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Next-generation Nanocarriers from the Ocean: A Perspective on Fucoidan in Precision Medicine

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Abstract: Fucoidans are natural polysaccharides that are fucose-rich and sulfate-dense and are found in brown seaweed of marine origin. Fucoidan is rapidly becoming a key material for creating state-of-the-art nanocarriers. Whereas traditional synthetic nanocarriers are mostly used for their functionality rather than their biological properties, fucoidan-based nanocarriers are biodegradable and biocompatible and can even exhibit intrinsic bioactivities. Here, we demonstrate that the highly sulfated nature and adjustable molecular weight of fucoidan make it a strong candidate for selectively binding to targets (e.g., selectins, scavenger receptors, and growth factors) and for regulating immune responses (e.g., NF-κB and MAPK signalling pathways). Furthermore, we cover the various methods for fabricating self-assembled fucoidan nanoparticles (NPs), hybrid nanosystems, and ligand-functionalized surfaces. The fucoidan nanocarrier has been used to treat cancer, prevent cardiovascular thrombosis, and regulate inflammation through different mechanisms (targeting tumor vasculature, delivering anticoagulants, and reprogramming immune cells). Finally, we address the challenges of formulation scale-up, pharmacokinetics, toxicity, and regulatory issues, as well as the need for sustainable fucoidan sourcing from marine sources. With continued interdisciplinary research and recent advances in marine biotechnology, fucoidan has bright prospects for the future of nanomedicine.

KEYWORDS: Fucoidan, nanocarrier, marine polysaccharide, precision medicine, therapeutic, diseases

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1. INTRODUCTION

Conventional chemotherapies and drug carriers often lack specificity and cause off-target toxicity. For instance, standard cancer treatments "often lead to severe side effects, such as immunosuppression, organ toxicity, and multidrug resistance". At the same time, a number of polymer-based or lipid nanocarriers can activate the immune system or be specifically targeted, thereby exerting limited clinical effects. Marine-derived polysaccharides, e.g., fucoidan, fill these gaps by combining safety with functionality. Fucoidan is not only a passive carrier but also has therapeutic properties, including scavenging reactive oxygen species and modulating cytokine levels, thereby enhancing its therapeutic effect (Mensah et al., 2023). Furthermore, the natural clearance and low immunogenicity of fucoidan and its derivatives slightly decrease the risk of side effects (Newehy et al., 2025). High-purity fucoidan extracts with up to FDA GRAS status have recently been produced through advances in extraction and manufacturing (Mary Saral & Mathew, 2020). A recent study also uses computer-aided design to tailor sulfated polysaccharide carriers (Lin et al., 2020; Mary Saral & Mathew, 2020).

In this commentary, we emphasize the potential of fucoidan, a marine biopolymer, to be developed into precision nanomedicines that overcome the drawbacks of synthetic carriers and deliver targeted, multifunctional therapies. Combining marine biotechnology with nanomedicine enables scientists to broaden the range of targeted treatments by sustainably using ocean resources (Lin et al., 2020; Mary Saral & Mathew, 2020).

2. FUCOIDAN: SOURCE, STRUCTURE, AND BIOACTIVITY

Fucoidans are high-molecular-weight sulfated polysaccharides derived mostly from marine brown macroalgae (Phaeophyceae), such as the genera Fucus, Laminaria, Sargassum, and Undaria (Mensah et al., 2023). They contain L-fucose backbones (usually 1,3 and 1,4-linked), which are decorated with sulfate ester groups and also include small amounts of other sugars (galactose, xylose, mannose) and uronic acids (Figure 1). The species, harvesting season, and extraction procedure result in a large variation in molecular weight and sulfate content. These characteristics are decisive for the biological activity: fucoidans with a high degree of sulfation and a moderate molecular weight are generally the most effective.

Fucoidans composition differentiates it from other marine polysaccharides, for example, alginate (from brown algae) is an anionic copolymer of D-mannuronate and L-guluronate (which form Ca, crosslinked hydrogels) (Choukaife et al., 2020), whereas carrageenan (from red algae) is a linear sulfated galactan, mainly used for gelation (Oliyaei et al., 2022).

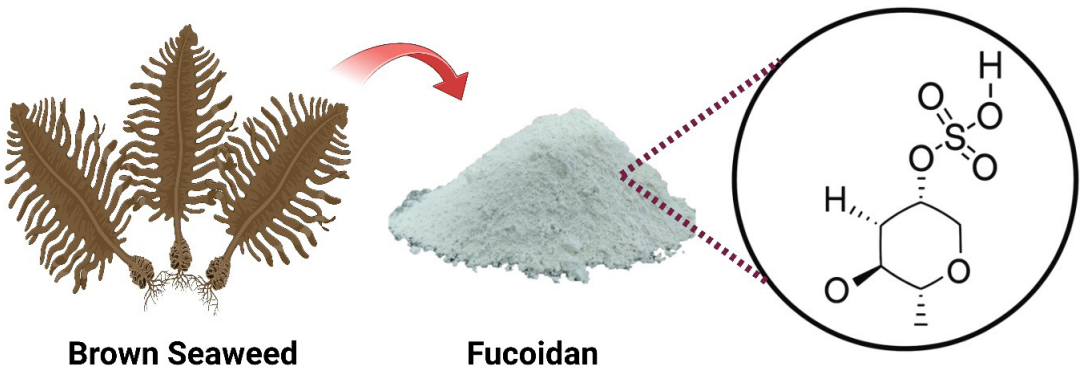


Figure 1. Fucoidan, a sulfated polysaccharide extracted mainly from brown macroalgae (seaweed)

