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# Bioactivity-Guided Assembly of Extracted Fucoidan from *Tubinaria decurrens* for Drug Delevery

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## INTRODUCTION & AIM

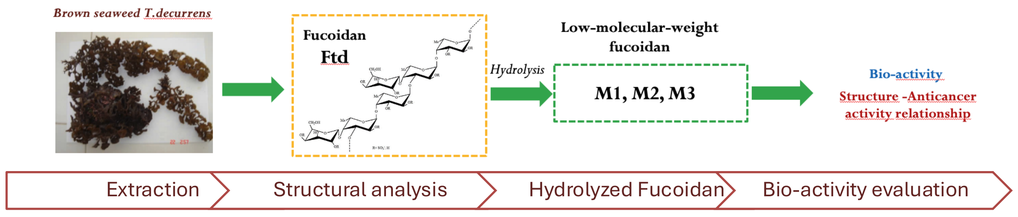
Fucoidan, a sulfated polysaccharide derived from brown seaweed, exhibits a broad spectrum of biological activities: Anticancer, antioxidant, immunomodulatory, and lipid-lowering effects. Despite this promising bioactivity, the clinical translation of fucoidan remains limited. To address this, transforming fucoidan into a multifunctional biomaterial is a rational strategy. By exploiting its polyanionic nature, fucoidan can be electrostatically assembled with cationic chitosan into polyelectrolyte complex nanoparticles. This nanoplatform preserves fucoidan's intrinsic bioactivity while acting as a structural and functional carrier to improving the stability, encapsulation efficiency, and controlled release of co-administered bioactive compounds such as curcumin.

This study bridges the fundamental structural characterization of fucoidan with its application in multifunctional drug delivery systems. Specifically, the objectives are to:

1. Elucidate the structure of fucoidan extracted from *Turbinaria decurrens* and establish its structure–anticancer activity relationship.
2. Fabricate unloaded and curcumin-loaded fucoidan–chitosan nanoparticles, evaluating their physicochemical properties and anticancer efficacy as a multifunctional drug delivery system.

## METHOD

### Isolation and Advanced characterization of Fucoidan




***Isolation:*** Fucoidan was extracted using a modified *Bilan et al.* [1] method. Low-molecular-weight fucoidan (LMWF) derivatives were subsequently obtained via acid hydrolysis (0.1 N HCl, 85°C) at various time intervals.

***Structural characterization:*** **FT-IR** (Fourier-Transform Infrared Spectroscopy)**, ESI-MS/MS(**Electrospray Ionization Tandem Mass Spectrometry)**, NMR (**Nuclear Magnetic Resonance Spectroscopy)**, SEC-MALLS (**Size Exclusion Chromatography with Multi-Angle Laser Light Scattering)**, SAXS(**Small-Angle X-ray Scattering)

***Biological Activity Evaluation***

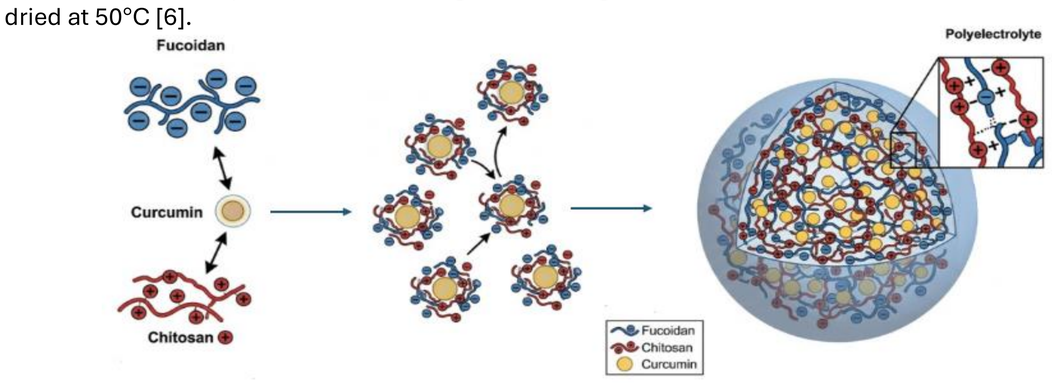
**Immunomodulatory Activity:** RAW264.7 macrophages → NBT dye reduction assay → Activation evaluation (*Manosroi et al.* [2]) **Hypolipidemic Activity:** Experimental hyperlipidemia model →Ftd administration →Lipid profile quantification (TC, TG, HDL) [3]. **In Vitro Cytotoxicity:** HT-29 colon cancer cells →*Skehan et al.* [4] method (0.8 – 100 $\mu$g/mL in 100% DMSO vs. Ellipticine) → $IC_{50}$ calculation (TableCurve).

### Bioactivity-Guided Assembly of Fucoidan-Chitosan Carriers

***Preparation of Fucoidan-Chitosan Carriers***

**Fucoidan/Chitosan Complexes (FC):** fucoidan (1 mg/mL in $H_2O$) + Chitosan (1mg/mL in 1% acetic acid) at a 3:1 (w/w) ratio [5]. Stirred (2–3 h) at, sonicated (15mins), washed, and dried at 50 °C.

