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Cytotoxic Activity of Ethanol Extract of Mangosteen Peel Extract (*Garcinia Mangostana* Linn.) Against T47D Breast Cancer Cells

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A B S T R A C T

Breast cancer continues to be a major worldwide health concern, necessitating safer and more efficient therapies. Natural substances as possible adjuvants to enhance chemotherapy results and lessen toxicity have been the focus of recent investigations. The purpose of the study was to assess mangosteen peel extract cytotoxic effects on T47D breast cancer cells. The MTT test was utilized to evaluate the cytotoxic effects of mangosteen peel extract (MPE) on T47D breast cancer cells. A microplate reader set to 550 nm wavelength was used to analyze the test findings. Both MPE and doxorubicin (Dox) demonstrated concentration-dependent cytotoxic effects according to the MTT assay with IC50 values of 8.9 µg/mL and 0.5 µg/mL on T47D cells, respectively. Our findings suggest that MPE might be a viable source of anticancer natural agents. The possibility of a new drug being developed in the future to treat breast cancer is increased by this discovery.

Keywords: Cytotoxic activity, *Garcinia mangostana*, T47D cells, Breast cancer

1. Introduction

Breast cancer remains one of the leading causes of death for women worldwide and a significant global health concern (Dange et al., 2017; Sun et al., 2017; Sung et al., 2021). The rates of morbidity and mortality caused by cancer rise each year, while chemotherapy continues to be the primary treatment choice despite its high cost and significant side effects (Globocan, 2020; Kaur et al., 2022). Chemotherapeutic drugs like doxorubicin often lose effectiveness when cancer cells develop multidrug resistance pathways (Kumar et al., 2024; Sen et al., 2024; Sun et al., 2017). Prolonged administration of doxorubicin has been reported to result in cardiotoxic effects (Dali et al., 2022; Jishala et al., 2020; Rawat et al., 2021). Although treatment has advanced, many current therapies for breast cancer are not selective, causing substantial harm to normal cells and reducing their overall efficacy (Jaibu et al., 2018; Perkins et al., 2024). Therefore, it is crucial to develop new cancer drugs that specifically target and eliminate cancer cells, preserving healthy tissues to enhance therapeutic effectiveness and minimize side effects (Navya et al., 2019; Wahyuni et al., 2022). One of the primary goals of current scientific studies is to explore strategies to maximize chemotherapy efficacy against cancer cells and reduce its harmful effects on non-cancerous tissue (Hanušová et al., 2011; Pal et al., 2024). Developing effective and targeted breast cancer treatments remains one of the most pressing and complex objectives in cancer research (Witzel & Müller, 2015). Numerous tropical plants have intriguing biological properties that may have medical uses (Ahmed et al., 2021; Shaikh et al., 2016). Plants with antioxidant and anti-inflammatory properties show potential as natural anticancer agents by mitigating oxidative damage and chronic inflammation (Ifora et al., 2023; Ifora & Rahmaddian, 2022). One of the plants that has the potential to be developed as a cytotoxic agent is *Garcinia mangostana*. Mangosteen peel has cytotoxic effects on MCF-7 cells (Laksmiani, 2019), and K-562 cells (Novilla et al., 2016) with IC_{50} each of them were 54 µg/mL and 2.79 µg/mL, respectively. Xanthones from the peel of *Garcinia mangostana* have been reported to have cytotoxic activity against human melanoma cells (Wang et al., 2011), MCF-7 and MDA-MB-231 cells (See et al., 2021). This demonstrates that the development of *Garcinia mangostana* as an anticancer agent is necessary. This study was conducted to investigated the cytotoxic effects of an ethanolic extract of *Garcinia mangostana* peel on T47D breast cancer cells.