It is important to note that fucoidan exhibits a wide range of pharmacological effects (Pereira & Valado, 2023). On the one hand, it is antitumorigenic and antioxidant; combinations that include fucoidan have been shown to induce apoptosis in cancer cells and to reduce angiogenesis (via VEGF/HIF-1 pathways) in *in vivo/in vitro* studies (Mensah et al., 2023; Turrini et al., 2023a). On the other hand, it can also reduce inflammation and modulate the immune system by interacting with immune mediators (e.g., toll-like receptors, scavenger receptors, and complement receptors) and lessening cytokine-driven damage (Lin et al., 2020). Because of its dense sulfation, it can be given anticoagulant and antithrombotic properties (heparin-like effects) (Turrini et al., 2023a). Taken together, these intrinsic properties (anticoagulant, antimetastatic, immunoregulatory) of fucoidan make it an appealing drug delivery scaffold: theoretically, a single nanocarrier can house drugs while reducing inflammation and thereby facilitating the clearance of reactive oxygen species (Moosavi-Nasab et al., 2020).

Table 1 (below) presents a comparative chart of marine polysaccharides and representative synthetic nanocarriers, with fucoidan as one of the main players. It demonstrates that fucoidan sulfate, with its complex structure, is the most likely candidate for selective cell/tissue targeting (e.g., P/L selectins), whereas alginate and carrageenan mostly serve as gelling/stabilizing agents. They are all natural polymers and biodegradable, but only fucoidan and carrageenan have significant bioactivity (Oliyaei et al., 2022). Nevertheless, synthetic carriers (e.g., PLGA), although biocompatible and FDA-approved, require ligand modification for targeting (Alsaab et al., 2022).

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Table 1. Comparative features of fucoidan versus other marine polysaccharides and representative synthetic carriers (PLGA, liposomes)

Material	Structure	Bioactivity	Biodegradability	Therapeutic Potential	References
Fucoidan	Sulfated fucose-rich heteropolymer (brown algae)	Anti-cancer, anticoagulant, anti-inflammatory, immunomodulatory	Enzymatically biodegradable; partially absorbed; excreted renally	Targeted drug delivery (e.g., P-selectin targeting); combined therapy (anti-tumor + anti-thrombotic)	(Lin et al., 2020; Oliyaei et al., 2022; Turrini et al., 2023a)
Alginate	Linear copolymer of β-D-mannuronic and α-L-guluronic acids (Ca^{2+}-cross-linkable)	Generally inert; supports cell adhesion and wound healing (no inherent drug bioactivity)	Biodegradable by alginate lyases; stable gel formation	Hydrogels for drug release (e.g., beads, scaffolds); wound dressings; encapsulation matrix	(Choukaife et al., 2020)
Carrageenan	Sulfated galactan (κ, ι, λ types from red algae)	Thickening agent; antiviral (e.g., topical), antioxidant, anti-tumor effects	Partially degraded by gut microbiota (prebiotic effects)	Food/biomedical films; vaccine adjuvants; potential in tumor inhibition (as shown in vitro)	(Oliyaei et al., 2022)
Synthetic (e.g., PLGA)	Synthetic polyester (polylactic-co-glycolic acid)	No intrinsic bioactivity (inert); biocompatible (FDA-approved)	Biodegradable by hydrolysis to lactic/glycolic acids	Widely used for controlled drug delivery (microparticles, micelles); requires surface ligands for targeting (e.g., antibodies, folate)	(Alsaab et al., 2022)

3. NANO FORMULATION STRATEGIES

3.1. Self-Assembled Fucoidan Nanoparticles

Fucoidan can form nanostructures via electrostatic and hydrophobic interactions. For instance, ionic gelation with polycations (e.g., chitosan) produces fucoidan-chitosan nanocomplexes that can trap drugs and release them upon pH change (Figure 2) (Venkatesan et. al., 2016). It has been demonstrated that such polyelectrolyte particles protect the payloads and also facilitate their sustained release.

On the other hand, the amphiphilicity of fucoidan enables fucoidan polysaccharides to self-assemble into nanoscale cores or membranes that encapsulate hydrophobic drugs. In one case, researchers prepared a fucoidan-stabilized oil-in-water nanoemulsion by mixing a Nigella sativa oil phase with fucoidan as an emulsifier, which enhanced the in vitro delivery of lipophilic antioxidants (Oliyaei et al., 2023). These self-assembled carriers are simple and environmentally friendly (no toxic crosslinkers), and their size or surface charge can be adjusted by varying fucoidan molecular weight and concentration.

Ionic gelation is quite straightforward to scale; however, maintaining batch-to-batch consistency

can be difficult due to natural variations in fucoidan (MW and sulfate content can fluctuate). Techniques with a high degree of automation (e.g., microfluidics, spray drying) are considered alternatives to improve reproducibility. For instance, nanoparticles must have a consistent size and drug loading; factors such as the fucoidan:chitosan ratio, pH, and stirring speed have a major impact on the results (Choukaife et al., 2020). This, in turn, calls for thorough process development (e.g., controlled emulsification parameters) to facilitate GMP production (Choukaife et al., 2020).