**Curcumin-loaded Complexes (FCC):** [Curcumin + Fucoidan (0.3% (w/v)]. Dropwise into Chitosan (0.3% w/v) continuous stirring → centrifugation, washed with 80% ethanol, and dried at 50°C [6].




***Curcumin Encapsulation Efficiency:*** Quantified indirectly using HPLC at 425 nm.

$$\mathrm{EE}(\%) = \frac{C_{\text{initial}} - C_{\text{free}}}{C_{\text{initial}}} \times 100; \quad \mathrm{LC}(\%) = \frac{m_{\text{total}} - m_{\text{free}}}{m_{\text{complex}}} \times 100$$

*Where:* $C_{\text{initial}}$ *and* $m_{\text{total}}$ *represent the initial concentration/mass of curcumin introduced;* $C_{\text{free}}$ *and* $m_{\text{free}}$ *denote the mass of free uncomplexed curcumin;* $m_{\text{complex}}$ *is the total dry weight of the collected complex.*

***Characterization of Fucoidan-Chitosan Carriers* (Structure & Morphology):** Analyzed via FTIR, XRD, DLS, SEM, and AFM.

***Anticancer Assay:*** Evaluated against human breast (MCF-7) and lung (A549) cancer cell lines following the *Monks et al.* [7] protocol.

***Swelling Behavior:*** Tested in simulated gastric (pH 1.2) & intestinal (pH 7.2) fluids over 0–72 h.

$$SI = \frac{W_t - W_0}{W_0} \times 100$$

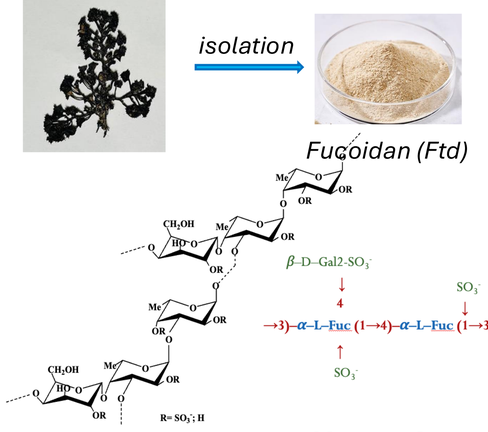
*Where:* $W_0$*: Initial dry weight of the nanoparticles;* $W_t$*: Weight of the swollen nanoparticles at time t(tested in SGF pH 1.2 and SIF pH 7.2)*

## CONCLUSIONS

*T. decurrens* fucoidan is a highly potent bioactive compound. Its enhanced anticancer activity is driven by a low molecular weight; low polydispersity (Mw/Mn); and rod-like conformation with short side chains. When formulated into a fucoidan-chitoan carrier, the system encapsulated curcumin and exhibited smart, pH-dependent swelling—restricted in SGF to prevent gastric degradation and enhanced in SIF for sustained intestinal drug delivery. Consequently, this multifunctional nanoplatform significantly improved targeted anticancer efficacy against MCF-7 and A549 cells compared to free curcumin.

## RESULTS & DISCUSSION

### Fucoidan - Brown Seaweed T. *decurrens:* *Composition & Structure*




| Yield (%) | Chemical composition of fucoidan | | | | | | |
|---|---|---|---|---|---|---|---|
| | **Sulfate (%)** | UA (%) | Monosaccharide composition | | | | |
| | | | **Fuc** | Gal | Xyl | Man | Glu |
| 2.9 | **15.78** | 7.5 | **1.00** | 0.5 | 0.03 | 0.04 | 0.02 |

Ftd is a sulfated galactofucan composed of alternating (1→3)– and (1→4)–α-L-fucopyranose residues. Branching occurs at the C-4 position, and sulfate groups are mainly located at C–2, C–3 and C–4 of the fucose residues. The side chains are composed of (1→4)-β-D-galactopyranose units sulfated at C-2. The sulfate content was 15.79%, indicating a moderate charge density for polyelectrolyte interactions.

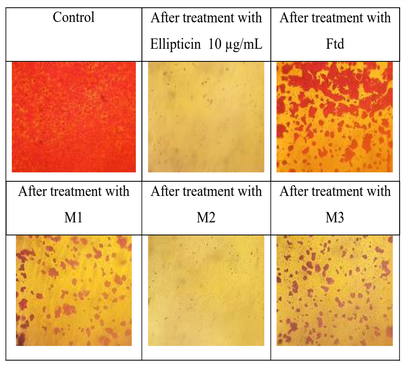
***Proposed chemical structure of fucoidan from T.decurrens (Ftd)***

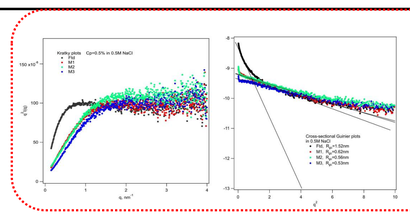
### Bio-activity of Fucoidan (Ftd)

Ftd exhibited immunomodulatory activity (NBT index ~1.51 at 100 µg/mL), anticancer activity against HT-29 cells ($IC_{50}$≈ 5.4 µg/mL), and lipid-lowering effects, reducing total cholesterol and triglycerides by 5.62% and 13.81%, respectively, while increasing HDL by 8.03%.

