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Purification and identification of novel cytotoxic oligopeptides from soft coral *Sarcophyton glaucum*[*#]

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Abstract: Globally, peptide-based anticancer therapies have drawn much attention. Marine organisms are a reservoir of anticancer peptides that await discovery. In this study, we aimed to identify cytotoxic oligopeptides from *Sarcophyton glaucum*. Peptides were purified from among the *S. glaucum* hydrolysates produced by alcalase, chymotrypsin, papain, and trypsin, guided by a methylthiazolyldiphenyl-tertrazolium bromide (MTT) assay on the human cervical cancer (HeLa) cell line for cytotoxicity evaluation. Purification techniques adopted were membrane ultrafiltration, gel filtration chromatography, solid phase extraction (SPE), and reversed-phase high-performance liquid chromatography (RP-HPLC). Purified peptides were identified by de novo peptide sequencing. From papain hydrolysate, three peptide sequences were identified: AGAPGG, AERQ, and RDTQ (428.45, 502.53, and 518.53 Da, respectively). Peptides synthesized from these sequences exhibited cytotoxicity on HeLa cells with median effect concentration (EC_{50}) values of 8.6, 4.9, and 5.6 mmol/L, respectively, up to 5.8-fold stronger than the anticancer drug 5-fluorouracil. When tested at their respective EC_{50}, AGAPGG, AERQ, and RDTQ showed only 16%, 25%, and 11% cytotoxicity to non-cancerous Hek293 cells. In conclusion, AERQ, AGAPGG, and RDTQ are promising candidates for future development as peptide-based anticancer drugs.

Key words: Anticancer therapy; Bioactive peptide; Cytotoxicity; HeLa cells; *Sarcophyton glaucum*; Soft coral
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1 Introduction

Cancer is one of the leading causes of morbidity and mortality worldwide. There were about 14 million new cancer cases and 8.2 million cancer deaths in 2012 globally. It was projected that in the next 20 years, new cases will increase by about 70% (Ferlay et al., 2013). Unfortunately, chemotherapy, a common cancer

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