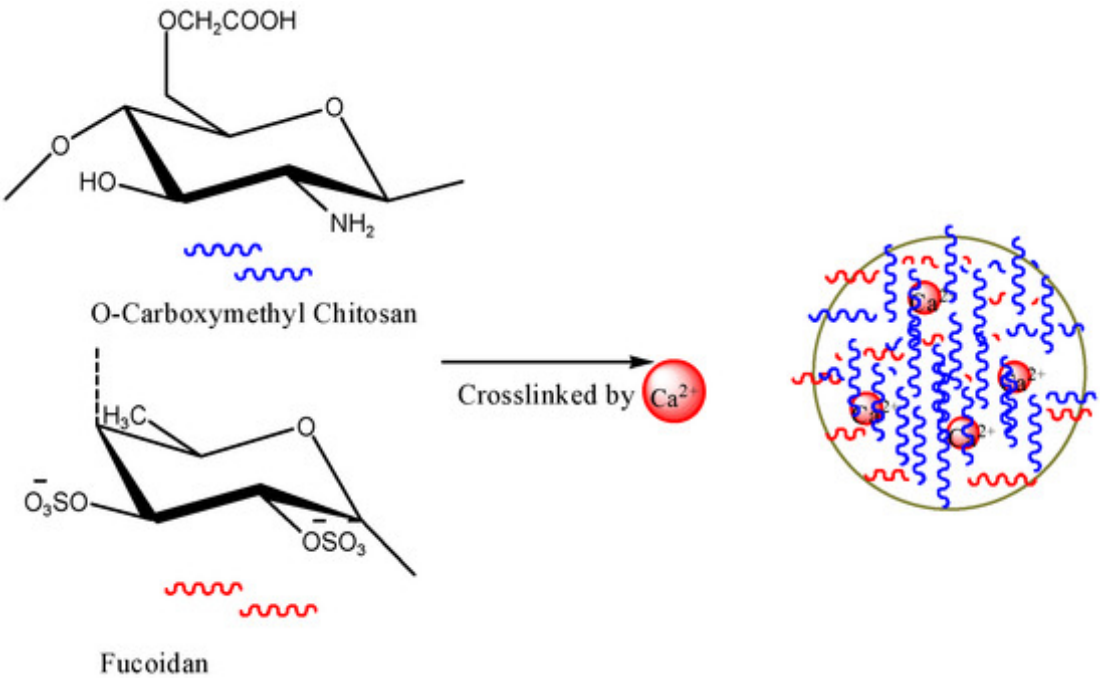


Figure 2. Diagram depicting the formation of fucoidan-based nanoparticles by ionic gelation. Calcium ions (Ca) in this method facilitate interactions between the negatively charged sulfate groups of fucoidan and the positively charged amino groups of O-carboxymethyl chitosan, thereby forming stable nanoparticles. This technique offers mild, biocompatible conditions for drug encapsulation (Boly et al., 2023)

3.2. Hybrid Systems

Hybrid nanocarriers utilize fucoidan in combination with inorganic or polymeric cores. For instance, fucoidan-coated gold nanoparticles (AuNPs) utilize fucoidan as both a reducing agent and a surface ligand. (Newehy et al., 2025). These F-AuNPs possess potent anticancer activity. Such hybrids merge inorganic core functionalities (e.g., imaging contrast, photothermal heating) with fucoidan's bioactivity. Likewise, fucoidan can sheath iron oxide or silica cores to create theranostic agents. For example, magnetic nanoparticles with a fucoidan shell can target the tumor endothelium while enabling magnetic resonance imaging (MRI). On the polymeric side, fucoidan can sheath synthetic NPs. For example, PEG–PLGA NPs coated with fucoidan have been used to deliver chemotherapeutics with enhanced tumor targeting. (In Table 2, Younus 2024 reports fucoidan PLGA NPs delivering epirubicin to colorectal tumors). The fucoidan coating binds to P-selectin and CLRs, while PLGA provides a controllable, biodegradable matrix (Alsaab et al., 2022). Liposomes can also be functionalized with fucoidan; several FDA-approved liposomal drugs demonstrate the feasibility of this approach (Filipczak et al., 2020; Maja et al., 2020).

Hybrid NPs may face additional manufacturing hurdles. Inorganic NP synthesis (e.g., colloidal AuNPs) is well established, but scaling laboratory methods to an industrial scale requires strict control of particle size and surface chemistry. Polymeric hybrids (fucoidan–PLGA) require solvent-based processes (e.g., nanoprecipitation) that must be optimized for scalability. Each added component

(fucoidan, polymer, targeting ligands) increases regulatory complexity. Batch variation in natural fucoidan remains an issue, so standardized, GMP-grade extracts are needed for clinical translation.

3.3. Surface Functionalization

Fucoidans' numerous functional groups (sulfates, hydroxyls) grant the biopolymer with further opportunities for precise targeting. Antibody, peptide, or small-molecule ligand, conjugated carriers can be prepared by post-functionalizing the fucoidan shell. For example, research inspired by the fucoidan-selectin interaction has decorated vasculature, targeting peptides on the surface of fucoidan nanoparticles to guide carriers to tumor vasculature. Furthermore, fucoidan may be linked to antibody fragments to produce dual-ligand systems, in which the antibody provides immunospecificity, and fucoidan contributes electrostatic stabilization and its own bioactivity. To sum up, these three formulation approaches, self-assembly, core-shell hybrids, and surface engineering, provide a repertoire that is collectively capable of designing fucoidan nanocarriers tailored for specific therapeutic applications.

