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ANTICANCER ACTIVITY OF GUAVA LEAF EXTRACT (PSIDIUM GUAJAVA)

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ABSTRACT
Free radicals are chemical compounds that are highly reactive and potentially harmful to the body's cells. At high levels, free radicals can be a serious health risk, causing damage to key components of cells. Cellular damage caused by free radicals, especially to Deoxyribonucleic Acid (DNA), can result in the development of cancer and other health problems. Guava seed leaf (Psidium guajava) was the focus of the study due to its potential in reducing breast cancer cell growth. This research details the results of two literature review studies that support this claim. Bioactive compounds such as polyphenols, flavonoids, phenolic acids, and ascorbic acid found in guava seeds have been linked to antioxidant and anti-inflammatory properties. The first study by showed that guava leaf extract has anti-proliferative activity against breast cancer cells (MDA-MB-231 and MG-63). The second study highlighted the cytotoxic activity of 70% ethanol extract of guava leaves against T47D breast cancer cells. The results of both studies showed that guava seeds have the potential to inhibit breast cancer cell growth, indicating a possible role for guava seeds in breast cancer prevention strategies.

INTRODUCTION

In Indonesia, guava (Psidium guajava) leaves are one of the plant assets that have an important role in the context of health and agriculture. This plant is not only widespread in various parts of Indonesia but also an integral part of people's daily lives. Guava leaves are characterized by their wide shape, and glossy green color, and are often used in various forms of traditional medicine (Asiandu, Sari, Sari, & Majid, 2023). Indonesians have recognized and utilized its benefits for generations, both as an herbal concoction and part of their daily diet.

Indonesia's tropical climate provides a very favorable environment for the growth and development of guava plants. This plant can be easily found in home yards, gardens, or even growing wild in various locations (Ashraf et al., 2016). Guava leaves are known to contain various active compounds, including flavonoids, tannins, and phenolic acids, which contribute to the antioxidant and anti-inflammatory properties of this plant. Therefore, in the context of natural resource utilization and public health, guava leaves play a significant role in Indonesia.

Herbal plants have long been the focus of research to explore the potential of natural treatments for various diseases, including cancer. One plant that has caught the attention of

researchers is Psidium guajava, better known as the guava plant. Guava leaves have been traditionally recognized as a source of various bioactive compounds that have health potential. In this context, our study aims to explore guava (Psidium guajava) leaf extracts that have anticancer activity as a potential alternative in the development of cancer therapy.

Guava (Psidium guajava) has long been recognized as a valuable herbal plant in the natural medicine tradition. The success of guava as an herbal plant can be seen from its phytochemical content. Bioactive compounds such as flavonoids, alkaloids, tannins, polyphenols, and triterpenoids are some of the main ones that are often utilized in guava leaves (Dwitiyanti, 2015). The unique combination of these compounds gives guava its antioxidant, anti-inflammatory, and antimicrobial properties. These properties naturally make guava an attractive option in the prevention and treatment of various diseases.

The utilization of guava as an herbal plant is also linked to its diverse health benefits. Guava leaf extract (Psidium guajava) has been known to have anticancer potential, boost the immune system, and aid in the management of diabetes. In addition, the anti-inflammatory content found in guava leaves can relieve various inflammatory conditions and have a positive effect on the health of the digestive tract (Indriani, 2006). The continued growth of this plant in various tropical and subtropical regions, including in Indonesia, makes guava leaves a sustainable choice as an herbal plant that can support overall public health.

Guava, which is widespread in various tropical and subtropical regions, has long been used in traditional medicine as an herbal remedy (Indriani, 2006). Although its properties have been empirically recognized, more in-depth scientific research is still needed to identify and understand the active compounds contained in guava leaves, as well as their potential to inhibit cancer cell growth. This research is expected to contribute significantly to further understanding of the anticancer potential of this plant.

In our research, we will use qualitative methods by collecting data related to active compounds contained in guava leaves and testing anticancer activity using certain cancer cell models. The results of this study are expected to provide new insights into the development of plant-based cancer therapies and increase our understanding of the potential of guava leaves (Psidium guajava) as a potential source of anticancer compounds. Thus, this research can open the door toward further utilization of natural resources for the development of more effective and sustainable cancer therapies.

