ANTIPROLIFERATIVE AND APOPTOTIC EFFECTS OF S-NITROSOTHIOIS O-CHLORO AND M-CHLORO S-NITROSO-ARYL-AMIDES (SNOKs) IN HUMAN BREAST CANCER CELL LINES.  
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Cancer is a multifactorial pathology, characterized by disorganized and abnormal growth. Nitric oxide (NO) has an important role regulating tumors signaling processes associated to aggressiveness and progression. Increasing expression of inducible NO synthase is a poor prognostic marker for breast cancer. Control of intracellular NO production and/or exposure of malignant breast tumor cells to NO donors are potential chemotherapeutic strategies. S-Nitrosothiols a specific class of NO donors react with thiol and thiol proteins making them potential chemotherapeutic agents in the treatment of various cancer types. In this study we tested the susceptibility of MDA-MB-231 (metastatic human breast cancer) and MCF10-A (non-tumorigenic human breast cell) to different concentrations of the s-nitrosothiols o-chloro and m-chloro S-nitroso-aryl-amides (SNOKs). A selective cytotoxic action of the o-chloro and m-chloro SNOks was evidenced in the MTT cell viability assay. Upon exposure to 50 μM m-chloro SNOK there was a 65% loss of cell viability of MDA-MB-231 cells, whereas MCF10-A cells lost only 40% of their viability. Intracellular NO detection using the fluorophore DAF-2DA revealed after 2 h exposure of both cell lines to 50 μM m-chloro SNOK, a 50% increase on NO production on MCF10-A cells and a 700% increase on NO production in MDA-MB-231 breast cancer cells. Loss of cell viability of MDA-MB-231 cells after incubation with 50 μM m-chloro SNOK was related to apoptosis as shown in the AnexinV/PI Apoptosis/necrosis assay. Data from western blot assays for Caspase-3, Caspase-9, PARP, Thioredoxin-1, JNK, and Phospho-JNK are currently being analyzed. S-nitrosothiols o-chloro and m-chloro SNOKs are preferentially cytotoxic towards MDA-MB-231 breast cancer cells as compared to MCF10-A non-tumorigenic cell line. Preferential cytotoxicity was directly related to the intracellular NO levels detected in both cell lines after exposure to 50 μM m-chloro SNOK. Nitric oxide, breast cancer, s-nitrosothiols.