One of the newest publications describes the utilisation of fucoidan-coated selenium nanoparticles carrying co-loaded curcumin (Alduais et al., 2025). for colorectal cancer treatment, resulting in increased cytotoxicity. On the other hand, intricate functionalization can require multiple steps in chemical synthesis, thereby lowering yields and raising costs. At the same time, in theory, ligand attachment, especially when bulky, may alter nanoparticle stability or trigger an immune clearance response. Functionalities thus need to be carefully balanced with manufacturability during the design process.

4. DISEASE-FOCUSED APPLICATIONS

4.1. Oncology

Fucoidan-based nanodelivery vehicles combine physical targeting of the tumor with therapeutic synergism in cancer therapy. Different mechanisms, such as downregulation of VEGF/HIF-1 and inhibition of CXCR4/SDF-1 chemotaxis, have been identified through which fucoidan can trigger apoptosis and prevent metastasis ((Lin et al., 2020; Turrini et al., 2023a). Chemotherapy drugs encapsulated in fucoidan showed enhanced anti-tumor effects in animal tumor models. For example, F-AuNPs showed strong anticancer effects in hepatoma models ((Newehy et al., 2025). Fucoidan naturally targets tumors by binding to P-selectin, which is overexpressed on cancer vasculature and on activated platelets in the tumor microenvironment ((Zheng et al., 2025). This "passive plus active" targeting strategy ensures that fucoidan-coated carriers preferentially accumulate in tumor tissue and intracellular tumor thrombi, thereby facilitating drug access to the tumor ((Lin et al., 2020). Currently, fucoidan is being tested as an adjuvant in clinical trials because it could improve the effectiveness of chemotherapeutic agents and immunotherapies by modulating immune checkpoints and reducing treatment toxicity. To sum up, fucoidan nanocarriers are in early development for tumor-selective drug delivery and combination chemoimmunotherapy (Lin et al., 2020; Turrini et al., 2023a). Tumor heterogeneity may complicate targeting efforts. Some tumors express low levels of P-selectin, and the stroma may impede NPs' penetration. Additionally, non-specific uptake by the liver and spleen (through scavenger receptors) may redirect nanoparticles. In vivo data indicate that tumors are likely to grow, but more research is needed in large-animal models before this can be used in humans.

4.2. Cardiovascular and Thrombotic Disorders

Fucoidan exhibits strong anticoagulant and antithrombotic effects due to its high sulfate density, which is comparable to that of heparin. This particular property of fucoidan can be exploited in designing nanocarriers for the treatment of cardiovascular diseases (Turrini et al., 2023a). Fucoidan-based nanoparticles, by interacting with P- and L-selectins on activated platelets and endothelial cells, have great potential for targeted drug delivery to the thrombotic site (Lin et al., 2020). In fact, the binding of fucoidan to selectins on activated platelets can be used to direct the carrier specifically to sites of thrombosis. In animal experiments, fucoidan-based systems with nanoparticles have shown greater effectiveness in preventing clot formation than fucoidan alone (Pereira et al., 2024). These targeted delivery systems can also release heparin locally over time, while limiting the risk of systemic bleeding. The use of fucoidan nanomedicines to treat atherosclerosis

and deep vein thrombosis is very attractive because they target blood vessels and prevent blood clot formation. Studies on the use of fucoidan gold nanoparticles in atherosclerosis models have shown a reduction in plaque formation. However, the translation to the clinic is not straightforward: the in vivo coagulation system is highly complex, and animal models of coagulation differ from human physiology. The dosage has to be just right between preventing blood clotting and causing bleeding. Also, NPs that remain in the body for an extended time can unintentionally cause bleeding. Hence, for these uses, it is very important to keep manufacturing sterile and control endotoxins.

4.3. Inflammation and Autoimmune Diseases

Fucoidan is a good choice for treating inflammatory conditions because it can reduce inflammation and change the immune system. Fucoidan-coated or fucoidan-based nanoparticles can selectively engage with macrophages and dendritic cells, potentially reprogramming an inflammatory environment (Lin et al., 2020). Studies on edible fucoidan films suggest that oral fucoidan nanocarriers could deliver anti-inflammatory agents to the gut and interact with immune cells in the Gut-Associated Lymphoid Tissue (GALT). In models of autoimmune arthritis, fucoidan derivatives have mitigated cytokine storms (Boly et al., 2023). Consequently, fucoidan-based delivery systems could be customized for conditions like inflammatory bowel disease or rheumatoid arthritis, integrating targeted drug delivery with fucoidan's macrophage-modulating properties (Lin et al., 2020). A recent study showed that fucoidan–heparin co-loaded nanoparticles targeted the inflamed endothelium in colitis and were more effective than free drugs at reducing IL-6 and TNF-α levels. But autoimmune diseases last a long time, so you have to take them again. We don't yet know how safe it is to be around fucoidan NP for long periods. Batch reproducibility of intricate formulations (e.g., multi-drug loaded) is a significant practical consideration. To give a better picture of recent progress, a detailed table (Table 2) below lists fucoidan-based nanocarrier formulations, their ingredients, methods, disease targets, and experimental models.

