



## Research article

# Microalgal metabolites as anti-cancer/anti-oxidant agents reduce cytotoxicity of elevated silver nanoparticle levels against non-cancerous vero cells

Hanaa Ali Hussein<sup>a,b</sup>, M. Maulidiani<sup>c</sup>, Mohd Azmuddin Abdullah<sup>a,\*</sup><sup>a</sup> Institute of Marine Biotechnology, Universiti Malaysia Terengganu, 21030, Kuala Nerus, Terengganu, Malaysia<sup>b</sup> College of Dentistry, University of Basrah, Basrah, Iraq<sup>c</sup> Faculty of Science and Marine Environment, Universiti Malaysia Terengganu, 21030, Kuala Nerus, Terengganu, Malaysia

## ARTICLE INFO

## Keywords:

Environmental science  
Toxicology  
Cell biology  
Biochemistry  
Heavy metals  
Microalgal metabolites  
Silver nanoparticles  
Apoptosis  
Cell-cycle  
Metabolite profiling

## ABSTRACT

Heavy metal pollution has become a major concern globally as it contaminates eco-system, water networks and as finely suspended particles in air. In this study, the effects of elevated silver nanoparticle (AgNPs) levels as a model system of heavy metals, in the presence of microalgal crude extracts (MCEs) at different ratios, were evaluated against the non-cancerous Vero cells, and the cancerous MCF-7 and 4T1 cells. The MCEs were developed from water (W) and ethanol (ETH) as green solvents. The AgNPs-MCEs-W at the 4:1 and 5:1 ratios (v/v) after 48 and 72 h treatment, respectively, showed the IC<sub>50</sub> values of 83.17–95.49 and 70.79–91.20 µg/ml on Vero cells, 13.18–28.18 and 12.58–25.7 µg/ml on MCF-7; and 16.21–33.88 and 14.79–26.91 µg/ml on 4T1 cells. In comparison, the AgNPs-MCEs-ETH formulation achieved the IC<sub>50</sub> values of 56.23–89.12 and 63.09–91.2 µg/ml on Vero cells, 10.47–19.95 and 13.48–26.61 µg/ml on MCF-7; 14.12–50.11 and 15.13–58.88 µg/ml on 4T1 cells, respectively. After 48 and 72 h treatment, the AgNPs-MCE-CHL at the 4:1 and 5:1 ratios exhibited the IC<sub>50</sub> of 51.28–75.85 and 48.97–69.18 µg/ml on Vero cells, and higher cytotoxicity at 10.47–16.98 and 6.19–14.45 µg/ml against MCF-7 cells, and 15.84–31.62 and 12.58–24.54 µg/ml on 4T1 cells, respectively. The AgNPs-MCEs-W and ETH resulted in low apoptotic events in the Vero cells after 24 h, but very high early and late apoptotic events in the cancerous cells. The Liquid Chromatography-Mass Spectrometry-Electrospray Ionization (LC-MS-ESI) metabolite profiling of the MCEs exhibited 64 metabolites in negative ion and 56 metabolites in positive ion mode, belonging to different classes. The microalgal metabolites, principally the anti-oxidative components, could have reduced the toxicity of the AgNPs against Vero cells, whilst retaining the cytotoxicity against the cancerous cells.

## 1. Introduction

Heavy metals are elements occurring naturally, and have high atomic weight and a density of at least 5 times the density of water. The presence and wide distribution of heavy metals in the environment are attributed to the anthropogenic activities such as mining and electro-plating industries, and also from agricultural and electronic wastes. There have been major concern on the potential effects of heavy metal pollution on the environment and human health that constant monitoring has become an essential part of the integrated remediation strategies [1, 2]. The toxicity of heavy metals depends on dosage, exposure route and duration, and chemical types. Exposure and impacts on individuals vary based on gender, age, genetics, and nutritional uptake. Heavy metals such as

cadmium, arsenic, chromium, mercury, and lead, have high degree of toxicity, and are known to cause damage to many organs, even at low levels. These are among the priority metals of public health concern and classified as human carcinogens according to the International Agency for Research on Cancer and the U.S. Environmental Protection Agency [3].

Toxic level of heavy metals in drinking water and marine organisms such as fish, and in the food chains from unsustainable agricultural practices, and also released from vehicles and fumes could be among the factors that contribute towards the spike in cancer incidence globally. Breast cancer is the most prevalent cancer in women and early stage diagnosis to identify cancerous cells could decrease the mortality rates in the long term. The screening methods include mammography,

\* Corresponding author.

E-mail addresses: [azmuddin@umt.edu.my](mailto:azmuddin@umt.edu.my), [joule1602@gmail.com](mailto:joule1602@gmail.com) (M.A. Abdullah).