

ABSTRACT

Alpinia scabra (Blume) Náves belonging to the botanical family Zingiberaceae, is an aromatic, perennial and rhizomatous herb, which is sometimes known by its vernacular name '*Lengkuas raya*' among the locals. It is a wild species which grows largely on mountains at moderate elevations in Peninsular Malaysia, but it can also survive in lowlands like in the states of Terengganu and Northern Johor. The experimental approach in the present study was based on bioassay-guided fractionation. The methanol and fractionated extracts (hexane, chloroform and water) of *A. scabra* leaves, rhizomes, roots and pseudo stems were investigated for their cytotoxic effect against selected human cancer cell lines, namely hormone-dependent breast carcinoma cell line (MCF7) and ovarian cancer cell line (SKOV-3) using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. The identified cytotoxic extracts were then subjected to chemical investigations in order to identify the active ingredients. A normal human lung fibroblast cell line (MRC-5) was used to determine the specificity for cancerous cells. The cytotoxic extracts were also subjected to morphological assessment, DAPI nuclear staining and DNA fragmentation analysis. The leaf (hexane and chloroform) and rhizome (chloroform) extracts showed high inhibitory effect against the tested cell lines. Ten fractions (LC1-LC10) were obtained after purification of the leaf chloroform extract. Fraction LC4 which showed excellent cytotoxic activity was further purified and resulted in seventeen sub-fractions (VLC1-VLC17). Sub-fraction VLC9 showed excellent cytotoxicity against MCF7 and SKOV-3 cells but not toxic against normal MRC-5 cells. Meanwhile, eighteen fractions (RC1-RC18) were obtained after purification of the rhizome chloroform extract, by which fraction RC5 showed cytotoxicity against SKOV-3 cells with high selectivity index. There were marked morphological changes when observed using phase-contrast inverted

microscope, DAPI nuclear staining and also DNA fragmentation in MCF7 and SKOV-3 cells after treatment with the cytotoxic extracts and fractions which were indicative of cell apoptosis. Methyl palmitate and methyl stearate were identified in the hexane leaf extract by GC-MS analysis. The data obtained from the current study demonstrated that the cytotoxic extracts and fractions of *A. scabra* inhibited the tested cancer cells mainly through apoptosis induction which were characterized by apoptotic morphological changes and DNA fragmentation. The active ingredients in leaf sub-fraction VLC9 and the rhizome fraction RC5 may lead to the discovery of valuable compounds that have the ability to kill cancer cells but not normal cells.