Arsenic is a major contaminant in drinking water that is associated with various cancers, skin lesions, peripheral vascular disease and hypertension. The main sources of arsenic in drinking water are erosion of natural deposits; runoff from orchards, run off from glass and electronics production wastes. Arsenic accumulates in the skin. A well-established exposure-response relationship exists between arsenic level of drinking water and various pathological conditions. Arsenic is a well-established human carcinogen, however, the exact mechanism by which it causes cancer is not known. Most of the effects of arsenic on human diseases have been established on the basis of epidemiologic studies, which have shown a significant association between the consumption of arsenic through drinking water and cancers of the skin, lung, bladder, liver, and kidney, neurologic disease, cardiovascular disease and other nonmalignant diseases. We analyzed the effects of Arsenic on MCF-7 breast cancer cells using Sodium Arsenite. At low concentrations, Sodium Arsenite increased the proliferation of MCF-7 cells. However, at high concentrations, it inhibited the cell proliferation and induced apoptosis. Activation of p53 and its target p21 protein was observed at high concentrations. Sodium Arsenite also activated extracellular signal-regulated kinases (ERK) pathway in MCF-7 cells. Cell signaling pathways modulated by Arsenic in MCF-7 breast cancer cells are discussed.

**BACKGROUND**

Arsenic is a natural element that is found in the environment. Arsenic has chemical properties that include inorganic and organic compounds. The inorganic compounds have been linked to cancer and other health problems. The form used in our research is sodium arsenite. Sodium Arsenite is the trivalent form of arsenic which is the most deadly and passes more rapidly through the tissues.

\[ O \quad As \quad O^- \quad Na^+ \]

**OBJECTIVES**

The objective of this study was to determine the effects of Sodium Arsenite on MCF-7 breast cancer cells.

**MATERIALS AND METHODS**

**Cell Culture and Reagents:** MCF-7 cells were grown as monolayer in Dulbecco’s modified Eagle medium (DMEM) (Invitrogen) supplemented with 5% heat-inactivated fetal bovine serum and 25 μg/ml gentamicin. The cells were grown and maintained in T-25 or T-75 tissue culture flasks in a humidified atmosphere of 5% CO2 and 95% air at 37°C. VES was obtained commercially from the Sigma Chemical Company.

**Cell Viability Assay:** The cell viability and proliferation of MCF-7 breast cancer cell lines were determined using a cell viability detection kit (4-[3-(4-iodophenyl)-2-(4-nitrophenyl)-2H-5-tetrazolio]-1,3-benzene disulfonate, WST-1) according to the manufacturer’s instructions (Roche Applied Science, Indianapolis, IN).

**DAPI Staining:** MCF-7 cells were grown on cover slips in 6-well plate and treated as indicated. The cells were fixed in methanol and stained with 4′,6-diamidino-2-phenylindole (DAPI) nuclear stain to visualize the apoptotic nuclei by fluorescent microscopy.

**Western Blotting:** Expression of various signaling proteins was determined by Sodium Oxytetracycline Gel Electrophoresis (SDS-PAGE) and Western Blotting.

**RESULTS**

1. **Cell Culture, Reagents and Materials**

2. **Effects of Sodium Arsenite on the proliferation of MCF-7 cells**

3. **Sodium Arsenite causes apoptotic phenotype in MCF-7 cells**

4. **Sodium Arsenite activates ERK Signaling in MCF-7 Cells**

5. **Sodium Arsenite upregulates p53 signaling at higher concentrations in MCF-7 cells**

**CONCLUSIONS**

- Sodium Arsenite at higher concentrations inhibits the proliferation of MCF-7 breast cancer cells.
- Arsenic exposure causes apoptotic phenotype in MCF-7 cells.
- Low doses of Sodium Arsenite activates ERK signaling pathway.
- Higher concentrations of Sodium arsenite activates p53 signaling in MCF-7 cells.

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**REFERENCES**

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