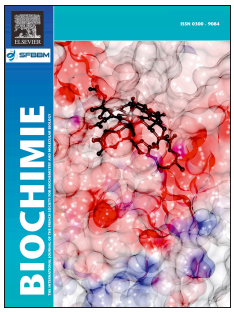
# Accepted Manuscript




The mycosporine-like amino acids porphyra-334 and shinorine are antioxidants and direct antagonists of Keap1-Nrf2 binding

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**ABSTRACT**

Mycosporine-like amino acids (MAAs) are UVR-absorbing metabolites typically produced by cyanobacteria and marine algae, but their properties are not limited to direct sun screening protection. Herein, we examine the antioxidant activities of porphyra-334 and shinorine and demonstrate that these MAAs are prospective activators of the cytoprotective Keap1-Nrf2 pathway. The ability of porphyra-334 and shinorine to bind with Keap1 was determined using fluorescence polarization (FP) and thermal shift assays to detect Keap1 receptor antagonism. Concomitantly, the ability of porphyra-334 and shinorine to dissociate Nrf2 from Keap1 was confirmed also by measurement of increased mRNA expression of Nrf2 targeted genes encoding oxidative stress defense proteins in primary skin fibroblasts prior and post UVR exposure. Surprisingly, enhanced transcriptional regulation was only promoted by MAAs in cells after exposure to UVR-induced oxidative stress. Furthermore, the *in-vitro* antioxidant activities of porphyra-334 and shinorine determined by the DPPH free-radical quenching assay were low in comparison to ascorbic acid. However, their antioxidant capacity determined by the ORAC assay to quench free radicals via hydrogen atom transfer is substantial. Hence, the dual nature of MAAs to provide antioxidant protection may offer a prospective chemotherapeutic strategy to prevent or retard the progression of multiple degenerative disorders of ageing