The flowchart (Figure 3) outlines the major disease targets for fucoidan-based nanoparticles, including oncology, cardiovascular and thrombotic diseases, and inflammatory or autoimmune diseases. Within these disease categories, major therapeutic modalities are detailed: tumor targeting via P-selectin binding, anticoagulation via platelet inhibition, and immunomodulation via cytokine regulation. Such modalities demonstrate the dual role of fucoidan as both a delivery strategy and a bioactive therapy.

Table 2. Fucoidan-based nanocarrier systems: composition, synthesis methods, target disease, and experimental model types

Nanocarrier	Compositions	Methods	Type of Diseases	*In Vitro*/ *In Vivo*	Outcome/ Remarks	Ref.
Cancer Diseases						
Fucoidan Gold NPs (F-AuNPs)	Fucoidan + Gold Nanoparticles	Reduction	Liver Cancer (HepG2), Leukaemia (THP-1)	*In Vitro*	Enhanced anti-cancer/antioxidant activity	Newehy et al., 2025
Fucoidan-Coated Se NPs & N-Cur	Fucoidan + Selenium NPs + Curcumin	Nanoprecipitation	Colorectal Cancer (CaCo-2, HT-29)	*In Vitro*	Strong colorectal cancer cytotoxicity (IC_{50} ≈10.3 mg/L for CaCo-2, 19.4 mg/L for HT-29, exceeding cisplatin) with DNA damage/ apoptosis induction	Alduais et al., 2025

4.4. Clinical Trials Involving Fucoidan

In the last three years, fucoidan has entered clinical investigations, primarily as an oral supplement or adjunct therapy. One example is a completed Taiwanese trial (NCT02875392) that evaluated a combined fucoidan + fucoxanthin supplement

Table 2. Continued

Nanocarrier	Compositions	Methods	Type of Diseases	*In Vitro*/ *In Vivo*	Outcome/ Remarks	Ref.
Fucoidan-Epirubicin NPs	Fucoidan + Polyethylene Glycol–Polylactic Acid (mPEG–PLA) + Epirubicin	Nanoprecipitation/ Solvent Evaporation	Colorectal Cancer (HCT116, C26)	*In Vitro, In Vivo*	Significantly enhanced tumor suppression with reduced systemic toxicity	Khan et al., 2024
Fucoidan-Cu NPs	Fucoidan + Copper	Self-assembly	Liver Cancer (HuH-7)	*In Vitro, In Vivo*	Efficient tumor growth inhibition and ROS-mediated cytotoxicity	Chen et al., 2024
Fucoidan-PEI NPs + Cytarabine	Fucoidan+ Polyethyleneimine + Cytarabine	Polyelectrolyte Complexation	Breast Cancer (MCF-7)	*In Vitro*	Enhanced intracellular drug delivery and apoptosis-related gene expression	Geethakumari et al., 2024
Quercetin-Fucoidan NPs (QU@FU-TS)	Fucoidan + Quercetin (QC) + Sodium tripolyphosphate + Tea Saponins	Self-Assembly	Lung Cancer (A549)	*In Vitro, In Vivo*	Superior tumor inhibition over free quercetin	Lin et al., 2024
Fucoidan Nanoparticles (FuNPs)	Fucoidan	Emulsion	Mouse Breast Cancer (4T1)	*In Vitro, In vivo*	Significant tumor volume reduction and suppression of lung metastasis & standalone therapeutic agents.	Chiang et al., 2021
Fucoidan-PLGA NPs (FPN-DTX NPs)	Fucoidan + PLGA + Docetaxel	Emulsion/ Solvent Evaporation	Breast Cancer (MDA-MB-231)	*In Vitro*	Improved cellular uptake and cytotoxic efficacy	Lai et al., 2020
Fucoidan-Coated CuS NPs	Fucoidan + Copper Sulfide	Solution-based Coating	Cervical and Lung Cancer (HeLa, A549), Leukaemia (K562)	*In Vitro, In Vivo*	Enhanced photothermal ablation and selective cancer cell killing	Jang et al., 2018
Cardiovascular Diseases						
Fucoidan-modified PLGA NPs	Fucoidan + PLGA	Self-assembly Method	Thrombosis, Myocardial Infarction	*In Vitro, In Vivo*	Selective thrombus targeting via P-selectin binding	Ma et al., 2025
CS/PANI/ Fucoidan 3D Scaffold NPs	Chitosan + Polyaniline + Fucoidan	3D-Printing	Cardiac Tissue Injury	*In Vitro*	Enhanced cell adhesion, conductivity, and cardiac tissue regeneration	Moradi et al., 2024
Fucoidan Nanoparticles	Fucoidan	Ball Milling	Diabetic Aortic Endothelial Cell Dysfunction	*In Vitro, In Vivo*	Improved endothelial function and reduced oxidative stress	Wardani et al., 2023

Table 2. Continued

Nanocarrier	Compositions	Methods	Type of Diseases	*In Vitro*/ *In Vivo*	Outcome/ Remarks	Ref.
Inflammatory Diseases						
Fucoidan-based Macrophage Membrane Bio-nanoparticles (MF@CB)	Fucoidan, Macrophage Cell Membrane	Dialysis Method and Membrane Coating	Lung Inflammation	*In Vitro*, *In Vivo*	High inflammation-site targeting and cytokine suppression	Yang et al., 2025
Fucoidan-based PEGylated PLGA-NPs (FuP2)	Fucoidan + PEGylated PLGA	Emulsion/ Solvent Evaporation	Inflammation	*In Vitro*, *In Vivo*	Sustained anti-inflammatory activity with improved circulation time	Abdelkader et al., 2022
FU/PVP/Hes Nanoparticles	Fucoidan + Polyvinylpyrrolidone + Hesperitin	Solvent Evaporation	Corneal Inflammation	*In Vitro*, *In Vivo*	Significant reduction in corneal inflammation and oxidative stress	Liu et al., 2025

