Evaluation of the cytotoxicity, cell-cycle arrest, and apoptotic induction by *Euphorbia hirta* in MCF-7 breast cancer cells

Abstract

**Context:** *Euphorbia hirta* L. (Euphorbiaceae) has been used as a folk remedy in Southeast Asia for the treatment of various ailments.

**Objective:** The current study evaluates the cytotoxicity, cell-cycle arrest, and apoptotic induction by *E. hirta* in MCF-7 breast cancer cells.

**Materials and methods:** Cytotoxic activity of methanol extract of whole part of *E. hirta* was determined by the MTT assay at various concentrations ranging from 1.96 to 250.00 µg/mL in MCF-7 cells. Cell morphology was assessed by light and fluorescence microscopy. Apoptosis and cell-cycle distribution were determined by annexin V staining and flow cytometry. DNA fragmentation, caspase activity, and reactive oxygen species (ROS) assays were performed using the commercially available kits. To identify the cytotoxic fraction, *E. hirta* extract was subjected to bioassay-guided fractionation.

**Results:** *Euphorbia hirta* exhibited significant inhibition of the survival of MCF-7 cells and the half inhibitory concentration (IC\(_{50}\)) values was 25.26 µg/mL at 24 h. Microscopic studies showed that *E. hirta*-treated cells exhibited marked morphological features characteristic of apoptosis. *Euphorbia hirta* extract also had an ignorable influence on the LDH leakage and generating intracellular ROS. The flow...
cytometry study confirmed that *E. hirta* extract induced apoptosis in MCF-7 cells. *Euphorbia hirta* also resulted in DNA fragmentation in MCF-7 cells. Moreover, *E. hirta* treatment resulted in the accumulation of cells at the S and G_{2}/M phases as well as apoptosis. The caspase activity study revealed that *E. hirta* extract induced apoptosis through the caspase-3-independent pathway by the activation of caspase-2, 6, 8, and 9. *Euphorbia hirta* hexane fraction, namely HFsub4 fraction, demonstrated highest activity among all the fractions tested with an IC_{50} value of 10.01 µg/mL at 24 h.

Discussion and conclusion: This study revealed that *E. hirta* induced apoptotic cell death and suggests that *E. hirta* could be used as an apoptosis-inducing anticancer agent for breast cancer treatment with further detailed studies.

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- Anticancer,
- caspase,
- G_{2}/M phase arrest,
- S phase arrest

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Author affiliations

- a Institute for Research in Molecular Medicine (INFORMM), Universiti Sains Malaysia, USM, Penang, Malaysia,
- b RIKEN-USM Joint Research Unit, RIKEN, Wako, Saitama, Japan,
- c School of Biological Sciences, Universiti Sains Malaysia, Penang, Malaysia,
- d Advanced Medical and Dental Institute, Universiti Sains Malaysia, Penang, Malaysia,
- e Faculty of Dentistry, Dental Research & Training Unit, and Oral Cancer Research and Coordinating Centre (OCRCC), University of Malaya, Kuala Lumpur, Malaysia, and
- f Faculty of Health, Nanomedicine – Laboratory of Immunology and Molecular Biomedical Research (LIMBR), School of Medicine (SoM), Institute for Frontier Materials (IFM), Deakin University, Waurn Ponds, Victoria, Australia

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