Abstract

Cancer is an uncontrolled cell proliferative disease in humans and currently there is a significant scientific and commercial interest in discovering new antitumor drugs from natural sources. Use of herbal drug as an alternate form in health care is increasing and screening of plants for bioactive compounds became an essential source of cancer-related drugs. Regarding the presence of active anticancer compounds in medicinal plants, present study was undertaken to investigate the antiproliferative effect from selected medicinal plants on A-549 (lung cancer) cells and primary cell culture (chick embryo fibroblast cells) using MTT assay. Here primary cell culture of chick embryo fibroblast cells was used as normal cells. *V. negundo, B. racemosa* and *B. monosperma* were potent plant among all selected plants showing anticancer activity against lung cancer cell-line compare to normal cells. Based on their anticancer activities, methanolic extracts of these plants were selected and their partition in hexane, chloroform, ethylacetate, butanol and water was done. All this fractions were again screened for their anti-proliferative activity.

Among them ethylacetate fraction of *V. negundo* (VnEAE) has most potent antiproliferative activity. Phytochemical analysis of the extract revealed the presence of different secondary metabolites in *V. negundo*. Antioxidative activity of VnEAE was investigated through DPPH and ABTS activity. VnEAE was found to cause characteristic apoptotic morphological changes and generation of ROS in A-549 cells. Ethylacetate extract of *V. negundo* inhibit growth of cancer cells by apoptosis pathway was confirmed using different apoptosis assay. VnEAE induced apoptosis in A-549 was supported by DNA fragmentation and DAPI staining.

To investigate molecular mechanism behind cytotoxic effect of VnEAE, quantitative real time PCR was used to measure expression levels of p53, Bax, Bcl2, caspase-3 and caspase-9. It showed up regulation of p53, Bax, caspase-3 and caspase-9 but down regulation of Bcl2 apoptotic gene also providing supportive data. Using LC-MS and ¹H-NMR technique cytotoxic compounds (luteolin and p-hydroxy benzoic acid) were identified which increased caspase-3 activity in a dose and time dependent manner in A-549 treated cells. Overall, the antiproliferative activities of both compounds give some support to their use in traditional medicine used to treat cancer.