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Protective Role of ~-Tocopherol and Ascorbic Acid Against Cadmium Induced Neurotoxicity in Rats

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ABSTRACT

Cadmium (Cd) is a neurotoxic heavy metal, which induces oxidative stress and membrane disturbances in the nervous system. Vitamin C and E is an effective antioxidants and free radical scavengers against oxidative stress. The present study was carried out to investigate the efficacy of vitamin C and E in protecting the cadmium induced changes in the activity of brain acetylcholinesterase (AChE), membrane bound ATPases, lipid peroxidation (LPO) and antioxidant status in rats. Oral treatment with cadmium chloride (5 mg/kg body wt/day) for 284 days resulted in a significant elevation in the levels of lipid peroxidation and lipid hydroperoxides along with a significant decrease in the level of reduced glutathione (GSH) and the activities of acetylcholinesterase (AChE), total ATPases, superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) in the brain tissue. Prior oral administration of vitamin C and E (50 mg/kg body wt./day) individually as well as in combination with cadmium significantly ($p<0.05$) diminished the level of LPO, lipid hydroperoxides and significantly ($p<0.05$) increased the activities of AChE, total ATPases, antioxidant enzymes and reduced glutathione in brain. These results suggested that vitamin C and E protects the brain tissue from the oxidative stress elicited by cadmium.

Key words : Neurotoxicity, α-tocopherol, Ascarfic acid, Cadmium

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Heavy metal toxicities have received widespread attention because of increasing amounts being released into the environment and their extended persistence and toxicity to a wide variety of organisms. Cadmium is perhaps one of the most toxic industrial and environmental pollutant and it poses a continuing health hazard. Cadmium is able to induce neurotoxicity with a wide spectrum of clinical entities including neurological disturbances (Viaene *et al.*, 2000) and changes the normal neurochemistry of the brain tissue (Gutierrez-Reyes *et al.*, 1998).

The brain is highly vulnerable to lipid peroxidation (LPO) because of its high rate of oxygen utilization, an abundant supply of polyunsaturated fatty acids, a deficient antioxidant defense and a high content of transition metals like copper and iron in several regions (Calabrese *et al.*, 2000). The enhanced susceptibility of membrane to LPO can lead to the loss of adenosine triphosphatases (ATPases) activity and depletion of thiols in brain (Bonting, 1970). ATPases are lipid dependent membrane bound enzymes which are involved in active transport, maintenance of cellular homeostasis and also involved in neurotransmission process (Ohinishi *et al.*, 1982).

Cadmium enhances the production of free radicals in the brain and interferes with the antioxidant defense system which inturn leads to cadmium induced alterations of the structural integrity of lipids and secondarily affects the membrane bound enzymes (Acan and Tezcan, 1995; Shukla *et al.*, 1996). In adult rats chronic cadmium exposure leads to the increase of LPO in the corpus striatum and cerebral cortex (Pal *et al.*, 1993) and it also inhibits the choline transport in synaptosomes (Chandra *et al.*, 1994). Several studies have reported that cadmium induces the LPO and it has an inhibitory action on the antioxidant enzymes and membrane bound ATPases is brain (Gutierrez-Reyes *et al.*, 1998; Garcia and Corredor, 2003; Carageorgiou *et al.*, 2004).

Antioxidants are becoming increasingly popular in oxidative stress related disorders and hold promise as therapeutic agents. The antioxidant compounds can counteract the decrease in ATPase activity and the increase in oxidative stress that are induced by cadmium (El-Missiry and Shalaby, 2000). Vitamin E is a major antioxidant in biological systems and acting as a powerful chain breaking agent through its scavenging action on peroxyl radicals (Beyer, 1994). Vitamin E terminates the chain reaction of lipid peroxidation in