RESEARCH METHODS

In conducting this research, the researcher will adopt a qualitative approach as the methodological foundation. This approach was chosen because it is more capable of providing an in-depth understanding of the phenomena observed, by the research objectives to explore quality information related to the anticancer activity of guava leaf extract (Psidium guajava) (Dwitiyanti, 2015). The advantages of qualitative methods lie in their ability to detail complex aspects of the object of research, identify patterns, and describe the context holistically, leaving room for rich and in-depth interpretations.

In the data collection process, the researcher will use the literature review technique. A literature review is an effective method for compiling a comprehensive understanding of previous research and recent developments in the field of study. A literature review study is a research method that refers to the collection, evaluation, and synthesis of information that has

been published in the scientific literature related to a particular research topic. The main purpose of the literature review study is to present a comprehensive understanding of existing knowledge, identify knowledge gaps, and develop a theoretical basis for the research to be carried out. The researcher will focus the literature review on peer-reviewed journals that are relevant to the research title. This step aims to collect high-quality scientific information that can support the theoretical basis of the research. The literature review study process will be carried out through searches on Google Scholar, ResearchGate, ScienceDirect, and others to ensure that the understanding of previous research accessed is up-to-date and has high scientific credibility.

RESULTS AND DISCUSSION

No	Extract(s)	Dose	Cell line models	Experimental Methods	Chemical Extraction Results	Mechanisms of anticancer	Reference
1	Leaf extracts of *Psidium guajava*	50µl	MCF-7 cancer cell lines	Trypan blue exclusion	5-fluorouracil	-	(Yadav & Mohite, 2020)
2	Leaf extracts of *Psidium guajava*	20µL	The EA.hy926 human vascular endothelial cell line and the HCT116 human colon carcinoma cell line	The maceration method.	2,2-diphenyl l-1-picrylhydraz l	inhibition of angiogenesis	(Lok et al., 2020)
3	Leaf extracts of *Psidium guajava*	50µl	HT-29 cell line	Method by Gutfinge and vanillin method	(3-(4,5 dimethylthiaz ol -2 yl) -2,5, diphenyltetraz olium bromide).	activated by various stimuli, including chemotherap eutic agents and radiation.	(Lee & Park, 2010)
4	Leaf extracts of *Psidium guajava*	50µg, 100g and 200µg /mL	HeLa cell-Line (ATCC#H TB-22)	Maceration with methanol and chloroform	-	HeLa cell-line proliferation inhibition	(Abbas, Ansari, ul Hassan, Alvi, & Abbas, 2020)
5	Leaf extracts of *Psidium guajava*	10,25, 50 dan 100M g/mL	KBM5, SCC4, and U266,	Folin-Ciocalteu and aluminum chloride methods	Phenolic and flavonoid	mitochondria l dehydrogenas e enzyme in metabolically active cells convert	(Ashraf et al., 2016)

						yellow tetrazolium salt to dark blue formazan and the intensity of blue color predicts cell viability	
6	Ekstrak etanol 70% daun jambu biji.	27,54 µg/m.	Sel T47D (continous cell line)	Metode perhitungan sel	Alkaloid,saponin, flavonoid, tanin dan triterpenoid	-	(Dwitiyanti, 2015)
7	Leaf extracts of *Psidium guajava*	0.0379mg/ml	(HeLa), (MDA-MB-231) and (MG-63)	Extraction method	Anti-proliferative	-	(Sul'ain, Zazali, & Ahmad, 2012)

One of the factors that cause cancer is the presence of free radicals, which can cause cell mutations due to excessive oxidation caused by pollution or chemicals. To prevent cancer, it is important to understand that nutrition plays an important role, including increased consumption of vegetables and fruits that contain natural antioxidants. Many types of antioxidants in food, such as vitamin C, vitamin E, carotenoids, and phenols, can help fight the effects of free radicals. According to research by Putri et al. (2020), the combination of vitamin C with other substances such as flavonoids, anthocyanins, carotenoids, and phenols can be more effective in inhibiting cancer cell growth than consuming vitamin C alone. Guava is one of the fruits rich in vitamin C, and phytochemical research on its leaves shows the content of amino acids tryptophan, lysine, vitamin C, vitamin B1, calcium, phosphorus, iron (Fe), phosphorus, and phytonutrient compounds such as pectin and tannins. According to research by Lim (2006) and Thunytong (2011), guava contains lycopene and fiber with high antioxidant content, including ascorbic acid and phenols, which exceeds that of white guava with 112 mg/g of ascorbic acid (Vitamin C) and 163.36 mg of phenols, respectively.

