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Biochemical evidence on the potential role of organophosphates in hepatic glucose metabolism toward insulin resistance through inflammatory signaling and free radical pathways

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Abstract

Several studies show that organophosphate pesticides exert several effects on glucose homeostasis. The current study investigates the influence of subchronic exposure to malathion (MT) on hepatic gluconeogenesis in relation to acetyl cholinesterase (AChE) inhibition, oxidative stress and inflammatory response in the rat. MT was administered by gavage at doses of 25, 50 and 100 mg/kg for 32 days. Fasting hyperglycemia was seen in line with an increased activity of hepatic phosphoenolpyruvate carboxykinase, glucose 6-phosphatase and tumor necrosis factor α. In addition to the impaired glucose tolerance and inhibition of AChE in a dose-dependent manner, there were significant increases in hepatic lipid peroxidation, carbonyl groups and 8-deoxyguanosine as the biomarkers of reactive oxygen species–mediated damage to lipid, protein and DNA, respectively. Altered quality of the liver in glucose production especially gluconeogenesis could be a compensatory mechanism against MT toxicity or even result in tissue damage. MT-induced insulin resistance in the liver occurs through oxidative and inflammatory signaling pathways.

Keywords

Organophosphate, inflammation, glucose metabolism, oxidative stress, malathion

Introduction

Malathion (MT) belongs to the organophosphate (OP) class of pesticides that are widely used in agricultural and public health programs. There is a major concern regarding the side effects these OPs have on the ecosystem and biological systems (Gupta, 2006). It is well known that the primary mechanism of toxicity of OPs is inhibition of the enzyme acetyl cholinesterase (AChE) and subsequent accumulation of the neurotransmitter acetylcholine in different parts of the body (Rahimi et al., 2006; Ranjbar et al., 2002). Although intensive activation of cholinergic receptors is significant in acute poisoning, but other mechanisms especially, oxidative stress are important in prolonged low level exposures (Abdollahi et al., 2004a,b; Ranjbar et al., 2005). Oxidative stress itself is involved in the progress of different pathological situations particularly chronic diseases, such as Parkinson, Alzheimer, atherosclerosis, colitis, and diabetes (Abdollahi et al., 2004c; Rahimi et al., 2005; Rezaie et al., 2007).

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