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Original article

Anticancer and antioxidant activities of *Nannochloropsis oculata* and *Chlorella* sp. extracts in co-application with silver nanoparticle

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ABSTRACT

This study examined the formulation of Microalgal Chloroform Extracts (MEs) and Silver nanoparticles (AgNPs) co-application for anticancer activity against MCF-7 and 4T1 cells, without affecting the non-cancerous Vero cell-lines. The concentration, ratios and duration of treatments were optimized, and the flow cytometric and cell cycle analyses were carried out. The metabolites based on Gas Chromatography-Mass Spectrometry (GC–MS) were determined and the antioxidant activities evaluated. The main compounds detected in *Chlorella* sp. and *N. oculata*, respectively, were hexanedioic acid, bis (2-ethylhexyl) ester (23.94, 36.47%), neophytadiene (16.82, 4.79%), eicosane (4.37, 15.04%), hexatriacontane (0, 12.77%), and 13-Docosenamide, (Z) (9.22, 0%). The AgNPs-*N. oculata*-CHL at (w/w) 1.5:1 and 2:1 ratios (w/w) exhibited cytotoxic IC_{50} of 10.47 and 17.78 μg/mL on MCF-7 cells; and 79.43 and 52.7 μg/mL against 4T1 cells after 72 h, respectively. The AgNPs-*Chlorella* sp.-CHL at 1:1 and 2:1 ratios exhibited IC_{50} of 19.05 and 14.45 μg/mL against MCF-7 cells; and 79.43 and 50.11 μg/mL on 4T1 cells after 72 h, respectively. There was no cytotoxicity against Vero cells at any of the treatments tested. The co-applications showed higher early and late apoptotic events and significant increase in sub G1 phase as compared to the single-applications. At the 2:1 ratio, the strongest anti-oxidant activities were shown by the AgNPs-*Chlorella* sp.-CHL (IC_{50} 2.11 mg/mL) and *N. oculata*-CHL (IC_{50} 2.98 mg/mL), as compared to the AgNPs-*T. suecica*-CHL (IC_{50} 1.77 mg/mL). The AgNPs-MEs co-application exerted high anticancer and antioxidant activities, with no cytotoxic activity against Vero cells. The formulation could lead to the development of potent therapeutic agents against breast cancer with reduced or no side effect.

1. Introduction

Free-radical chain reactions can lead to many diseases such as diabetes, cancer, arthritis, and increased aging process. Effective free-radical scavenging activities is therefore important to quench the initiator radical (Saha et al., 2004). Biogenic compounds from plant and microalgal extracts are Generally Regarded As Safe (GRAS) to be developed as complementary anticancer, antitumor and antioxidant therapeutics, with little or no side effects (Abdullah et al., 2016, 2017; Martínez Andrade et al., 2018). Unicellular green algae *Nannochloropsis oculata* (Ochrophyta, Eustigmatophyceae) and *Chlorella vulgaris* Beijerinck (Chlorellaceae), have been explored for functional food, nutraceutical, pharmaceuticals, biochemicals, and animal feed applications (Abdullah et al., 2016, 2017; Shah and Abdullah, 2018).

Abbreviations: AgNPs, Silver nanoparticles; NPs, Nanoparticles; MEs, Microalgae extracts; SPR, surface-plasmon resonance; ROS, reactive oxygen species; MET, Methanol; CHL, Chloroform; HEX, Hexane; ETH, Ethanol; W, Water; PI, Propidium iodide; XRD, X-ray Diffraction; DMSO, Dimethyl sulfoxide; MTT, 3-(4,5-dimethylthiazol-2-yl)- 2,5-diphenyltetrazolium bromide TMX, Tamoxifen; SEM, Scanning Electron Microscopy; GC–MS, Gas-chromatography mass spectrometry.

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