

## The Study of Cytotoxic Effects of Boldine Derivatives on Human Breast Cancer Cells- MCF-7 and MDA-MB231 Cell Lines

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DOI: 10.21859/mci-supp-01

### Keywords:

Breast Cancer  
Boldine Derivatives  
Cytotoxicity Assay

### Abstract

**Introduction** Boldine is an aporphine alkaloid that is found in high amount in boldo tree and *Lindera* aggregate. It is used as homeopathic and herbal medicine that has various antioxidant and anti-cancer. Our previous study has reported anti-telomerase effect of this alkaloid. In order to enhance this valuable inhibitory effect, several new synthetic substitutes have been synthesized in Prof. Bruce Cassel's Lab.

**Materials and Methods:** LD50 values of the derivatives in both MCF-7 and MDA-MB231 cell lines were measured by MTT test. Cells seeded in 96 well plates were treated with six different concentrations of each compound (400 $\mu$ M, 200 $\mu$ M, 100 $\mu$ M, 50 $\mu$ M, 25 $\mu$ M and 12.5 $\mu$ M). MTT solution was added after 48 hours, then incubated for four hours. IC50 values were measured through Gen5 software of Powerwave XS2 Biotek plate reader. Data was collected by at least 3 independent repeats of the experiment.

**Results:** The collected data showed that B2 with LD50= 16.25  $\mu$ M in MCF-7 and 21.88  $\mu$ M in MDA-MB231 was the most potent anti-proliferative derivative. The IC50 values for the other three compounds, B3, B4 and B5 in the MCF-7 cell line were 156.4 $\mu$ M, 610 $\mu$ M and 252.5 $\mu$ M, and in the MDA-MB231 cell line were 107.5 $\mu$ M, 363.8 $\mu$ M, 217.5 $\mu$ M, respectively. Also in microscopic observations, the survival percentage of both cell lines in presence of B2 was significantly reduced dose dependently.

**Conclusions:** B2, the most potent anti-proliferative derivative of boldine, showed stronger cytotoxic effects in MCF-7 than MDA-MB231 cell line. The higher hydrophobicity and more flexible structure of this derivative may play critical role in enhancing the interaction with important molecular targets inside the cell.