

Comparative bioactivities of native, degraded, and sulfated fucoidan derivatives from *Sargassum crassifolium*: insights from apoptosis, migration, immunostimulation, and multivariate analysis

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Received 11 November 2025; revised 17 January 2026

Native fucoidan (designated as SC) was extracted from *Sargassum crassifolium* following an extrusion-puffing pretreatment. SC was subjected to hydrogen peroxide (H₂O₂)-mediated degradation to yield a lower molecular weight derivative, SC-H₂O₂. Subsequently, two oversulfated derivatives were synthesized from SC-H₂O₂, namely SC-H₂O₂-S1 (mild sulfation), and SC-H₂O₂-S2 (intensive sulfation). All fucoidan derivatives induced apoptosis in A-549 cells via mitochondrial pathways, as evidenced by decreased MMP and Bcl-2 levels, increased Bax expression and cytochrome c release, and activation of caspases. Among them, SC-H₂O₂-S1 exhibited the strongest pro-apoptotic and anti-migration effects by modulating RANK and MMP-9 expressions. Additional experiments revealed that SC-H₂O₂ showed reduced immunostimulatory activity in RAW 264.7 murine macrophages compared to SC, whereas SC-H₂O₂-S1 enhanced the immunostimulatory effects relative to SC-H₂O₂. Principal component analysis (PCA) and hierarchical clustering analysis (HCA) indicated that SC and SC-H₂O₂ were characterized by modulation of apoptosis and immune-enhancing factors, whereas SC-H₂O₂-S1 and SC-H₂O₂-S2 exhibited stronger associations with apoptosis and cell migration.

Keywords: Cell migration, Fucoidan modification, Immunomodulatory activity, Mitochondrial apoptotic pathway