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ScienceDirect
C. R. Biologies 331 (2008) 655–662
COMPTES RENDUS BIOLOGIES
http://france.elsevier.com/direct/CRASS3/

Pharmacology, toxicology / Pharmacologie, toxicologie

Biochemical evaluation of hepatic damage in subchronic exposure to malathion in rats: Effect on superoxide dismutase and catalase activities using native PAGE

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Received 15 February 2008; accepted after revision 11 June 2008

Available online 3 July 2008

Presented by Pierre Buser

Abstract

The aim of this study was the evaluation of the hepatic damages following a subchronic exposure to malathion, an organophosphorus (OP) insecticide. Malathion was administered intragastrically in 1 ml corn oil containing 100 mg/kg Body Weight daily for 32 days. Malondialdehyde (MDA) concentration superoxide dismutase (SOD) and catalase (CAT) activities were analysed using a non-denaturing electrophoresis. The serum activities of Pseudocholinesterase (PchE), aspartate aminotransferase (ASAT) and alanine aminotransferase (ALAT) were determined. Malathion exposure leads to a significant decrease in AchE activity, an increase in hepatic MDA, and in serum ASAT and ALAT activities. A positive correlation between serum transaminases levels and hepatic MDA was demonstrated. These results indicate that malathion exposure induced lipid peroxidation LPO, a process of degradation of membrane lipids, involving the deterioration of the cellular integrity. We have recorded a slight increase in antioxidant enzymes activities. This leads us to suggest an insufficient elimination of free radicals, causing cytotoxic effects. ***To cite this article: R. Rezg et al., C. R. Biologies 331 (2008).***

Résumé

Évaluation biochimique des dommages hépatiques induits après une exposition subchronique au malathion chez le rat. Effets sur les activités de la superoxide dismutase et la catalase en utilisant la technique du *native PAGE*. Cette étude s'intéresse à l'évaluation des dommages hépatiques induits chez le rat à la suite d'une exposition subchronique à un insecticide organophosphoré, le malathion. Le malathion, solubilisé dans 1 ml d'huile de maïs à raison de 100 mg/kg de poids corporel/jour, est administré par gavage durant 32 jours. À la fin de l'expérience, le foie a été isolé pour la détermination du taux du malondialdéhyde (MDA) et la révélation native par électrophorèse en gel de polyacrylamide (*native PAGE*) des activités de la superoxide dismutase (SOD) et de la catalase (CAT). Les activités plasmatiques de *la pseudocholinesterase (PchE)*, l'aspartate-amino-transférase (ASAT) et l'alanine-amino-transférase (ALAT) ont été également déterminées. Notre étude montre que l'exposition subchronique au malathion a induit chez le rat une diminution significative de l'activité de *la PchE* et une élévation hautement significative du taux du MDA hépatique, couplée à une augmentation significative des activités sériques des transaminases indicatrices de cytolyse. De plus, une corrélation positive et hautement significative a été démontrée entre l'élévation du taux de MDA et l'augmentation

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1631-0691/$ – see front matter
doi:10.1016/j.crvi.2008.06.004

concomitante des activités sériques des transaminases. Ceci indique probablement que l'exposition subchronique au malathion entraîne la dégradation des lipides membranaires et donc l'altération de l'intégrité des hépatocytes, provoquant la libération de ces enzymes dans la circulation. Par ailleurs, une faible augmentation des activités des enzymes antioxidantes a été enregistrée, ce qui nous laisse suggérer une élimination insuffisante des radicaux libres, causant des effets cytotoxiques. ***Pour citer cet article : R. Rezg et al., C. R. Biologies 331 (2008).***

Keywords: Malathion; Lipid peroxidation; Transaminases; Cytolysis; Cytotoxicity; Superoxide dismutase; Catalase

Mots-clés : Malathion ; Peroxydation lipidique ; Transaminases ; Cytolyse ; Cytotoxicité ; Superoxide dismutase ; Catalase

1. Introduction

The widespread use of pesticides in public health and agricultural programs has resulted in the pollution of water, air, and food that has lead to severe acute and chronic cases of human poisonings [1–6]. The World Health Organization estimates that the incidence of pesticide poisoning in developing countries has doubled between 1987 and 1997 [7]. However, the use of organophosphorus pesticides (OP) has increased considerably due to their low potency and durability as compared to organochlorine pesticides [8], in spite of their risks to human health and the environment. The OP compound malathion [S-1,2(bis ethoxycarbonyl) ethyl O,O dimethyl phosphorodithioate] is used extensively throughout the world, especially in developing countries, to control major arthropods in public health programs, animal ectoparasites, human head and body lice, household insects and to protect grain in storage [9–12]. It kills insects by contact or vapour action. OP compounds are primarily recognized for their ability to induce toxicity in mammals through the inhibition of acethylcholinesterase (AChE), leading to the accumulation of acetylcholine and subsequent activation of cholinergic muscarnic and nicotinic receptors [13]. Also, a study suggests that OP compounds may exert direct action on muscarnic and nicotinic receptors, when their concentration in the circulation exceeds micromolar levels [14]. The toxicity of OP agents may be due, at least in part, to the formation of reactive oxygen species (ROS), leading to lipid peroxidation LPO, which is generally assessed by an increase in the levels of thiobarbituric acid reactive substances (TBARS) [13, 15,16]. In addition, malathion is a lipophilic substance; it may enhance LPO by directly interacting with the cellular plasma membrane [13]. It is evident that LPO is accompanied by an alteration (inhibition or activation) in the antioxidant defence system in different organs following acute, subchronic and chronic exposure to OP compounds [13,17–22]. Nevertheless, recent evidence suggests that exposure to different stress models and concentrations (acute, repeated and chronic restraint stress) have an important implication in the alteration of the antioxidant defence system [23]. The liver is the major metabolizing and the most active organ for mediating bio-activation of thiono-organophosphates [24]. It is considered among the primarily targets for malathion toxicity [25]. Thus, the aim of the present investigation was the evaluation of liver damage after subchronic exposure to malathion and the estimation of the antioxidant status using non-denaturing electrophoresis followed by activity-staining [26].

2. Materials and methods

2.1. Chemicals

Malathion (fyfanon 50 EC 500 g/l) of commercial grade was used in this study. 2-thiobarbituric acid (TBA); 2,6,-di-tert-butyl-4-methylphenol (BHT); trichloroacetic acid (TCA); Acetylthiocholine iodide; 5,5-dithio bis(2-nitrobenzoic acid)(DTNB); 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), phenazine methosulfate (PMS), magnesium chloride ($MgCl_26H_2O$); potassium iodide; sodium thiosulfate ($Na_2S_2O_3$) were obtained from sigma-Aldrich Co (Germany).

2.2. Animals and treatment

Adult male *wistar* rats (170–180 g), procured from Tunisian Society of Pharmaceutical Industries, were kept in clean plastic cages and allowed to acclimatize in the laboratory environment from 7 days. The ambient temperature was ($22 \pm 1\,^{\circ}C$) with a 12-h dark/light cycle. Balanced food and drinking water were given to the animals ad-libitum.

Animals were randomly divided into two groups of 12 animals and treated for 32 days. The first group received orally 1 ml corn oil via gavage. The second received instead 1 ml corn oil containing 100 mg Mal/kg body weight per day. The test concentration