Research Article

Induction of Apoptosis of 2,4',6-Trihydroxybenzophenone in HT-29 Colon Carcinoma Cell Line

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2,4',6-Trihydroxy-4-methoxybenzophenone was isolated from the ethyl acetate fraction of Phaleria macrocarpa (Scheff.) Boerl. fruits. It was found to inhibit cell proliferation in HT-29 human colon carcinoma cell line but caused little damage to WRL-68 normal human liver and MRC-5 normal human fibroblast lung cell lines. The compound was found to sharply affect the viability of HT-29 cells in a dose- and time-dependent manner. HT-29 cells treated with the compound showed morphological changes under microscopic examination such as cell shrinkage, membrane blebbing, DNA fragmentation, and the occurrence of apoptotic nuclei. The percentage of early apoptotic, late apoptotic, and dead or necrotic cells was determined by flow cytometry using annexin V-FTIC/PI staining. In addition, flow cytometry showed that, when the HT-29 cells were treated with 115 μM of the compound, it resulted in G0/G1 phase arrest in a time-dependent manner. Western blot revealed an upregulation of PUMA, Bak, Bcl-2, and Mcl-1 proteins suggesting that the compound induced apoptosis in HT-29 cells by regulating these proteins.

1. Introduction

Cancer refers to a family of diseases in which tissues multiply and spread unregulated throughout the body, the result of which may lead to death [1]. It is a major public health problem and has significantly increased the worldwide death rate. One of the most common types of cancer is colon cancer. Modern advances in cellular and molecular biology have increased our understanding of the various mechanisms of cancer [2]. Nowadays, there are many natural compounds and mechanism-based approaches to cancer treatment that have the potential to be successful. The development of anticancer drugs has also seen a massive contribution from natural products [2].

Phaleria macrocarpa (Scheff.) Boerl. is a medicinal plant belonging to the Thymelaeaceae family and in Indonesia it is locally known as Mahkota Dewa. The edible fruits of this plant are usually mixed with other Indonesian herbs and used in herbal medicine [3]. The fruits of P. macrocarpa consist of the skin which have a bright red color, a white, fibrous, and watery flesh, a shell, and a seed. In alternative medicine, it is used in the treatment of cancer, diabetes mellitus, nerve pain, kidney failure and disorder, liver dysfunction, serious illnesses, hypertension, skin diseases, and management of cholesterol levels.

Research on the use of the extracts of P. macrocarpa fruits as a possible anticancer agent is extensive. Prior research has shown that an ethanol extract from the flesh of the P. macrocarpa fruit toxic towards HeLa cell line derived from cervical carcinoma [4]. It has been shown that different parts of P. macrocarpa fruit showed excellent antioxidant activities and good anti-inflammatory and high cytotoxic activities against HT-29, MCF-7, and HeLa cell lines [5]. Gallic acid isolated from P. Macrocarpa has been shown to possess anticancer properties against human esophageal cancer cells (TE-2) but no cytotoxic effect was observed on noncancerous (CHEK-1) cells [6]. The major compound of Phaleria obtained from P. macrocarpa fruits has been found to have high cytotoxic effect on MDA-MB231 breast cancer cell lines [7]. DLB1425 of the extraction of P. macrocarpa flesh fruits inhibited proliferation of MDA-MB231 and MCF-7 cells, activation of caspase 9, and downregulation of Bax and Bcl-2 at the