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Prospective study of cytotoxic and genotoxic effects of Combretastatin A4

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Combretastatins are a class of natural phenols found in the bark of Combretum caffrum, commonly known as South African Bush Willow. Despite having a similar name, combretastatins are unrelated to statins, a family of cholesterol-lowering drugs.

Combretastatin A4 have been shown to be one of the most potent tubulin-depolymerizing agent. Microtubules control chromosomal segregation and cytokinesis during mitosis in both cancer and stromal cells and contribute to overall tumor growth. Consequently, microtubule inhibitors interfere with cell cycle progression and induce apoptosis in cancer cells *in vitro.*

The aim of this study was to investigate the potential gentoxic effect of Comretastatin A4 (CA4) in isolated peripheral blood mononuclear cells (PBMC) in Comet assay in order to establish is there any DNA damage in healty non-dividing cells. The aim also was to explore potential cytotoxic activity of CA4 against human cervical carcinoma (HeLa) cell line.

Genotoxicity of CA4 was evaluated on PBMC in a range of 9 concentrations (from 1 nM to 200μM). Non of the tested concentrations showed genotoxiceffect. The same range of different concentrations of CA4 (from 1 nM to 200μM) were applied to evaluate potential cytotoxicity in a monolayer culture of HeLa cells using the 3-[4,5-dimethylthiazole-2-yl]-2,5-diphenyltetrazolium bromide (MTT) assay. After 24h incubation with CA4, there was a significant reduction in cell viability in all concentrations above 250 nm, while IC50 (half maximal inhibitory concentration) was 123 ± 0.06396 μM.

We concluded that CA4 does not have gentoxic effect on PBMC, and that it reduce cell viability of cancer HeLa cell lines. These results are especialy importanat because they showed that CA4 does not damage the DNA molecule in healthy human cells, but achieves its cytotoxic effect on malignant cells in the same range of concentrations.

Keywords:
DNA damage, genotoxicity, cytotoxicity, Comet assay, MTT assay.