Apoptosis induced in MCF-7 human breast cancer cells by 2',4'-dihydroxy-6-methoxy-3,5-dimethylchalcone isolated from *Eugenia aquea* Burm f. leaves

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Abstract. During a previous study that aimed to identify anticancer agents within primate-consumed plants, the present group identified that *Eugenia aquea* (*E. aquea*) possessed potential as a source of anticancer agents. The ethanol extract of *E. aquea* leaves exhibited strong inhibitory activity against the proliferation of the human breast adenocarcinoma MCF-7 cell line. The inhibition of proliferation was determined using an MTT assay. The present study was performed to isolate the active compound within the *E. aquea* leaves that generated the aforementioned activity, and resulted in the isolation of 2',4'-dihydroxy-6-methoxy-3,5-dimethylchalcone, which was identified through the analysis of spectroscopic data. This compound was examined for its inhibitory activity against the MCF-7 cell line using a MTT assay, and the ability of 2',4'-dihydroxy-6-methoxy-3,5-dimethylchalcone to induce apoptosis through the activation of the poly(adenosine diphosphate-ribose) polymerase (PARP) protein was also investigated. The results of the present study revealed that the isolated compound inhibited cell proliferation in a dose-dependent manner, possessed an IC_{50} of 74.5 μg/ml (250 μM) and promoted apoptosis via the activation of PARP. It was concluded that these results indicated a requirement for additional investigations into 2',4'-dihydroxy-6-methoxy-3,5-dimethylchalcone in order to provide a basis for the use of this compound in the management of cancer.

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Introduction

Breast cancer is a type of cancer that accounts for >1.2 million new cases worldwide and 500,000 mortalities annually, resulting in breast cancer being the most malignant form of cancer among females (1). Numerous clinically-used drugs are available for the treatment of cancer, including breast cancer, but the use of these agents does not provide optimum effectiveness for the treatment of the disease. The majority of the drugs result in serious side-effects, which generates excessive damage to normal cells (2). Therefore, investigating anti-cancer drugs of plant origin continues to provide novel and significant possibilities for anti-cancer agents. Numerous types of bioactive compounds from medicinal plants have been isolated at present and several of these compounds are currently undergoing further investigation (3-5).

Plants consumed by primates are considered to be a promising source of therapeutic agents for the management of human diseases, including cancer (6). Previous investigations have been performed on primate-consumed plants to assess their anti-tumor activity (6). Additional investigations led to the isolation of kaempferol-3-*O*-rhamnoside from the leaves of *Schima wallichii* Korth, a plant commonly consumed by primates. Kaempferol-3-*O*-rhamnoside exhibited inhibitory activity against MCF-7 breast cancer cell proliferation through the activation of the caspase cascade pathway (7). In another study, 42 species of primate-consumed plants that grow in Indonesia were evaluated for their antiproliferative activity against MCF-7 human breast cell lines using a MTT bioassay. The results revealed that certain plant extracts demonstrated strong inhibitory activity against MCF-7 cell proliferation, and one of these was the extract from the leaves of *Eugenia aquea* (*E. aquea*) (8). The present study aimed to identify the active compound derived from the leaves of *E. aquea,* responsible for the antiproliferative activity against MCF-7 cell lines, and to examine the pro-apoptotic activity of this compound.