Based on the results of the literature review study conducted by (Sul'ain et al., 2012) titled "Screening on the anti-proliferative activity of Psidium guajava leaves extract towards selected cancer cell lines" aims to evaluate the antiproliferative activity of Psidium guajava leaves extract against some selected cancer cell lines. The study was conducted through an experimental method, in which three specific cancer cell lines were selected for testing, namely cervical cancer (HeLa), breast cancer (MDA-MB-231), and osteosarcoma (MG-63). In this study, Psidium guajava leaves were extracted using three different solvents, namely petroleum ether, methanol, and water. In addition, to see the antiproliferation effect relatively, Madin Darby canine kidney (MDCK) non-malignant cells were used as negative control cells, while the cisplatin area acted as a positive control. The results showed that extraction of Psidium guajava leaves with petroleum ether exhibited the most effective anti-proliferation activity against breast cancer (MDA-MB-231) and osteosarcoma (MG-63) cell lines. Nonetheless, it should be noted that these extracts also exhibited cytotoxic effects against non-malignant cells

(MDCK). These findings provide important insights into the potential of Psidium guajava leaves in inhibiting the growth of certain cancer cells, although it is worth considering the cytotoxic impact against non-malignant cells which also needs to be further evaluated.

Research conducted (Dwitiyanti, 2015) entitled "Guava Leaf (Psidium guajava L.) as Breast Anticancer" aims to evaluate the ethanol extract of guava leaf on cytotoxic activity against T47D cancer cells, which are breast cancer cells. This study used an experimental method with a viable cell count technique to measure the level of cancer cell proliferation. Previously, other studies have proven that quercetin content with a level of 61.71% is found in guava leaves, a compound that has been identified as having cytotoxic potential. In this study, a cytotoxicity test was conducted with the test solution of six different concentrations, namely 130.62; 67.98; 35.98; 18.43; 9.56; and 5 µg/ml. The results showed that the LC50 value (concentration that can kill 50% of cells) of the ethanol extract of guava leaves against T47D cells was 27.54 µg/ml.

With the LC50 value obtained, this study concluded that guava leaf extract significantly showed cytotoxic activity against T47D cancer cells. This finding provides further evidence regarding the potential of guava leaves (Psidium guajava) as a source of bioactive compounds that can be used in the development of anticancer therapy, especially against breast cancer. The statement is based on the findings of literature review studies that show the potential of guava (Psidium guajava) in reducing breast cancer cell growth. In the first study conducted by (Sul'ain et al., 2012), Guava leaf extract was extracted using petroleum ether, and the results showed significant antiproliferative activity against breast cancer cell lines (MDA-MB-231). Similarly, the second study conducted by (Dwitiyanti, 2015), in which 70% ethanol extract from guava leaves showed strong cytotoxic activity against T47D breast cancer cells. In both studies, researchers used experimental methods and direct counting (viable cell count) to measure the antiproliferative or cytotoxic effects of guava extract on breast cancer cells. The results showed that guava leaf extract was able to inhibit the growth of breast cancer cells at certain concentrations. For example, in the study (Dwitiyanti, 2015), The LC50 value (concentration that can kill 50% of cells) of 70% ethanol extract of guava leaves against T47D breast cancer cells was 27.54 µg/ml. This value indicates that the extract can significantly reduce the growth of breast cancer cells at this concentration level.