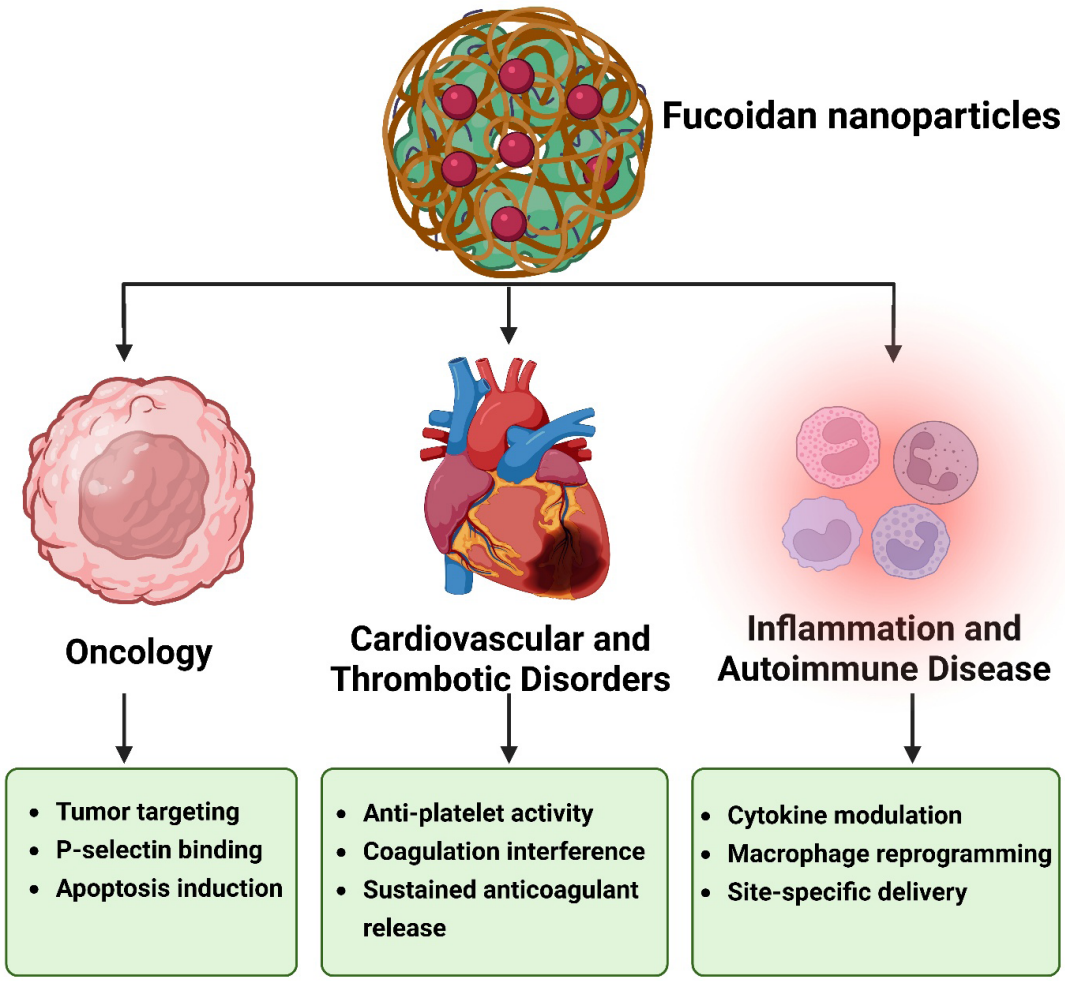


Figure 3. Flowchart representing the therapeutic uses of fucoidan-derived nanocarriers

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(FucoHiQ) in patients with non-alcoholic fatty liver disease (NAFLD). The study (57 participants) examined changes in liver enzymes and fibrosis markers, which are believed to be the mechanisms by which fucoidan exerts its liver-protective effects. In oncology, a Mayo Clinic trial (NCT06855524, active) is testing high-purity fucoidan versus placebo to prevent chemotherapy-related fatigue in patients with GI cancer. Several other Phase I/II studies are registered, including fucoidan supplementation in cancer survivors (immune recovery), metabolic syndrome (NAFLD; NCT02875392), and as an anti-inflammatory in atopic dermatitis (NCT05420410). To date, no trials have evaluated fucoidan-loaded nanoparticles in humans, so clinical data on nanocarriers remain limited. Nevertheless, these trials (most of which were registered after 2020) underscore the growing translational interest. Fucoidan, recognized as GRAS and with a history as a dietary supplement, makes it easy to include in human studies (Mary Saral & Mathew, 2020). Early reports suggest good safety, but efficacy endpoints remain to be confirmed.

