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Cyclic tetrapyrrolic photosensitizers from *Cladophora patentiramea* (Cladophoraceae, Chlorophyta) and *Turbinaria conoides* (Sargassaceae, Phaeophyta) for photodynamic therapy

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Abstract In screening for novel photosensitizers for photodynamic therapy, 14 seaweed samples from Port Dickson in Malaysia were collected. Methanolic extracts of these samples were prepared and evaluated for phototoxicity using a short-term cell viability assay, where promyelocytic leukemia cells, HL60 were incubated with the extracts prior to irradiation with a broad spectrum light at 9.6 Jcm^{-2} (equivalent to 10.5 mW cm^{-2} for 10 min). Four of the methanolic extracts demonstrated moderate to strong phototoxicity and bioassay-guided isolation of photosensitizers was carried out on two selected seaweeds to yield a total of eight cyclic tetrapyrrolic compounds which are derivatives of chlorophyll-*a* and -*b*. Seven of these compounds showed >50% phototoxicity at 5 μg mL^{-1} while exhibiting minimal cytotoxicity in the dark, which is an important characteristic of an ideal photosensitizer.

Keywords Photodynamic therapy · Photosensitizer · Seaweeds · Cyclic tetrapyrroles · Chlorophylls

Introduction

Photodynamic therapy (PDT) of cancer involves administration of a photosensitizer which preferentially accumulates in cancerous tissues followed by site-directed activation of the photosensitizer with focal light irradiation to generate reactive oxygen species that remove the tumor via direct cell damage, shutting down of tumor vasculature and recruitment of immune response cells (Pervaiz 2001). Upon activation, the reactive free radicals are generated by photosensitizers via either Type I which involves reactions of the photosensitizers directly with biological substrates such as cell membrane to form radicals such as superoxides, hydroperoxyls, and hydroxyls, or Type II pathway which involves the transfer of the photosensitizer energy directly to produce reactive oxygen species (Pervaiz 2001).

To date, a number of photosensitizers have been clinically approved for treatment of specific cancers, including Photofrin®, Foscan® and Levulan®. Many of the photosensitizers that are clinically approved or in clinical trials are derived from naturally occurring structures based on cyclic tetrapyrroles such as hematoporphyrin from blood, and chlorophyll-based compounds from higher

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