA: Analysis, Writing original draft. AS: Conceptualization, Supervision, Reviewing & editing the original draft. All authors approved the final version.

Author Declaration Statements

Declaration: The authors hereby declare that the manuscript submitted for consideration is an original work and has not been published or submitted elsewhere for publication. The authors take full responsibility for the integrity, accuracy, and ethical compliance of the work presented in the manuscript.

Conflict of Interest: All authors confirm that:

- Any potential conflicts of interest, whether financial or non-financial, have been fully disclosed. – **Yes / Not Applicable**✓
- All sources of funding and financial support received for the conduct of the study have been appropriately acknowledged. – **Yes / Not Applicable**✓
- Necessary ethical approvals have been obtained from the relevant institutional or regulatory bodies for studies involving human participants, animals, or sensitive data, wherever applicable. – **Yes / Not Applicable**✓

AI Usage Statement: Authors declare that AI tools, if used, were solely employed to improve the clarity, grammar, and language of the manuscript (as indicated in the reviewer's comments). No data, results, or scientific content were generated or altered using AI.

9.0 References

1. Carrasqueira, J., Bernardino, S., Bernardino, R., & Afonso, C. (2025). Marine-derived polysaccharides and their potential health benefits in nutraceutical applications. *Marine drugs*, 23(2), 60.
2. Cha, M., Yan, S., Zhang, Y., & Wang, P. (2025). Progress in the application of marine polysaccharide drug delivery systems in tumor immunotherapy: Multiple mechanisms and material forms. *Marine Drugs*, 23(10), 384.
3. FDA Access Information (2024). Premarket Notification 510(k) and Premarket Approval (PMA) clearances for polysaccharide-based topical devices. U.S. Food and Drug Administration.
4. Hsu, C. Y., Allela, O. Q. B., Hussein, A. M., Mustafa, M. A., Kaur, M., Alaraj, M., ... & Farhood, B. (2024). Recent advances in polysaccharide-based drug delivery systems for cancer therapy: a comprehensive review. *Artificial cells, nanomedicine, and biotechnology*, 52(1), 564-586.
5. Jeong, S., Lee, S., Lee, G., Hyun, J., & Ryu, B. (2024). Systematic characteristics of fucoidan: intriguing features for new pharmacological interventions. *International Journal of Molecular Sciences*, 25(21), 11771.
6. Jia, H., Li, Y., Zheng, Y., Wang, H., Zhao, F., Yang, X., ... & Man, C. (2025). Recent advances in fucoidan-based improved delivery systems: Structure, carrier types and biomedical applications. *Carbohydrate Polymers*, 352, 123183.
7. Li, B. K., Raziuddin, R., Tylawsky, D., Singhania, M., Becher, O., Heller, D. A., & Raju, G. P. (2025). SURG-01. Fucoidan nanoparticle encapsulation of targeted therapies facilitates BBB penetration and tumor-specific localization in DMG. *Neuro-Oncology Pediatrics*, 1(Supplement_1), wuaf001-252.
8. Liang, X., Sun, Y., Guo, Y., Liu, B., Gu, Y., & Gao, W. (2026). Dual-Functional Chitosan-Hyaluronic Acid Dialdehyde Nanoparticles for CD44-Targeted Bcl-2 siRNA Delivery and Photothermal Therapy in Bladder Cancer. *Journal of Biotechnology*.
9. Liu, T. C., Shih, C. J., & Chiou, Y. L. (2024). Oral administration of oligo fucoidan improves the survival rate, quality of life, and immunity in patients with lung cancer. *Food & nutrition research*, 68, 10-29219.
10. Lukova, P., Katsarov, P., & Pilicheva, B. (2023). *Application of Starch, Cellulose, and Their Derivatives in the Development of Microparticle Drug-Delivery Systems*. *Polymers* 15: 3615.

11. Pramanik, S., Singh, A., Abualsoud, B. M., Deepak, A., Nainwal, P., Sargsyan, A. S., & Bellucci, S. (2024). From algae to advancements: laminarin in biomedicine. *RSC advances*, *14*(5), 3209-3231.
12. Silva, O. L. T., et al. (2024). Exploring the pharmacological potential of carrageenan. *Marine Drugs*, *22*(6), 271–289.
13. Tamzi, N. N., Rahman, M. M., & Das, S. (2024). Recent advances in marine-derived bioactives towards cancer therapy. *International Journal of Translational Medicine*, *4*(4), 740-781.
14. Tripathi, A., Pandey, V. K., Rustagi, S., Lai, W. F., & Samrot, A. V. (2025). Alginate-based NPs for targeted ovarian cancer therapy: Navigating current progress and biomedical applications. *International Journal of Biological Macromolecules*, *319*, 145365.
15. Tylawsky, D. E., Kiguchi, H., Vaynshteyn, J., Gerwin, J., Shah, J., Islam, T., ... & Heller, D. A. (2023). P-selectin-targeted nanocarriers induce active crossing of the blood–brain barrier via caveolin-1-dependent transcytosis. *Nature materials*, *22*(3), 391-399.
16. Xue, P., Yu, Z., Shang, Y., Liu, S., Zhang, M., Zhu, F., Xiao, J., Long, L., & Guo, C. (2026). Dual-targeted fucoidan-TPP nanoparticles delivery system potently inhibit breast cancer via mitochondrial dysfunction and cGAS-STING activation. *Colloids and surfaces. B, Biointerfaces*, *258*, 115279. <https://doi.org/10.1016/j.colsurfb.2025.115279>.
17. Yao, W., Qiu, H. M., Cheong, K. L., & Zhong, S. (2022). Advances in anti-cancer effects and underlying mechanisms of marine algae polysaccharides. *International Journal of Biological Macromolecules*, *221*, 472-485.