From marine metabolites to cosmeceuticals: Optimizing bioactive compounds for improved skin health

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Marine macroalgae are an underexplored source of structurally diverse secondary metabolites. Their exposure to extreme and fluctuating environmental conditions has driven the evolution of complex metabolic pathways, leading to the biosynthesis of chemically unique compounds. These include phenolic acids, phlorotannins, terpenoids, sterols, etc., which serve, among others as UV protection, and oxidative stress mitigation, mechanisms also relevant to anti-aging skincare.

This work focused on two such underexploited species, *Gongolaria abies-marina* and *Caulerpa prolifera*, applying an integrated strategy of phytochemical profiling, optimized extraction, and structural modification of selected metabolites. While both yielded enzyme-inhibitory extracts, the most impactful results came from the semi-synthesis of key lipophilic constituents.

Targeting enhanced bioactivity, phytol, β-sitosterol, and stigmasterol were selected for semi-synthesis. Ten ester derivatives of each molecule were obtained using benzoic, cinnamic, furanoic, and thiophene-carboxylic acids, yielding compounds with distinct substitution patterns. Several derivatives showed markedly enhanced inhibition of hyaluronidase and tyrosinase compared to parent compounds and controls (Figure 1). β-sitosterol 3-(2-methoxybenzoate) was the most potent hyaluronidase inhibitor (IC_{50} = 2.88 µM), over nine times stronger than sodium aurothiomalate. Substituent positioning on the aromatic ring significantly influenced activity, highlighting key structure–activity relationships. For tyrosinase, phytyl 4-methoxybenzoate outperformed phytol with a 2.8-fold increase in potency (IC_{50} = 27.94 µM).

These results show that strategic derivatization of macroalgal metabolites enhances their anti-aging bioactivity, especially enzyme inhibition. This work expands the chemical space of marine natural products and provides promising semi-synthetic candidates for future cosmeceutical applications.

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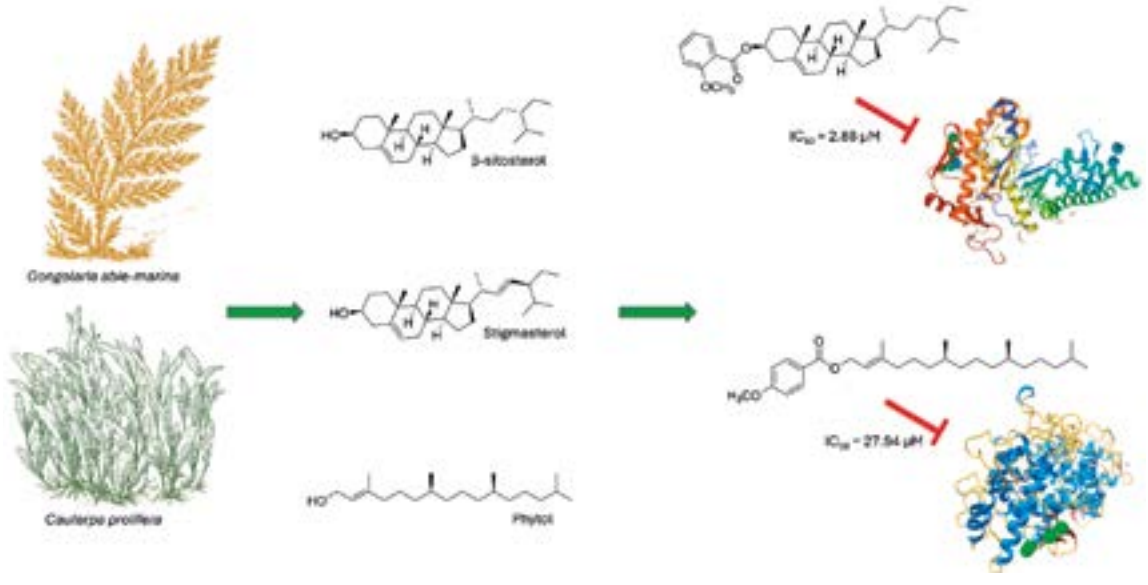

FIGURE 1
Schematic representation of the workflow for the semi-synthesis of derivatives from compounds of *Gongolaria abies-marina* and *Caulerpa prolifera*.