ABSTRACT

Cancer statistics show that 13% of all death globally results from cancer. In Kenya, about 80,000 new cases of cancer are reported each year. From these new cases, about 50 people die every day as a result of cancer.

To manage cancer, there are various treatment modes including; surgery, immunotherapy, chemotherapy, phototherapy among others. However, chemotherapy is the most common. As much as chemotherapy is useful to the patient, it comes with adverse side effects like, nausea, vomiting, loss of appetite etc. To make it even worse there is emergence of multi drug resistance (MDR) cancer cell lines. This has made the treatment of cancer to be difficult due to treatment failures by contemporary drugs.

The extracts of Zanthoxylum species like Z. gilletii showed good activities against drug sensitive and drug resistant cancer cell lines and this motivated us to investigate other Zanthoxylum species. In this research work, the stem barks of Zanthoxylum paracanthum and Zanthoxylum chalybeum were examined for their chemical components and the compounds tested for their cytotoxicity against drug sensitive and MDR leukemia cell lines.

The stem bark material of Z. paracanthum was collected from Msambweni forest in Kwale County which is about 37 Km from Mombasa town, while that of Z. chalybeum was collected from Kakamega forest in Kakamega County which is about 10 Km from Kakamega town. The plant materials were identified by Mr. Patrick Mutiso a technologist with experience in plant identification techniques, from the School of Biological Sciences (SBS), University of Nairobi. The plant materials were then dried under shade for 1 week and then ground to fine particles. The ground materials of the two Zanthoxylum species were extracted exhaustively using 50% MeOH in CH2Cl2 to yield 97g (9.7%) crude extract of Z. paracanthum and 84g (9.3%) of Z. chalybeum. The crude extracts were subjected to a combination of chromatographic techniques with varying solvent systems to yield four compounds from Z. paracanthum namely; an indole alkaloid, canthin-6-one (1), one benzophenanthridine alkaloid, dihydrochelerythrine (2), one terpenoid, lupeol (3) and one lignin, sesamin (4) and three compounds for Z. chalybeum namely; one new amide, 3-(1-isoprenoloxy)-4-methoxyfagaramide (5) and one known one, fagaramide (6) together with sesamin (4) that was also isolated from Zanthoxylum chalybeum.

The isolated compounds were tested for their cytotoxicity against drug sensitive and MDR leukemia cell lines using resazurin test (metabolic capacity of viable cells reduce resazurin dye to resorufin which is highly fluorescent). Canthin-6-one (1) exhibited the highest activities against both the drug sensitive and drug resistant leukemia cell lines, with only < 1% of the drug sensitive leukemia cells remaining viable (99% inhibition) and <3% resistant leukemia cells remaining viable (97% inhibition) at 10 µg/ml. The other compounds were considered inactive as they exhibited cell inhibition of less than 70% at 10 µg/ml in accordance to criteria evaluation of the cytotoxicity of pure compounds.