SHORT COMMUNICATION

INHIBITION OF DNA TOPOISOMERASE I AND II, AND GROWTH INHIBITION OF MDA-MB-231 HUMAN BREAST CANCER CELLS BY BIS-BENZIMIDAZOLE DERIVATIVES WITH ALKYLATED MOIETY

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The purpose of the present study was to identify the cellular processes and targets affected by treatment with bis-benzimidazole derivatives with chloroalkyl and bromoalkyl moieties (1–4) in the estrogen receptor-negative MDA-MB-231 human breast cancer cells. Treatment of the cells revealed that these compounds inhibited DNA synthesis and irreversibly inhibited the proliferative activity of the cells. All drugs 1–4 inhibited relaxation of pBR 322 DNA induced by both topoisomerases, although topoisomerase I was 2- to 9-fold more sensitive than topoisomerase II. This suggests that DNA-binding may be implicated in the cytotoxicity of bis-benzimidazole derivatives with alkylating moieties, possibly by inhibiting interactions between topoisomerases and their DNA targets.

Key words: breast cancer MDA-MB-231 cells, DNA topoisomerase, bis-benzimidazole derivatives, DNA binding

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