

## Arsenic toxicity and controlling measures through black tea polyphenols

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Arsenic (As) has been classified by the International Agency for Research on Cancer (IARC) and the Integrated Risk Information System (IRIS) of the United States as a known human class I carcinogen. Arsenic is found abundantly in the rivers of West Bengal, Bihar, Orissa and in the north-eastern part of India. It has been found that out of its many chemical states, arsenite (As III) causes cytotoxicity in the human keratinocytes (human skin cells), leading to alterations in transcription factors such as activation of activator protein 1 (AP-1) and inhibition of nuclear factor-kappa B (NF-kB). The exposure could occur through ROS (reactive oxygen species) production and an electrophilic metabolite of arsenic, e.g. monomethylarsonous acid (MMA III) that reacts readily with the reactive thiols of Kelch-like ECH-associated protein 1 (Keap1). Arsenic has been reported with constitutive activation of nuclear factor erythroid 2-related factor 2 (Nrf2), a protein that regulates the pathway of antioxidants. Arsenic-mediated Nrf2 activation has been proposed to be due to dysregulation of autophagy and over-expression or accumulation of ubiquitin-binding protein p62 protein, which has been observed to bind directly with Keap1 and hinder Nrf2 ubiquitination.

Nrf2/Keap 1 axis plays a major role in maintaining redox homeostasis of the cells, hence the cellular expression of Nrf2 and Keap1 both in the protein level as well as mRNA level of cultured human keratinocytes (HaCaT) cells has been investigated and it has been found that As III induced higher expression of Nrf2 protein forming carcinomas. However, in the case of simultaneous treatment with black tea polyphenols (BT) and As III, the expression of Nrf2 was significantly downregulated with an increase in the expression of Keap1. A similar trend was also observed in the mRNA level of Nrf2 and Keap1, as found by real-time polymerase chain reaction. A microscopic study revealed that the morphological alteration of HaCaT cells caused due to arsenite was effectively regained upon administration of black tea extract. Therefore, it can be concluded that black tea extract can be used as an efficient agent to ameliorate the cytotoxicity caused by arsenite in human keratinocytes.

*Keywords: Arsenic, Skin cancer, Cytotoxicity, Human keratinocytes, Black tea polyphenols*

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### Citation:

Shinjini Roy. Arsenic toxicity and controlling measures through black tea polyphenols. The Torch. 2021. 2(38). Available from: <https://www.styvalley.com/pub/magazines/torch/read/arsenic-toxicity-and-controlling-measures-through-black-tea-polyphenols>.