2. Materials and Method

2.1 Plant material

The *Garcinia mangostana* L.. peel was collected at Kota Baru, Luhak Nan Duo District, West Pasaman Regency, and West Sumatra. Dr. Nurainas, a botanist from Andalas University's Herbarium in West Sumatera, Indonesia, identified the *Garcinia mangostana* L. peel. Plant materials were sliced into tiny pieces and air-dried in a shaded area. Before extraction, the dehydrated plant components were ground into a powder.

2.3 Sample preparation

Plant materials were sliced into tiny pieces (3-5 mm thick) and air-dried in a shaded area for 7 days. The dried bark of mangosteen peel was ground into a powder using a traditional grinder. The materials were then soaked for 24 hours at room temperature in 70% ethanol with intermittent stirring and then filtered. This process was repeated thrice. The filtrates were combined and concentrated under a vacuum using a rotary evaporator at 45℃ till a semisolid extract was formed. The extract was kept in a refrigerator at 4℃ for further pharmacological testing.

2.3 Cell culturing procedure

T47D cells were grown in *Dulbecco's modified Eagles medium*, which contained 10% fetal bovine serum (Gibco, Grand Island, NY, USA), 1% penicillin-1% streptomycin (Gibco, Grand Island, NY, USA), and 0.5% fungizon (Gibco, Grand Island, NY, USA), in a flask in a humidified atmosphere (5% CO2) at 37˚C.

2.4 Cytotoxic assay

T47D cells were seeded in a 96-well plate with 1.71 x 10^5 cells/well and divided into control and treatment groups. Then, incubated at 37˚C with 5% CO_2 for 24 hours. Cells were treated with final concentrations of MPE were 0.1, 1, 10, and 100 µg/mL while the concentrations of Dox were 0.1, 1, 10, and 100 µg/mL. The culture media was withdrawn and the cells were cleaned with PBS (Sigma) after a 24-hour incubation period. 100 µL of diluted 5 mg/mL MTT on PBS (Sigma) was applied to each well after being diluted with Dulbecco's Modified Eagle Medium (DMEM). After four hours of incubation, 10 µL DMSO was added to stop the reaction. After that, the plate was incubated for 30 minutes at room temperature. The plate was agitated for ten minutes to ensure that the formazan had dissolved, and then the absorbance was measured at a wavelength of 550 nm using an ELISA reader (Bio-Rad, USA). Every treatment was administered in triplicate, and the cytotoxic activity was quantified using the IC_{50} method, which determines the quantity needed to lower the population's absorbance of cells by 50% in comparison to the untreated (control) cells.

2.5 Analysis

The in vitro experiment data were presented as mean ± S.E.M. Using the obtained absorbance, the percentage (%) of cell viability was determined. A plot of log concentration against % cell viability produced the equation y=ax+b, which was utilized to calculate the IC_{50} value, representing the concentration required to inhibit 50% of cell proliferation. Graphical illustration of the viability percentage was analyzed and presented using GraphPad Prism (GraphPad Prism, 9.0.0).

3. Results and Discussion

The National Cancer Institute (NCI) classifies cytotoxicity according to IC_{50} values. Extracts with IC_{50} values less than 20 µg/mL are considered highly active, moderately active if IC_{50} 21-200 µg/mL, weakly active if IC_{50} = 201–500 µg/ml and IC_{50} values above 500 µg/mL indicate inactive or no cytotoxicity (Anywar et al., 2022). The inhibitory concentration (IC_{50}) is the amount needed to prevent 50% of cell growth. Lower IC_{50} values signify larger efficacy in inhibiting cell division (He et al., 2016). The MPE exhibited an IC_{50} of 8.9 µg/mL on T47D cells, indicating highly active and dox showed a significantly lower IC_{50} of 0.5 µg/mL, highlighting its potent cytotoxicity as a chemotherapeutic agent. Both substances displayed a dose-dependent response, indicating increased cell death with increasing concentrations (Figure 1.).

