

Exploring the Anti-Cancer Effects of *Psidium guajava* L. and *Curcuma longa* L. against Breast Cancer

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Abstract: Background: Breast cancer is a prevalent and fatal disease in women, with the boundaries of traditional remedies such as radiation, surgery and chemotherapy that damage healthy cells. Natural sources, rich in phytochemicals, provide possible options for cancer treatment. The objective of this study is to review the anticancer properties of guava leaves (*Psidium Guajava* L.) and turmeric rhizome against breast cancer. Methodology: This study employed a literature review functioning, which is to analyze phytochemical composition and guava leaves and an anticancer capacity of turmeric rhizomes. A total of 25 relevant studies were reviewed from journals, including 15 studies on guava leaves and 10 studies on turmeric. Secondary data was obtained and analyzed through several stages to draw a conclusion. The findings of these studies were synthesized to provide a comprehensive understanding of the anticancer properties of guava leaves and turmeric. The purpose of the review is to provide a strong theoretical basis for their possible use as drug agents against breast cancer. Results: Guava Leaf Extracts contain flavonoids, tannins, alkaloids, saponin and terpenoids that prevent cancer cell proliferation. Turmeric contains curcumin, tannins, alkaloids, terpenoids, flavonoids, glycosides, and sterols, which display the anticancer properties. Curcumin reduces histamine production in turmeric, breast cancer motivates dehydration in cells, and promotes apoptosis. The presence of phytochemicals in guava leaves and turmeric rhizomes shows their ability as anticancer agents. Bioactive compounds in these plants can provide a promising approach to the treatment of breast cancer, in which curcumin is playing an important role in induction of apoptosis in cancer cells. Conclusion: Guava leaves and turmeric rhizomes demonstrate important anticancer properties, making them a potential natural agent for the treatment of breast cancer. Further research has been warned to detect their medical applications and develop effective treatment.

Keywords: breast cancer; apoptosis; curcumin; natural sources; phytochemical

1. Introduction

Cancer is a common term for a large group of diseases that can affect any part of the body. Other words used are malignant tumors and neoplasm. A defined characteristic of cancer is the rapid construction of abnormal cells that grow beyond their normal boundaries, and which can then invade parts of the body nearby and spread to other organs; The latter process is known as metastasis. Comprehensive metastases are the primary cause of death from cancer. Cancer occurs from the change of normal cells in tumor cells in a multi-step process that usually grows from a pre-cancer wound to a deadly tumor. These changes are the result of interaction between a person's genetic factors and three categories of external agents, including:

- Physical carcinogenes, such as ultraviolet and ionizing radiation;
- Chemical carcinogenes, such as asbestos, tobacco smoke components, alcohol, aflatoxine (a food contaminated), and arsenic (a drinking water contaminated); and
- Organic carcinogenes, such as some viruses, bacteria, or parasites infections.

The use of tobacco, alcohol consumption, unhealthy diet, physical inactivity and air pollution is a risk factor for cancer and other non -gourd people. Some chronic infections are risk factor for cancer; It is a special issue in lower and medium-oriented countries. About 13% of cancer globally diagnosed in 2018 was attributed to carcinogenic infection, including *Helicobacter Pylori*, Human Papillomavirus (HPV), Hepatitis B virus, Hepatitis B virus and Epstein-bar viruses.

The occurrence of cancer increases dramatically with age, most likely that risk for specific cancer growing with age is created. The overall risk accumulation is combined with the tendency of cellular repair mechanisms, as a person is less effective with being large. Cancer is the second biggest cause of death after heart disease. Depending on WHO data, the death rate worldwide reached 13% due to cancer. Every year, 12 million people in the world were suffering from cancer and 7.6 million of them died. The number of cancer patients will continue to increase. In 2030, it is estimated that it will reach 26 million people with death, expecting about 17 million (Ministry of Health 2015).

Based on basic health research data in 2007, the national rate of cancer patients in Indonesia was 4.3 per 1000 population, with high cancer rates in women than men. Among women, 5.7 per 1000 people in Indonesia were suffering from cancer. Meanwhile, 2.9 per 1000 male population experience Cancer (Ministry of Health of Indonesia; Davi and Hendrati 2015). In 2020, 9.23 million women worldwide detected cancer, and 4.43 million women died of cancer. By 2040, these numbers are estimated to increase to 13.3 million new cases and 7.1 million deaths, which represent a 44% increase in new cases and 60% increase in deaths. Properly, this remarkable increase in new cases is much higher in low - income countries than high -income countries, and only one -third of differences can be explained by demographic changes.

Common types of cancer on women are breast cancer that causes death in women. The American Cancer Society (2008) reported that 1.3 million women worldwide had detected breast cancer. Every year, about 465,000 women

died of breast cancer. Within 25 years, the number of patients in developed countries increased by about 30% (Vahuni 2015). Breast cancer is considered one of the major causes of death in women after menopause for 23% of all cancer deaths. This is now a global issue, but still diagnosed in their advanced stages due to the self-inspection of the breast and the negligence of the clinical examination. According to the World Health Organization (WHO), increasing the results and existence of breast cancer by early detection is the foundation of the rules of breast cancer. Various modern drugs are prescribed to treat breast cancer. Breast cancer therapy with anti-estrogens such as Roccifen or Tamoxifen can avoid breast cancer in individuals that increase the chances of developing it

Breast cancer is usually treated with radiation techniques, surgery and chemotherapy. However, these techniques have side effects as they sometimes increase cancer cells to spread to other parts of the body, damage healthy cells, and can also trigger cancer cells to mutate cells. Surgery of both breasts is an additional preventive measure in some increased possibility of cancer development in women. In patients identified with breast tumors, various strategies of management are used such as targeted therapy, hormonal therapy, radiation therapy, surgery and chemotherapy. In individuals with distant metastasis, management is usually aimed at increasing the quality of life and survival rate. Unpleasant side effects of the treatment of breast cancer are one of the most inspiring factors to find some alternative methods. The use of herbs to treat patients with breast cancer is considered a natural option, as some plants may have properties that naturally have the ability to treat breast cancer. Thus, the discovery of new drugs that are safe with less side effects, it is necessary to overcome this problem (Muhartono and everyone's 2015).

