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Pleotropic Effects of Epoxyazadiradione in Human Triple Negative Breast Cancer Cells

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Background: For several decades the medicinal plants have been widely explored for the development of lead compounds with no or lesser side effects compared to the existing anticancer drugs. Epoxyazadiradione is a limonoid found in neem plant, with several pharmacological properties.

Aim: To investigate the anticancer activity of Epoxyazadiradione (EAD) on human triple negative breast cancer cell line (MDA-MB-231).

Methodology: MTT, staining techniques (DAPI, Acridine orange/EtBr, Annexin V, JC-1), LDH release assay, caspase 3 &9 activity assay, ELISA, gelatin zymography, scratch wound assay, western blotting, FACS analysis, colony formation assay, Anoikis assay and Immunostaining were employed.

Result & conclusion: The results revealed that EAD caused 50% inhibition in MDA-MB-231 cells at 12±1.04μM, with no significant toxicity on normal cell lines (H9C2) up to 50 μM. The apoptotic cell death was revealed by increased nuclear fragmentation, membrane breakage, phosphatidyl serine translocation, mitochondrial membrane depolarization, activation of caspases (3,9) and upregulation of apoptosis -indicator proteins (bax, cleaved parp). The EAD also reduced cell migration, matrix metalloprotease 9 (MMP9) activity, fibronectin expression and colony formation, which in turn indicates the compound's antimetastatic potential. EAD was also found to reduce glucose uptake, increase intracellular ROS, induce cell cycle arrest at G2/M phase and revert anoikis resistance. And finally nuclear translocation of NF-kb and EGFR is found to be reduced under the treatment in a dose dependent manner. Taken together, our results strongly suggest that EAD has dose- and time-dependent antineoplastic effects, suggesting its potential usage against triple negative breast cancer.

Biography:

Lakshmi S did her graduation in zoology (2008) from St. Xavier's college for women, Aluva and post -graduation in Bioinformatics (2010) from Union Christian college, Aluva. She is qualified CSIR-NET (eligibility for lectureship) in 2012 and joined for PhD under Mahatma Gandhi University, Kottayam in 2013. She is currently doing PhD in Biological sciences (final year) under AcSIR (Academy of scientific and innovative research).