### *Structure- Anticancer activity relationship*

| Sample | *Mw* (*k*Da) | *Mw/Mn* | Sulfate content (%w) | Sulfate group position | $IC_{50}$ (µg/mL) | $R_{gc}$ (nm) |
|---|---|---|---|---|---|---|
| Ftd | 122.6 | 4.10 | 15.79 ± 0.29 | C3<C2<C4 | 73.52 ± 2.54 | 1.52 |
| M1 | 42.6 | 1.97 | 16.81 ± 0.53 | C3<C2<C4 | 11.72 ± 1,24 | 0.62 |
| **M2** | **28.2** | **1.94** | **16.84 ± 0.26** | **C3<C2<C4** | **5.41 ± 0.36** | **0.56** |
| M3 | 24.0 | 2.24 | 15.85 ± 0.36 | C3<C2<C4 | 6.55 ± 0.31 | 0.53 |



**Conformational structure (by SAXS)**

**Rod-like; The small cross-sectional radius of gyration (Rgc) indicates short side-chain length.**

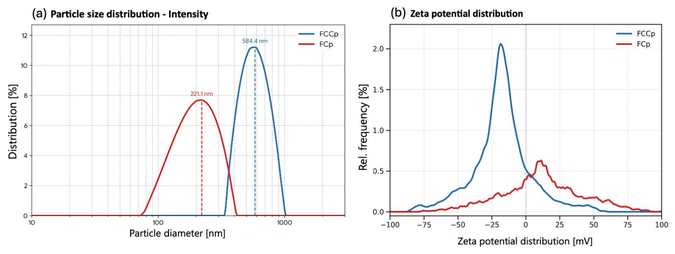
**New insights** into the structure–anticancer activity relationship of fucoidan

**Structure–Anticancer Relationship**

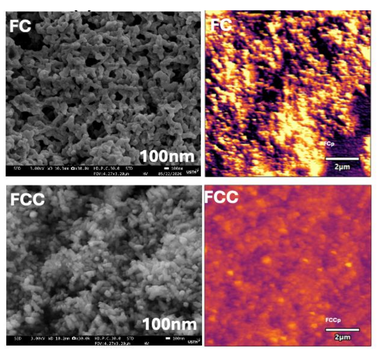
**Fucoidan with enhanced anticancer activity is characterized by low molecular weight; low polydispersity *(Mw/Mn);* and rod-like conformation with short side chains.**

### Bioactivity-Guided Assembly of Fucoidan-Chitosan Carriers

***Particle Morphology and Size Analysis (DLS, SEM, and AFM)***

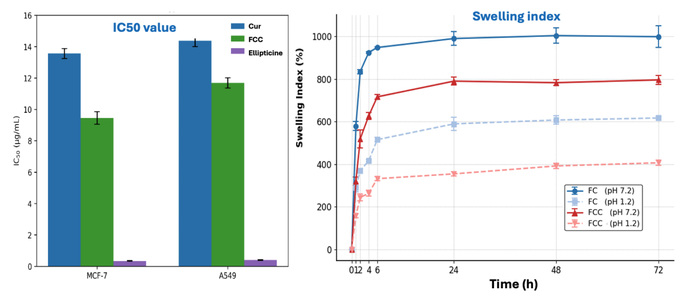



| Sample | Size (nm) | ζ-potential (mV) |
|---|---|---|
| FC | 197.8 ± 0.15 | 29,97 ± 0,07 |
| FCC | 526.7 ± 0.42 | -18,27 ± 0,25 |

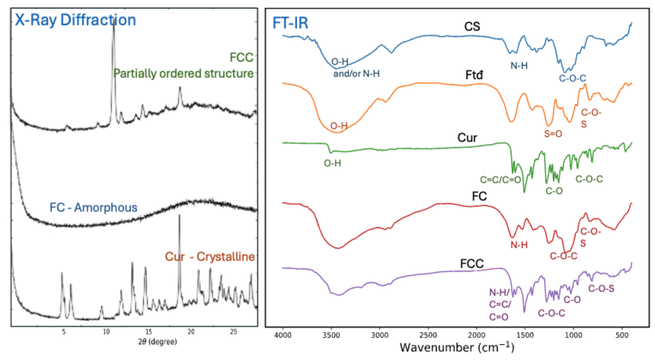



Fucoidan was assembled with chitosan via electrostatic interactions between ($–SO_3^-$) and ($–NH_3^+$) groups to form FC and further loaded with curcumin to FCC systems.

***Anticancer activity & pH-Responsive Swelling***




***Structural Characterization***




**FCC significantly enhances anticancer efficacy** and **improves bioavailability** over free curcumin.

**pH-Responsive Swelling:** Fucoidan-chitosan carriers showed pH-dependent swelling—low in SGF (pH 1.2) and high in SIF (pH 7.2). This prevents premature gastric degradation and enables sustained, intestinal drug release.

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