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Encapsulation and controlled release of halogenated natural products in nanoformulations for enhanced stability and biological activity

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Nanotechnology has emerged as a transformative tool in the life sciences to offer innovative solutions to overcome the limitations of conventional drug delivery systems, particularly the poor solubility, lipophilicity, and instability of many bioactive compounds. Halogenated natural products (HNPs) are of great interest due to their potent biological activities, including notable antimicrobial effects. These are bioactive compounds derived from natural sources (e.g., marine organisms, plants, fungi) and contain halogen atoms that improve the biological activity, stability and membrane permeability. Marine-derived HNPs, especially those from *plocamium SSP.*, have attracted more attention for their strong antimicrobial properties. Despite their therapeutic potential, their clinical application remains limited due to poor solubility and instability under physiological conditions. To address these challenges, therefore this study aims to develop lipid-based nanoparticles formulation to improve the solubility, stability and biological efficacy of halogenated compounds.

HNPs were extracted and isolated from the red algal *Plocamium cornutum* and structurally characterized using nuclear magnetic resonance (NMR) spectroscopy. These bioactives were encapsulated into solid lipid nanoparticles (SLNs) using the hot homogenization method. The physiochemical properties of the resulting SLNs were characterized by dynamic light scattering (DLS) to determine particle size, polydispersity index (PDI), and the zeta potential parameters. The surface morphology were examined using scanning and transmission electron microscopy (SEM and TEM), while the entrapment efficiency was assessed via nuclear magnetic resonance (NMR) spectroscopy.

In addition, the antimicrobial activity was assessed using broth micro dilution and disc diffusion assay to evaluate the efficacy of the encapsulated HNPs against selected gram negative and positive microbial strains, *Escherichia coli* and *staphylococcus aureus*. The minimum inhibitory concentrations (MIC) were determined using the 96-well plates and the results were quantified using UV-Vis spectrophotometer. The encapsulated HNPs exhibited distinct zones of inhibition and lower MIC values compared to the free compounds which shows improved antimicrobial potency. This work offered an innovative strategy to address the stability and delivery limitations of bioactive compounds by combining marine natural product chemistry with nanocarrier technology. These findings provide proof of concept for developing effective, nanotechnology-based drug delivery systems for marine derived antimicrobials with potential applications in pharmaceutical and clinical settings.

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