Guava seeds have been the focus of research due to the possible presence of components that can exert anti-cancer effects. Some of the compounds that have been identified in guava seeds involve polyphenols, flavonoids, phenolic acids, and ascorbic acid. The presence of these compounds sparked research interest due to the antioxidant and anti-inflammatory properties that Psidium guajava has been shown to possess. Polyphenols, for example, have been recognized for their ability to fight oxidative stress and reduce inflammation in the body. Flavonoids, a group of compounds involving quercetin and kaempferol, have been linked to anticancer potential, being able to inhibit cancer cell growth and stimulate cancer cell death (Sul'ain et al., 2012). Phenolic acids are also known to have anti-cancer properties through various mechanisms, including inhibition of cancer cell proliferation. Additionally, ascorbic acid, or vitamin C, is known for its role in boosting the immune system and fighting free radicals. Therefore, while guava seeds offer potential as part of a cancer prevention strategy, more clinical research is needed to understand exactly their impact on breast cancer cell growth in humans.

CONCLUSIONS

Based on research results and literature review studies conducted, there is strong evidence to suggest that guava seeds (Psidium guajava) have the potential to reduce breast cancer cell growth. Guava seeds contain several bioactive compounds, including polyphenols, flavonoids, phenolic acids, and ascorbic acid, which have collectively been shown to have antioxidant and anti-inflammatory properties. Literature review studies conducted by and showed that guava leaf and seed extracts have antiproliferative and cytotoxic activities against breast cancer cells. These findings provide a basis for considering guava seeds as part of a breast cancer prevention strategy, with compounds such as polyphenols, flavonoids, and phenolic acids that may contribute to the inhibition of cancer cell growth.

BIBLIOGRAPHY

Abbas, Muhammad, Ansari, Muhammad Tayyab, ul Hassan, Saeed, Alvi, Muhammad Nadeem, & Abbas, Musharraf. (2020). The Phytochemical and Comparative Anticancer Study of Methanolic and Chloroform Extracts of Psidium guajava L. Leaves of Pakistani Origin. *Journal of Drug Delivery and Therapeutics*, *10*(1-s), 149–153.

Ashraf, Aisha, Sarfraz, Raja Adil, Rashid, Muhammad Abid, Mahmood, Adeel, Shahid, Muhammad, & Noor, Nadia. (2016). Chemical composition, antioxidant, antitumor, anticancer, and cytotoxic effects of Psidium guajava leaf extracts. *Pharmaceutical Biology*, *54*(10), 1971–1981.

Asiandu, Angga Puja, Sari, Widya, Sari, Septi Widiya, & Majid, Alif Syahrul Abdul. (2023). The Anticancer Properties of Guava Leaves (Psidium guajava L.) and Turmeric Rhizome (Curcuma longa L.) Against Breast Cancer: A Literature Study. *Biology, Medicine, & Natural Product Chemistry*, *12*(1), 407–412.

Dwitiyanti, Dwitiyanti. (2015). Daun Jambu Biji (Psidium guajava L.) sebagai Antikanker Payudara. *Pharmaceutical Sciences and Research*, *2*(2), 3.

Indriani, Susi. (2006). Aktivitas antioksidan ekstrak daun jambu biji (Psidium guajava L.). *Jurnal Ilmu Pertanian Indonesia*, *11*(1), 13–17.

Lee, Sang Bong, & Park, Hae Ryong. (2010). Anticancer activity of guava (Psidium guajava L.) branch extracts against HT-29 human colon cancer cells. *Journal of Medicinal Plants Research*, *4*(10), 891–896.

Lok, Bronwyn, Sandai, Doblin, Baharetha, Hussein M., Nazari, V. Mansoureh, Asif, Muhammad, Tan, Chu Shan, & Majid, A. M. S. Abdul. (2020). Anticancer effect of Psidium guajava (Guava) leaf extracts against colorectal cancer through inhibition of angiogenesis. *Asian Pacific Journal of Tropical Biomedicine*, *10*(7), 293–307.

Sul'ain, Mohd Dasuki, Zazali, Khaizil Emylia, & Ahmad, Norliza. (2012). Screening on the anti-proliferative activity of Psidium guajava leaves extract towards selected cancer cell lines. *Journal of US-China Medical Science*, *9*(1), 30–37.

Yadav, Akshay R., & Mohite, Shrinivas K. (2020). Anticancer activity of Psidium guajava leaf extracts on breast cancer cell line. *Research Journal of Pharmaceutical Dosage Forms and Technology*, *12*(4), 298–300.