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Taurine mitigates cognitive impairment induced by chronic co-exposure of male Wistar rats to chlorpyrifos and lead acetate

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ABSTRACT

Organophosphate pesticides and heavy metals are ubiquitous environmental pollutants and neurotoxicants. We investigated the effects of taurine (an antioxidant; TA) on oxidative stress and cognition in male Wistar rats co-treated with chlorpyrifos (an organophosphate pesticide; CPF) and lead acetate (heavy metal; LA). The Wistar rats were divided into 5 groups of 10 rats each. The first two groups were administered with distilled water and soya oil respectively. The remaining three groups were administered with taurine (TA), 50 mg/kg body weight, CPF + LA group [CPF (4.25 mg/kg, 1/20 LD50] and LA (233.25 mg/kg, 1/20 LD50) and TA + CPF + LA group [TA (50 mg/kg), CPF (4.25 mg/kg) and LA (233.25 mg/kg)]. The xenobiotics were administered once daily by oral gavage for 16 weeks. The results showed reductions in the activities of brain antioxidant enzymes and acetylcholinesterase, increased lipoperoxidation and histopathological alterations of the cerebral cortex in the CPF + LA group. However, TA mitigated perturbations in the activities of the antioxidant enzymes and acetylcholinesterase, counteracted oxidative stress and brain lipoperoxidation and attenuated neuronal degeneration induced by joint CPF and LA-induced neurotoxicity. The results suggested that TA is neuroprotective following chronic co-exposure of rats to CPF and LA.

1. Introduction

The entire ecosystem is constantly exposed to complex mixtures of environmental pollutants, including pesticides, toxic metals, industrial wastes and sewage effluents. This is due to the increasing and inevitable need for humans to feed, cloth and provide shelter for themselves. This has culminated in increased agricultural activities in several countries in order to ensure food security. Also, industrial operations

Abbreviations: CPF, chlorpyrifos; CAS, chemical abstract service; LA, lead acetate; TA, taurine; CPF + LA, chlorpyrifos + lead acetate; TA + CPF + LA, taurine + chlorpyrifos + lead acetate; DW, distilled water; SO, soya oil; BLL, blood lead levels; ROS, reactive oxygen species; DNA, deoxyribonucleic acid; ACh, acetylcholine; AChE, acetylcholinesterase; DTNB, 5,5′-dithiobis-2-nitrobenzoicacid; MDA, malondialdehyde; TBA, thiobarbituric acid; H&E, haematoxylin and eosin; SOD, superoxide dismutase; CAT, catalase; GPx, glutathione peroxidase.

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have been enhanced in several countries in order to facilitate food production and provide human needs such as clothing, shelter, transportation and even employment. It is noteworthy that pesticides and heavy metals are the most common environmental pollutants because of their widespread use for agricultural and industrial purposes (Ambali et al., 2011a). Pesticides are a diverse group of chemicals designed for the prevention and elimination of destructive plants, insects, rodents and fungi (Jones and Miller, 2008). It is notable that the intensive use of pesticides has resulted in serious environmental problems because they are either recalcitrant or biodegraded slowly (Mehta et al., 2009).

Organophosphate insecticides (OPs) are one of the most widely used classes of pesticides for agricultural, industrial, domestic and landscape pest control purposes (Ray et al., 2010; Wu et al., 2011), and chlorpyrifos (O,O-diethyl-3,5,6-trichloro-2-pyridyl-phosphorothionate; CPF) is a commonly used organophosphorus pesticide (Saulsbury et al., 2009). It elicits acetylcholinesterase (AChE) inhibition at cholinergic synapses and neuromuscular junctions (Oruç, 2010) resulting in cholinergic toxicity with nicotinic and muscarinic effects (Ojha et al., 2011). In addition, CPF has been reported to evoke oxidative stress in rodents (Ambali et al., 2011a,b; Elsharkawy et al., 2013). The main pathways of exposure to CPF are inhalation of vapours and aerosols, dermal absorption or ingestion of residues in the diet (Testai et al., 2010). CPF has been shown to cause adverse effects on learning and impairment of reference and working memory in animals (Icenogle et al., 2004; Ambali and Aliyu, 2012). Besides, the pesticide has been shown to reduce neuronal proliferation and evoke modification in neurotrophic signalling (Bagchi et al., 2006).

