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OliveNet™ Journal Club
Expert review of literature related to olives and olive oil
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Title

Protective effect of hydroxytyrosol against oxidative stress mediated by arsenic-induced neurotoxicity in rats

Author(s)

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Keywords

Hydroxytyrosol, arsenic, neurotoxicity, superoxide dismutase, glutathione, protein oxidation, apoptosis

Summary

Arsenic is a confirmed carcinogen and a major environmental contaminant which causes a wide range of health problems (*2*). Inadvertent exposure may result from various sources including tobacco use and contaminated food, and the most common is through drinking contaminated groundwater (*3, 4*). This represents a major problem affecting over 40 million people particularly in parts of India and Bangladesh (*5*). Arsenic crosses the blood-brain barrier and accumulates in brain tissue where it has been shown to impair learning and memory, and to cause wide range of neurological conditions (*6-8*). Given its high metabolic rate, and limited glutathione-producing capacity of neurons, the brain is particularly susceptible to detoxify damage by reactive oxygen species (*9, 10*). In this study the ability of the key olive polyphenol, hydroxytyrosol, to protect from arsenic-mediated neurotoxicity in rats was investigated.

Key points and implications

The study was performed in rats which were exposed to arsenic via oral gavage (25 parts per million in distilled water for eight weeks; equivalent to 2.5 mg/kg sodium arsenite). A hydroxytyrosol rich leaf extract was prepared from the Frantoio cultivar and administered at 10 mg/Kg for eight weeks. Therefore, the four groups used in these experiments were: 1) vehicle (distilled water) control group, 2) arsenic treated group, 3) hydroxytyrosol treated group, and 4) combination arsenic and hydroxytyrosol treated group. A series of conventional experiments including measurement of levels of protein peroxidation and carbonylation, detection of superoxide dismutase and glutathione activities, and analysis of apoptosis were performed. In summary, the findings highlighted that hydroxytyrosol inhibited arsenic-induced increases in protein peroxidation and carbonylation, and restored arsenic-mediated decreases in superoxide dismutase and glutathione content in rat brain. Further, by Western blot analysis of the Bcl-2, Bax, caspase-3, and cytochrome c release from mitochondria it was shown that hydroxytyrosol prevents arsenic-induced

apoptosis. An interesting experiment was lipid and protein analysis by Fourier-transform infrared spectrophotometry. For these experiments, brain powder was produced by lyophilisation (essentially drying the tissue), and preparing potassium bromide pellets for analysis. The findings confirmed that hydroxytyrosol prevented arsenic-induced oxidative damage to lipids and proteins. Overall, these findings highlight that the major olive polyphenol, hydroxytyrosol, has the ability to reduce oxidative stress in the brain, and suggests that further research aimed at identifying precise mechanistic insights is warranted.

Related publications

1. M. Soni, C. Prakash, R. Dabur, V. Kumar, Protective Effect of Hydroxytyrosol Against Oxidative Stress Mediated by Arsenic-Induced Neurotoxicity in Rats. *Applied biochemistry and biotechnology*, (2018).
2. B. C. Minatel *et al.*, Environmental arsenic exposure: From genetic susceptibility to pathogenesis. *Environment international* **112**, 183-197 (2017).
3. S. M. Cohen, A. Chowdhury, L. L. Arnold, Inorganic arsenic: A non-genotoxic carcinogen. *Journal of environmental sciences* **49**, 28-37 (2016).
4. M. B. Shakoor *et al.*, Human health implications, risk assessment and remediation of As-contaminated water: A critical review. *The Science of the total environment* **601-602**, 756-769 (2017).
5. U. K. Chowdhury *et al.*, Groundwater arsenic contamination in Bangladesh and West Bengal, India. *Environmental health perspectives* **108**, 393-397 (2000).
6. C. C. Yen *et al.*, Inorganic arsenic causes cell apoptosis in mouse cerebrum through an oxidative stress-regulated signaling pathway. *Archives of toxicology* **85**, 565-575 (2011).
7. V. M. Rodriguez, L. Carrizales, M. S. Mendoza, O. R. Fajardo, M. Giordano, Effects of sodium arsenite exposure on development and behavior in the rat. *Neurotoxicology and teratology* **24**, 743-750 (2002).
8. C. Prakash, M. Soni, V. Kumar, Biochemical and Molecular Alterations Following Arsenic-Induced Oxidative Stress and Mitochondrial Dysfunction in Rat Brain. *Biological trace element research* **167**, 121-129 (2015).
9. E. Birben, U. M. Sahiner, C. Sackesen, S. Erzurum, O. Kalayci, Oxidative stress and antioxidant defense. *The World Allergy Organization journal* **5**, 9-19 (2012).
10. S. J. Flora, S. Bhadauria, S. C. Pant, R. K. Dhaked, Arsenic induced blood and brain oxidative stress and its response to some thiol chelators in rats. *Life sciences* **77**, 2324-2337 (2005).