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# P199. ASSESSMENT OF SELECTIVITY OF A SERIAL 1,4-BENZOXAZINE-3-ONE DERIVATIVES INDUCED OXIDATIVE DNA DAMAGE ON CANCER CELLS USING THE MODIFIED ALKALINE COMET ASSAY

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It is important that anticancer agents affect selectively cancer cells to minimize possible side effects of therapy. It is reported that cancer cells may be more sensitive to ROS generated DNA damage than normal cells. So it is supposed that increased oxidative stress by exogenous ROS generation therapy has an effect on selectively killing cancer cells with little or no toxicity on normal cells. We evaluated selective genotoxic and ROS generating activities of a serial 1,4- benzoxazine-3-one derivatives previously synthesized and assessed in vitro anticancer and human topoisomerase I inhibitory activities.

In this present study, we evaluated their potentials of generating DNA strand breaks and oxidative DNA damage on cancer (HeLa) and normal (L929) cells with alkaline and modified comet assay, respectively. Cells treated with various non-cytotoxic doses of the test compounds. Following test procedures, slides were scored by comet assay IV analysis program. For modified comet assay, slides were incubated with damage specific DNA glycosylases (Fpg and Endo III) before electrophoresis. Tail moment results were statistically analyzed.

Test results showed that BS1, BS4, BS10, BS11 caused DNA strand breaks on HeLa, but not on L929. Fpg and Endo III-sensitive sites were both higher in cells treated with BS1 and BS4, whereas BS10 and BS11 increased only frequency of Fpg-sensitive sites.

This present study revealed that BS1, BS4, BS10 and BS11 exhibited selectively genotoxic and ROS generating activity on HeLa cells. Further mechanistic studies as well as in vivo studies with these compounds have planned in a new project.

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