5. PHARMACOKINETICS, SAFETY, AND REGULATORY OUTLOOK

The pharmacokinetics and safety characteristics of fucoidans differ from those of synthetic polymers. Whether given orally or parenterally, fucoidan is only partially absorbed and mostly excreted through the kidneys and broken down by enzymes (Figure 4) (Venkatesan et al., 2016). Its high molecular weight makes it difficult for passive tissue to penetrate, so it usually needs to be delivered by a nanocarrier to work. For instance, studies on the biodistribution of radiolabeled fucoidan show that small amounts are cleared by the kidneys and taken up by the liver and tumors. Research on animals shows that fucoidan has a good safety profile. For example, in rodent experiments, no notable toxic effects were observed even at doses up to 600-1000 mg/kg/day (Turrini et al., 2023b). Fucoidan is generally safe. Some places even list it as GRAS (Generally Recognized as Safe), and there have been a few documented cases of acute toxicity (Pereira et al., 2024). One issue is that when something is highly sulfated, it is more easily detected by the immune system, so products must strike a balance between potency and removal. Fucoidan is not considered a drug by current regulatory frameworks; instead, it is considered a food supplement or excipient. Therefore, the clinical translation of fucoidan nanomedicines needs to show that they are safe for humans and of consistent quality. Clotting times were only significantly prolonged at very high doses, owing to heparin-like anticoagulant effects (Turrini et al., 2023a). People are working to make fucoidan sources more consistent and to conduct formal toxicology studies on fucoidan nanoformulations. To sum up, the fact that fucoidan is a natural product gives it an advantageous safety margin; nevertheless, its pharmacokinetics and regulatory roadmap call for detailed characterization before it can be used as a medicine.

At present, fucoidan is mainly controlled as a dietary supplement or nutraceutical rather than as a pharmaceutical. It is worth noting that some fucoidan extracts, such as those from Undaria and Fucus, have been granted FDA GRAS status for consumption up to approximately 250 mg per day (Mary Saral & Mathew, 2020). In fact, companies market fucoidan as a dietary fiber that can help the gut and immune system. However, fucoidan nanocarriers intended for use as medicinal products will likely be classified as drugs or biologics, which means they would be strictly regulated. So far, no fucoidan drug (small molecule or NP) has been authorized. There are currently no standard pharmacopeial monographs for fucoidan, and the criteria for obtaining it remain unclear. Finding seaweed that is good for the environment and making sure that each batch is the same are two of the biggest problems. To produce clinical-grade material, you need to follow GMP extraction protocols that standardize temperature, pH, and purification. The FDA and EMA would need to know everything about the polysaccharide, including its molecular weight distribution, sulfate content, and impurity profile. Fucoidan nanomedicines may be considered combination products because they are biologically active. Showing that you can consistently make complicated NPs (which often require several steps) will be a challenge for regulators.

Nanoparticle formats are generally safe, but more specific studies are needed. Nanocarriers may alter biodistribution and immunogenicity. For example, intravenous fucoidan NPs could provoke complement activation or accumulate in the reticuloendothelial system. Regulatory guidance suggests extensive preclinical toxicity testing (acute and chronic, immunotoxicity, genotoxicity) for any new NP drug. To date, published toxicity studies on fucoidan NPs have been limited to rodents. These

show minimal systemic toxicity, but formal GLP studies are required.

Given its dual role (excipient + bioactive), fucoidan nanocarriers may fall under "nanomedicine" guidelines, an evolving regulatory space. Agencies encourage early discussion (e.g., FDA IND consultations) to address characterization of the polysaccharide. Depending on the indication, the number of fucoidan NPs (drug, biologic, device) could be classified differently. Toxicity endpoints will primarily monitor coagulation parameters (given the possibility of heparin-like effects) (Turrini et al., 2023a) immune reactions and organ deposition. To meet production scale, controlling raw fucoidan variability becomes part of the manufacturing process without requiring disruptive changes. Different analytical methods, such as HPLC for monomers and NMR for sulfation, will be extremely important. In summary, a proactive regulatory strategy is needed: early toxicology in relevant models, pilot pharmacokinetic studies, and continuous engagement with regulators. This will build confidence that fucoidan-based therapies are safe and consistent enough for clinical trials.

