



Cannabis 2019: Multidisciplinary modern scientific approaches for the discovery of natural products anticancer agent: From myth to science

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Abstract

From ancient time traditional medicinal plants based herbal formula has made countless contribution to the well-being of the human population. Currently, more and more evidence showing the efficacy and potential of medicinal plants through the multidisciplinary modern approaches for the discovery of natural products anticancer agent. The multidisciplinary modern scientific approaches will help to reveal and uncover the “mystery” of traditional medicinal plants properties to the modern science world. Therefore, the present study was conducted to investigate the anticancer effects and mechanism of *Calophyllum inophyllum* L. (*Calophyllaceae*) fruit extract against MCF-7 cells via multidisciplinary modern scientific approaches. *C. inophyllum* fruit extract was found to have markedly cytotoxic effect against MCF-7 cells in a dose-dependent manner with the IC₅₀ for 24 hours of 23.59 µg/mL. Flow cytometry analysis revealed that *C. inophyllum* fruit extract mediated cell cycle at G₀/G₁ and G₂/M phases and MCF-7 cells entered the early phase of apoptosis. Herbal medicine has become a very safe, non-toxic, and easily available source of cancer-treating compounds. Herbs are believed to neutralize the effects of diseases in a body because of various characteristics they possess [4]. For instance, among the many anticancer medicinal plants, *Phaleria macrocarpa* (local name: Mahkota dewa) and *Fagonia indica* (local name: Dhamasa) have been used traditionally for the anticancer properties of their active ingredients. Metabolites extracted from the plant material are used to induce apoptosis in cancer cells. Gallic acid as the active component was purified from the fruit extract of *P. macrocarpa* and has demonstrated a role in the induction of apoptosis in lung cancer, leukemia, and colon adenocarcinoma cell lines. It is a polyhydroxy phenolic compound and a natural antioxidant that can be obtained from a variety of natural products i.e., grapes, strawberries, bananas, green tea, and vegetables. It also plays a critical role in preventing malignancy transformation and the development of cancer [10]. Similarly, other compounds such as vinca alkaloids, podophyllotoxin, and camptothecin obtained from various plants are used for the treatment of cancer. The expression of anti-apoptotic proteins Bcl-2 was decreased whereas, the expression of the proapoptotic protein Bax, cytochrome C and p53 were increased after treatment. *C. inophyllum* fruit extract led to apoptosis in MCF-7 cells via the mitochondrial pathway in a dose dependent manner. This is evidenced by the elevation of intracellular ROS, the loss of mitochondria membrane potential ($\Delta\psi_m$) and activation of caspase-3. Meanwhile, dose-dependent genomic DNA fragmentation was observed after *C. inophyllum* fruits extract treatment by comet assay. These studies show that *C. inophyllum* fruits extract-induced apoptosis are primarily p53 dependent and mediated through the activation of caspase-3. *C. inophyllum* fruit extract could be an excellent source of the chemopreventive agent in the treatment of breast cancer and has potential to be explored as a green anticancer agent. Consequently, scientist hopes that more evidence-based multidisciplinary modern scientific approaches to studying traditional medicinal plants will be provided to lifting the mysterious veil.

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