On the other hand, heavy metals are toxic to many organisms at higher concentrations and several of them participate in important metabolic and signalling pathways (Valko et al., 2005). They exist in different forms in the environment and their toxicity is attributed to their oxidative state and ability to react with other compounds (Walker, 1995). Lead (LA) is a potent and ubiquitous neurotoxicant (Meyer et al., 2008) and it is implicated in oxidative damage to the heart, liver, kidneys, reproductive organs, brain and erythrocytes (Ahamed et al., 2005). The sources of LA exposure may include air and soil (Hashisho and El-Fadel, 2004), lead-based paint (Nduka et al., 2007), leaded gasoline (Lovei, 1999), battery manufacture and reclamation (CDC, 1992), pottery/ceramics (González-Soto et al., 2000), eye cosmetics (Sprinkle, 1995) and melting of LA for the manufacture of fishing sinkers (Nriagu et al., 2008). Several cases of LA poisoning have been reported after people have ingested medicinal products that contain LA in New Zealand, Italy and the United States (Roche et al., 2005). LA evokes several neurobehavioural and psychological alterations (Wilson et al., 2000) and central nervous system impairments and spatial learning deficits have been reported after chronic LA exposure in rodents (Kuhlmann et al., 1997; Sansar et al., 2011). In children, cognitive dysfunction is associated with mean blood LA levels (BLL) <10 μg/dL (Tellez-Rojo et al., 2006). It has been shown that low-level LA exposure can adversely affect cognitive functions such as attention, speech, memory, cognitive flexibility and visual-motor integration in children (Yuan et al., 2006). Numerous adverse effects of LA exposure have been attributed to its propensity to induce the production of reactive oxygen species (ROS), DNA damage and inactivation of anti-oxidant enzymes (Gurer-Orhan et al., 2004). It is known that LA induces oxidative stress by disrupting the intracellular pro-oxidant/antioxidant balance in normal tissues (Gurer and Ercal, 2000). In addition, LA inhibits delta-aminolevulinic acid dehydratase (ALAD) activities (Rendón-Ramirez et al., 2007). Consequently, delta-aminolevulinic acid (ALA) accumulates in the blood following the inhibition of ALAD by LA and this culminates in the generation of ROS that damage tissues (Ahamed and Siddiqui, 2007).

Indeed, the environment is heavily contaminated with many chemicals, which interact with one other and alter their toxic responses in humans and animals (Ambali et al., 2011a). In the real-world scenario, environmental contaminants exist as mixtures (Qin et al., 2011; Boatti et al., 2012). Therefore, we focused on the joint neurotoxicity of CPF and LA in the current study because it reflects the environmental reality of multiple chemical exposure and both neurotoxicants studied are ubiquitous in the environment. It is notable that pesticides and metals constitute important mixtures in polluted sites in developing countries (Yanez et al., 2002). According to Tilton et al. (2011), mixture exposures are a common occurrence in aquatic environments and exposures of fish to pesticides and metals can induce loss of olfactory-driven behaviours such as homing, predator evasion, prey selection and reproduction, which are critical for survival and hence, supply of protein to human and animal populations (Sandahl et al., 2004, 2005; Tierney et al., 2010). Therefore, the investigation of the toxicological impacts and amelioration of the adverse effects of mixtures of contaminants may provide results that are of better practical application than focusing only on individual contaminants.

Furthermore, CPF and LA have caused deleterious effects in man and animals due to their persistence in the environment and their toxicodynamics (Krishna and Ramachandran, 2009), and there is a high likelihood of co-exposure to CPF and LA in the environment (ATSDR, 2006). CPF and LA are common food contaminants and dietary exposure to both contaminants has been reported in the literature (Solon et al., 2008; Yan et al., 2012). Besides, pesticides and heavy metal residues have been detected in breast milk (a crucial food for newborns and infants) in several countries (Craan and Haines, 1998; Landrigan et al., 2002). Consequently, the nervous systems of the infants may be damaged because of their immature and porous blood–brain barrier (Landrigan, 1999).

It is apparent that CPF and LA are neurotoxicants that have permeated every sphere of human and animal existence. Therefore, we considered conducting the present study in order to investigate the mitigation of the neurotoxic effects of chronic co-exposure of male Wistar rats to CPF and LA. Although the mechanisms of toxicity of CPF and LA differ, oxidative stress has been identified as a common feature of CPF (Ambali and Aliyu, 2012) and LA (Khalaf et al., 2012) poisoning. In the present study, we hypothesized that taurine (a putative antioxidant and neuroprotective agent) might be capable of mitigating neurotoxicity induced by chronic co-treatment of male Wistar rats with CPF and LA. It has been established that oxidative stress may result from the production of excessive ROS or breakdown of the cellular