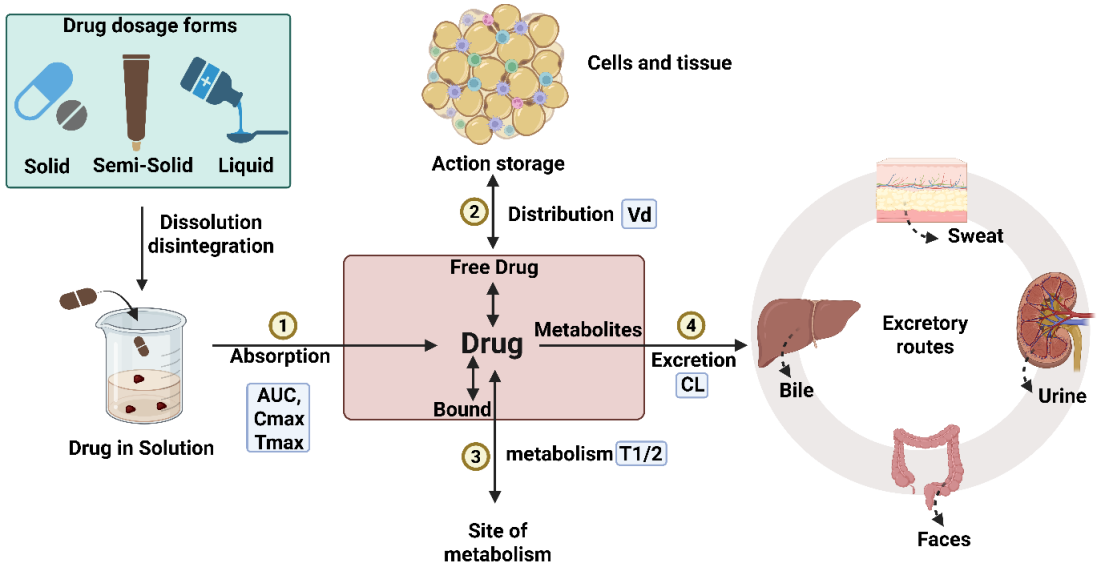


Figure 4. Conceptual overview of nanoparticle pharmacokinetics (ADME): pathways of absorption, distribution, metabolism, and excretion (Adapted from Abdifetah and Na-Bangchang, 2019)

6. SUSTAINABILITY AND BLUE-ECONOMY CONSIDERATIONS

Seaweed aquaculture for fucoidan is naturally sustainable: brown algae grow quickly and do not require arable land, freshwater, or fertilizers, and they absorb carbon dioxide (CO_2). Fucoidan can be extracted using green processes (enzymes, microwave, ultrasound) that require very little solvent. Besides, harvesting seaweed still supports the local economy and can be integrated into circular-economy biorefineries (e.g., other algal products such as biofuels and fertilizers). In the life cycle analysis, fucoidan production is generally less carbon and water-intensive than petrochemical polymers.

There are also ethical issues, such as avoiding the depletion of wild stocks and ensuring that marine communities receive a fair share of the benefits. In short, the use of fucoidan nanocarriers is a blue biotech approach that adds value to renewable biomass and aligns with the pharmaceutical industry's sustainability objectives.

7. EXPERT OUTLOOK AND FUTURE DIRECTIONS

Looking ahead, many emerging technologies appear poised to be major drivers of the fucoidan nanomedicine field. To begin with, the possibility of customizing fucoidan compositions through algae species or molecular weight fractionation might enable drug delivery systems to be adapted

 https://doi.org/10.37819/nanofab.2025.0023

to individual genotypes or disease phenotypes. Additionally, fucoidan nanoparticles serve as effective theranostic agents. To illustrate, radiolabeled fucoidan nanoparticles could make it possible for real-time Positron Emission Tomography PET/MRI analysis of drug distribution, at the same time treating the disease. Moreover, the advent of computational modeling and machine learning is expected to accelerate the design of advanced fucoidan nanostructures and formulations (Dong & Jiang, 2024). Lastly, combination therapies (such as co-delivery of small RNAs or peptides with fucoidan) could uncover new synergies. By merging marine biotechnology and nanomedicine, researchers can extend the range of targeted therapies.

The next steps in the field will be to thoroughly investigate the pharmacology of fucoidan and to develop scalable manufacturing. Standardization of extract chemistry (by enzymatic or microbial fermentation) will help to improve reproducibility. Early-stage clinical trials should be initiated without delay, leveraging the established safety profile of fucoidan. Through collaboration between chemists, pharmacologists, and engineers, new advances will be realized. Ultimately, fucoidan nanocarriers illustrate how the ocean can sustainably provide solutions to the most advanced biomedical needs. With further research and clinical development, we look forward to fucoidan becoming a versatile foundation of precision nanomedicine.

8. CONCLUSION

Fucoidan is a unique class of marine-derived nanocarrier materials that integrates biological functionality with cutting-edge nanofabrication. Compared to traditional synthetic systems, which primarily act as passive carriers, fucoidan nanocarriers integrate structural diversity with active biological properties stemming from sulfation patterns, molecular weight variability, and specific interactions with receptors. These properties enable synchronized targeting, therapeutic control, and biological feedback, which are in remarkable harmony with the concept of precision medicine. Recent advances have shown that fucoidan nanostructures can be designed to leverage selectin-mediated targeting, immune regulation, and control of major signaling pathways, such as PI3K/Akt, MAPK, and NF-κB. Such mechanism-based engagement provides the rationale for their proven efficacy in cancer, cardiovascular, and inflammatory disease models. Notably, the emerging clinical data, together with the attainment of FDA-notified GRAS status for specific fucoidan extracts, reflect a degree of translational readiness that is uncommon for emerging nanocarrier technologies. However, issues of structural variability, scalable nanofabrication, and regulatory standardization remain core challenges for clinical translation. Overcoming these hurdles through standardized nanocarrier characterization, scalable nanofabrication approaches, and mechanism-guided nanocarrier design will be critical. When viewed against other marine polysaccharides and traditional synthetic nanocarriers, fucoidan uniquely integrates bioactivity, biocompatibility, and targeting specificity, although precise optimization will be necessary to ensure reproducibility and controlled pharmacokinetics. Looking ahead, the combination of fucoidan with hybrid nanomaterials, biomimetic nanosystems, and stimuli-responsive nano-scaffolds holds great promise for improving therapeutic specificity. As nanomedicine advances with clinically relevant and sustainable approaches, fucoidan emerges as a biologically active, regulatory, and environmentally compatible platform, poised to make a meaningful contribution to the next wave of precision nanomedicine.

Author Contributions

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

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