

ABSTRACT

Griselda Minerva. 24020121130107. **The Synergistic Cytotoxic Effect of Ethyl Acetate Fraction from Key Lime Leaves (*Citrus aurantiifolia*) Combined with Doxorubicin on Breast Cancer Cells.** Under the guidance of Kasiyati and Marissa Angelina.

Breast cancer is the second most prevalent health issue after lung cancer, with nearly half of all cases resulting in mortality. Doxorubicin is a first-line therapy for breast cancer; however, prolonged use can lead to cardiomyopathy and induce cancer cell resistance. Combining doxorubicin with other cytotoxic agents has become a common strategy to overcome resistance. Key lime (*Citrus aurantiifolia*) leaf extract exhibits cytotoxic effects against cancer cells, attributed to compounds such as coumarins and furocoumarins. This study aimed to identify the bioactive compounds in the ethyl acetate fraction of key lime leaves and analyze their cytotoxic effects, both alone and in combination with doxorubicin, on MCF-7 breast cancer cells. Phytochemical screening, thin-layer chromatography (TLC), and LC-HRMS were employed for compound identification. Cytotoxicity was assessed using the MTT assay, and synergistic effects were determined by calculating the Combination Index (CI) with Chou-Talalay approach and calculated on CompuSyn software.. The ethyl acetate fraction demonstrated cytotoxicity against MCF-7 cells with an IC₅₀ of 59.2 ppm. Notably, 12 out of 16 tested concentration combinations exhibited synergistic interactions with doxorubicin, indicating enhanced cytotoxic effects. LC-HRMS analysis identified 23 compounds in the fraction, 13 of which are known to possess anticancer or cytotoxic properties.

Keywords: MCF-7 cells, breast cancer, *Citrus aurantiifolia*, combination therapy, doxorubicin