Apoptosis in human Breast cancer cell line MCF-7 induced by water soluble extracts and smoke of Artemisia princeps var orientalis

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Abstract

Dried leaves of *Artemisia princeps var orienatlis* (*A. princeps*) are used in oriental practice of moxibustion which is promoted for improving general health. In this study, we have evaluated the ability of *A. princeps* smoke and water extract to induce apoptosis in human breast cancer MCF-7 cells *in vitro*. Tumor cells were cultured with smoke or water extract (1.5-50% V/V) for 72 hrs and cytotoxicity and apoptosis were determined by MTT assay and TUNEL technique. Smoke and water extracts of *A. princeps*, in a dose dependent manner, inhibited the growth of breast cancer cells but they had no effect on the survival of normal blood lymphocytes. The IC50 values for smoke and water extract were 4±2% and 5± respectively. *A. princeps* smoke induced apoptosis in MCF-7 cells as determined by TUNEL assay and induction of apoptosis was associated with activation of caspases 3, 8 and 9, depolarization of mitochondrial membrane potential, and down regulation of BCL2 expression. Furthermore *A. princeps* smoke exerted synergistic cytotoxicity with, doxorubicin, a conventional chemotherapeutic agent. These data suggest that *A. princeps* smoke and extracts induce apoptosis in breast cancer cells via mitochondrial pathway and they may represent a novel adjuvants for the treatment of breast cancer.
Introduction

Breast cancer is now the second leading cause of cancer death in women. A prerequisite for successful treatment of breast cancer is the susceptibility of cancer cell to apoptosis. Indeed, most of the current conventional approaches to treating breast cancer including radiation, chemotherapy, biological and hormonal therapy with Tamoxifen and Herceptin induce apoptosis in breast cancer cells (1-6). Despite significant advances in primary and adjuvant treatment for local breast cancer, many patients suffer a systemic relapse. Therefore there is a need to identify new agents that induce apoptosis and develop complimentary and/or alternative treatments for the treatment of breast cancer.

Apoptosis is an orchestrated form of cell death in which cells commit suicide. Abnormal apoptosis is associated with a wide variety of human diseases such as cancer, autoimmune disease and neurodegenerative diseases. The two most common apoptotic pathways are the extrinsic pathway and the intrinsic pathway (mitochondrial pathway (7,8)). Extrinsic pathway is initiated by stimulation of death receptors (eg CD95, TNFR 1) in the plasma membrane (9,10). Intrinsic pathway is initiated by chemotherapeutic agents, radiation and other cellular stresses that disrupt mitochondrial integrity (11,12). Both apoptotic pathways culminate in the activation of caspases, a family of intracellular cysteine proteases, which can disrupts cells within a few minutes of their activation (13,14).