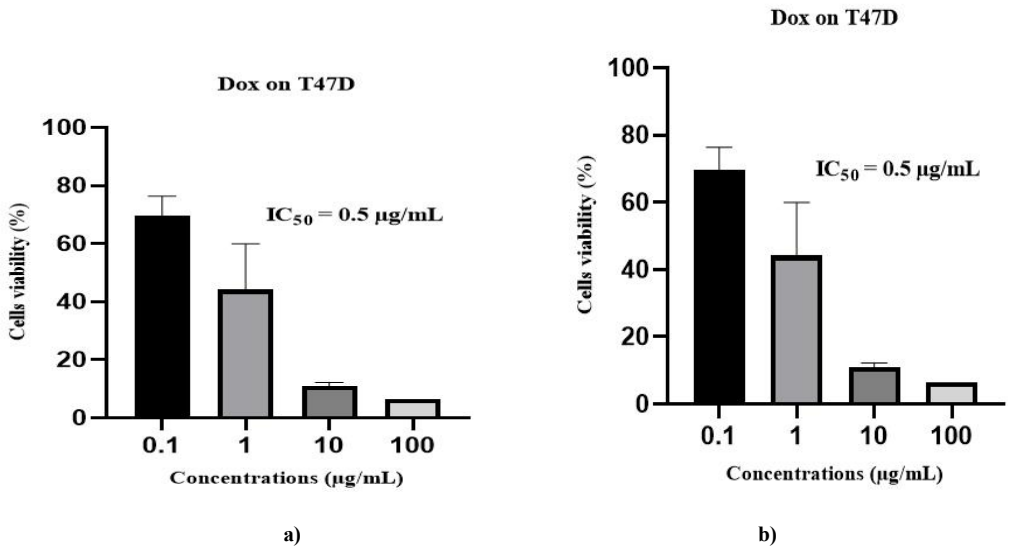

Figure 1. Cell viability (%) of T47D cells following treatment with MPE (a) and Dox (b) for 24 h single test application. Viability values are presented as mean (n = 3) ± SEM.

The results of the MTT assay demonstrated that both MPE and Dox exhibited cytotoxic effects on T47D breast cancer cells. However, the potency of these compounds differed significantly. Doxorubicin, a well-established chemotherapeutic agent, displayed a much lower IC_{50} value (0.5 µg/mL) compared to MPE (8.9 µg/mL), indicating that doxorubicin was more effective in reducing cell viability. The dose-dependent manner of cytotoxicity observed for both MPE and Dox suggests that increasing concentrations of these compounds led to a corresponding increase in cell death. This finding is consistent with previous studies that have reported the cytotoxic effects of MPE and doxorubicin on various cancer cell lines such as MCF-7 cells (Laksmiani, 2019), and K-562 cells (Novilla et al., 2016). The cytotoxic effect of MPE can be attributed to its bioactive compounds, such as xanthones, which have been shown to induce apoptosis (Fukuda et al., 2017), inhibit cell proliferation (Rech et al., 2021), and arrest the cell cycle in cancer cells (Thanh et al., 2021). Doxorubicin, on the other hand, exerts its cytotoxic effects by intercalating into DNA, causing DNA damage and inhibiting topoisomerase II (Thorn et al., 2012).

Future studies should focus on isolating and characterizing the bioactive components in MPE responsible for its cytotoxic properties. In vivo experiments will be critical to confirm its therapeutic value and safety in living systems. By creating targeted drug delivery systems, the efficacy of MPE can be maximized, while reducing dosages and minimizing toxic effects on normal cells. This study serves as a foundational step toward the development of MPE as a safe and effective natural anti-cancer therapy

4. Conclusion

This study revealed that Mangosteen Peel Extract (MPE) possesses significant cytotoxic activity against T47D breast cancer cells. Although its potency is lower compared to the standard chemotherapeutic agent, Doxorubicin, MPE shows promise as a potential natural-based anticancer agent.

Conflict of interest

The authors declare that there are no conflicts of interest.

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