DISERTASI

KAJIAN AKTIVITAS ANTIKANKER KOMBINASI *Garcinia cowa* Roxb. DAN DOXORUBICIN TERHADAP SEL T47D KANKER PAYUDARA: UJI SITOTOKSIK, APOPTOSIS, MIGRASI, SIKLUS SEL, DAN EKSPRESI PROTEIN REGULATOR

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ABSTRAK

KAJIAN AKTIVITAS ANTIKANKER KOMBINASI *Garcinia cowa* Roxb. DAN DOKSORUBISIN TERHADAP SEL T47D KANKER PAYUDARA: UJI SITOTOKSIK, APOPTOSIS, MIGRASI, SIKLUS SEL, DAN EKSPRESI PROTEIN REGULATOR

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Kanker payudara merupakan salah satu penyebab utama kematian perempuan di dunia. Doksorubisin (Dox) merupakan kemoterapi lini pertama, namun penggunaannya dibatasi oleh efek toksik sistemik dan resistensi. Penelitian ini mengevaluasi potensi ekstrak etanol kulit batang *G. cowa* sebagai adjuvan terapi terhadap sel kanker payudara T47D. Penelitian ini bertujuan untuk mengkaji potensi ekstrak etanol kulit batang *G. cowa* (GCBEE) sebagai adjuvan kemoterapi terhadap sel kanker payudara T47D melalui evaluasi sitotoksisitas, selektivitas, efek anti-migrasi, induksi apoptosis, gangguan siklus sel, serta ekspresi protein regulatornya. Sel kanker payudara T47D diberikan perlakuan dengan GCBEE 30 µg/mL, Dox pada 0,026 µg/mL, dan kombinasinya (GCBEE + Dox) dengan inkubasi selama 48 jam. Setelah perlakuan, uji sitotoksisitas dilakukan dengan metode MTT, apoptosis dianalisis menggunakan AO/PI dan *flow cytometry*, migrasi sel diuji dengan *scratch assay*, siklus sel dan ekspresi protein p53 dianalisis menggunakan *flow cytometry* berbasis antibodi spesifik. Hasil menunjukkan GCBEE memiliki aktivitas sitotoksik selektif terhadap sel T47D (IC_{50} = 130 µg/mL; SI = 15). Kombinasi GCBEE-Dox bersifat sinergis (CI<1). Kombinasi juga menghambat migrasi sel, meningkatkan apoptosis total, menghambat siklus sel fase G_2/M, menurunkan ekspresi *cyclin* D1/E, dan meningkatkan ekspresi p53. GCBEE berpotensi sebagai kandidat adjuvan dalam terapi kanker payudara. Temuan ini mendukung pengembangan kombinasi terapi berbasis bahan alam untuk meningkatkan efektivitas dan mengurangi toksisitas kemoterapi konvensional.

Kata kunci: *Garcinia cowa*, T47D, doksorubisin, apoptosis, p53, kombinasi sinergis, siklus sel.

ABSTRACT

ANTICANCER ACTIVITY STUDY OF *Garcinia cowa* Roxb. AND DOXORUBICIN COMBINATION ON T47D BREAST CANCER CELLS: CYTOTOXICITY, APOPTOSIS, MIGRATION, CELL CYCLE, AND REGULATORY PROTEIN EXPRESSION ASSAYS

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Breast cancer is one of the leading causes of death among women worldwide. Doxorubicin (Dox) is a first-line chemotherapy agent; however, its clinical use is limited by systemic toxicity and drug resistance. This study evaluated the potential of *Garcinia cowa* bark ethanol extract (GCBEE) as an adjuvant therapy against T47D breast cancer cells. The study aimed to assess GCBEE's potential as a chemoadjuvant by examining its cytotoxicity, selectivity, anti-migratory effects, apoptosis induction, cell cycle disruption, and modulation of regulatory protein expression. T47D breast cancer cells were treated with GCBEE (130 µg/mL), Dox (0.026 µg/mL), or their combination (GCBEE + Dox) for 48 hours. Post-treatment, cytotoxicity was evaluated using the MTT assay, apoptosis was analyzed via AO/PI staining and flow cytometry, cell migration was assessed via scratch assay, and cell cycle progression and p53 protein expression were measured using antibody-based flow cytometry. The results demonstrated that GCBEE exhibited selective cytotoxicity against T47D cells (IC_{50} = 130 µg/mL; Selectivity Index = 15). The GCBEE-Dox combination showed synergistic effects (Combination Index < 1). Additionally, the combination significantly inhibited cell migration, increased total apoptosis, induced G_2/M cell cycle arrest, downregulated cyclin D_1/E expression, and upregulated p53 expression. These findings suggest that GCBEE holds promise as an adjuvant candidate in breast cancer therapy. The study supports the development of natural compound-based combination therapies to enhance efficacy and reduce the toxicity of conventional chemotherapy.

Keywords: *Garcinia cowa*, T47D, doxorubicin, apoptosis, p53, synergistic combination, cell cycle.