Psidium Guajava L. and *Curcuma Longa* L. are two common plants, producing secondary metals such as tannins, flavonoids, alkaloids, and saponin (Korea et al. 2016). Turmeric (*Curcuma longa* L.) rhizome has curcumin which also has anticancer properties that can prevent carcinogenesis (Meiyanto 1999; Nurrochmad 2004). Thus, guava (*Psidium guajava* L.) and turmeric (*Curcuma longa* L.) can be used as an alternative to breast cancer without low side effects or without any side effects. This review focuses on the anticancer properties of guava leaves (*Psidium Guajava* L.) and turmeric rhizome against breast cancer.

2. Methodology

A literature study was carried out to support ideas that are based on a strong theoretical basis on several sources consisting of several leading journals.

A total of 25 relevant studies from leading journals were reviewed, including 15 studies on guava leaves and 10 studies on turmeric rhizome. Secondary data were obtained and analyzed through several stages to draw a conclusion. The findings from these studies were synthesized to provide a comprehensive understanding of the anticancer properties of guava leaves and turmeric rhizome. The review aimed to provide a strong theoretical basis for their potential use as pharmaceutical agents against breast cancer.

3. Results and Discussion

Guava (*Psidium guajava* L.) and turmeric (*Curcuma longa* L.) are two common plants obtaining compounds that inhibit the growth of cancer cells based on phytochemical properties.

Through the literature, guava leaf extract consists of flavonoids, tannins, alkaloids, saponins, terpenoids that inhibit the proliferation of cancer cells. Besides, turmeric also has tannins, alkaloids, terpenoids, flavonoids, glycosides, sterols, and curcumin.

The presence of curcumin reduces histamine production which induces inflammation and decrease toxin. Because of curcumin, breast cancer cells have dehydration before apoptosis

Guava extracts purified from leaf and bark has many bio-active molecules with anti-cancer activities. In addition, lycopene-rich extracts obtained from red guava fruit can induce apoptosis in estrogen receptor-positive breast cancers. Red guava extracts can, through caspase-3 activation and PARP cleavage signaling, induce apoptotic and necrotic death in TNBC cells. Based on Dwitianti (2015), 70% ethanol extract from guava leaves had cytotoxic properties against T47D breast cancer cells with a concentration of 130.62 µg mL⁻¹ capable of killing breast cancer cells by 88.52% which were incubated for 24h. Secondary metabolites such as tannins, alkaloids, and saponins contained in guava leaves also inhibited the growth and spread of cancer cells by inhibiting the proliferation of cancer cells (Correa et al. 2016). The mechanism of flavonoids and alkaloids have properties as antineoplastic agents that can inhibit and even kill cancer cells by inhibiting DNA synthesis and inhibiting mitosis at the metaphase and anaphase stages of cancer cells (Purwaningsih et al. 2015). Saponin compounds also play a role in inhibiting cancer cells because they are antiproliferative, antimetastatic, and also antiangiogenesis. Saponins induce apoptosis and cell differentiation (Xu et al. 2016).

Curcumin has been utilized for centuries in traditional medicine, particularly in traditional Chinese medicine herbal systems. Studies demonstrated that curcumin possesses potential chemical properties contributing to anti-breast cancer (anti-BC) effects on several phenotypes through the following mechanisms:

- (a) inhibition of P-glycoprotein activity and reduction in drug resistance;
- (b) induction of the cell cycle;
- (c) initiation of apoptosis and ferroptosis; and
- (d) Regulation of the progression of the epithelial-mesenchymal transition (EMT).

Turmeric rhizome extract suppressed the growth of MCF-7 and MDA-MB-231 breast cancer cells. Curcumin contained in turmeric rhizome extract triggered apoptosis. The rate of apoptosis of MCF-7 and MDAMB-231 breast cancer cells correlated with the curcumin concentration. It induced the Bax protein used in cell apoptosis and inhibited Bcl-2

protein expression as an antiapoptotic protein (Lv et al. 2014). Curcumin also acts as an autophagy modulator which is a tumor angiogenesis and metastatic inhibitor through the suppression of various growth factors including VEGF, COX-2, MMPs, and ICAMs (Wilken 2011; Kurniawan et al. 2016). Apart from curcumin, turmeric (*C.longa* L.) rhizome also contains several compounds that play a role in inhibiting or even killing cancer cells such as alkaloids, flavonoids, and tannins with certain mechanisms. They enhance the anticancer potential of turmeric.

4. Conclusion

Guava leaves (*Psidium guajava* Linn.) contain several compounds that act as anticancer consisting of alkaloids, flavonoids, saponins, and steroids. Turmeric (*Curcuma longa* Linn.) rhizome contains curcumin and several other compounds such as alkaloids, flavonoids, and tannins which have anticancer properties. The mechanisms of these compounds as anticancer include inhibiting the proliferation of cancer cells and inducing apoptosis of breast cancer cells. Further research is needed to determine the perfect combination of both ingredients in preventing other types of cancer.

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