Available online at www.sciencedirect.com
ScienceDirect
Pesticide Biochemistry and Physiology 91 (2008) 81–89
PESTICIDE
Biochemistry & Physiology
www.elsevier.com/locate/ypest

Prophylactic effect of green tea polyphenols against liver and kidney injury induced by fenitrothion insecticide

Manal E.A. Elhalwagy [a,*], Nevine S. Darwish [b], Enass M. Zaher [c]

[a] Department of Mammalian Toxicology, Pesticide Central Laboratory, Agriculture Research Center, Giza 12618, Egypt
[b] Department of Histology, Research Institute of Ophthalmology, Giza 12211, Egypt
[c] Department of Harmful Animals, Plant Protection Research Institute, Agriculture Research Center, Giza 12618, Egypt

Received 25 September 2007; accepted 9 January 2008
Available online 26 January 2008

Abstract

The ameliorative effect of daily administrated dose of green tea extract (60 mg polyphenols/animal/day) was investigated on albino rats *Rattus norvegicus* (150–180 gm) intoxicated with 1/30 and 1/60 LD_{50} fenitrothion organophosphate insecticide for 28 days. Blood samples were taken at 14 and 28 days for further biochemical parameters. Histopathological studies were carried out in the liver and kidney at the end of the experiment. Significant inhibition in plasma cholinesterase (ChE), a biomarker of Ops, was recorded. Damage in the liver and kidney tissues was observed and confirmed with elevation of plasma alanine aminotransferase (ALT), aspartate aminotaransferase (AST), albumin, urea and creatinine, as well as an elevation in the oxidative stress (OS) marker malondialdehyde (MDA). Decrease in total glutathione (GSH) content in erythrocytes and fluctuation in glutathione *S*-transferase (GST) activity in plasma was also observed. Green tea supplementation (60 mg/animal/day) partially counteracts the toxic effect of fenitrothion on oxidative stress parameters and repairs tissue damage in the liver and kidney, especially when supplemented to 1/60 LD_{50} intoxicated animals depending on the duration. It seems that enzyme and metabolite markers of these organs need more time to be restored to the control level.

Keywords: Organophosphorus insecticide; Fenitrothion; Green tea extract; Oxidative stress; Liver; Kidney; Alanine aminotransferase (ALT); Aspartate aminotransferase (AST); Albumin; Urea; Creatinine; Glutathione *S*-transferase; Total glutathione

1. Introduction

For centuries, pesticides have been used in agriculture to enhance food production by eradicating unwanted insects and controlling disease vectors. Among common pesticides; organophosphorus compounds (OP) are widely used in agriculture, medicine and industry. Fenitrothion(*O*,*O*-dimethyl-*O*-(3-methyl-4-nitrophenyl)phosphorothioate. Organophosphorus insecticide is now widely used for controlling a wide range of insects and other pests. Although fenitrothion exhibits low mammalian toxicity, biochemicals, morphological and functional alterations in animal tissues have been reported. The prolonged administration of fenitrothion increased the concentration of corticosterone and glucose in the plasma of male rats. It also increased the weight of the adrenal gland of male rats and altered its functions [1].

Dermal, inhalation and oral exposure to fenitrothion inhibit acetylcholinesterase enzyme (AChE)[1] in plasma, erythrocytes and brain of mammals [2,3], in addition to a considerable liver and kidney damage evidenced by elevation in serum aspartate and alanine aminotransferase

* Corresponding author.
E-mail address: manalelhalwagy2003@yahoo.com (M.E.A. Elhalwagy).

[1] *Abbreviations used:* Fn, fenitrothion; GT, green tea; OS, oxidative stress; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ChE, cholinesterase; AChE, acetylcholinesterase; GSH, reduced glutathione; GST, glutathione *S*-transferase; MDA, malondialdehyde; ROS, reactive oxygen species; GTE, green tea extract; GSH-Px, glutathione peroxidase; DTNB, 5,5′-dithiobis(2-nitrobenzoic acid); CDNB, 1-chloro-2,4-dinitrobenzene.

0048-3575/$ - see front matter © 2008 Elsevier Inc. All rights reserved.
doi:10.1016/j.pestbp.2008.01.006

(AST and ALT) [4,5]. Another studies recorded an increase in serum cholesterol and alternation in cell membrane fluidity and lipid content [6].

Acute and chronic exposure to fenitrothion induced ultra structural changes in liver and kidney cells of rats with complete distortion of the nuclear membrane, total loss of nuclear intactness and abnormally enlarged smooth endoplasmic reticulum [7]. These toxic effects probably occur through the generation of reactive oxygen species (ROS) causing damage to various membranous components of the cell [8]. The biochemical basis of oxidative damage is becoming clearer as recent studies point to the production of ROS as a secondary means of toxicity [9]. Cells succumb to oxidative damage when endogenous store of antioxidants is used up by the oxidant exposure. The antioxidant machinery is composed of enzymes like glutathione *S*-transferase (GST) [10], and non-enzymatic components are primarily composed of thiols and glutathione (GSH) [11]. Polyphenols have been recently recognized as functionally active molecules, possessing antioxidant, anticancer and antimutagenic properties, as well as exerting protective effects against cardiovascular and other diseases [12]. The essential polyphenols in foods are flavonoids and condensed tannins. These phenolic compounds occurring abundantly in vegetables, fruits and they showed high antioxidant property. Green tea extract represents the richest source of natural polyphenols, so it has generally a protective effect on liver, serum and central nervous tissue [13].

Green tea polyphenols has demonstrated a protective effect against a spectrum of offensive oxidants, like super oxide and peroxinitrite radicals [14]. It was found that Green tea increases the activity of liver antioxidant enzymes glutathione peroxidase GSH-Px and oxidized glutathione GSSG, as well as the content of reduced glutathione GSH and improves total antioxidant status (TAS) [15]. Polyphenols found in green tea show 20 times more powerful antioxidant activity than vitamin C [16].

The present work aims to investigate the effect of green tea polyphenols against toxicity induced by repeated different doses of fenitrothion insecticide. Their individual or combined effect on the antioxidant enzyme system, liver and kidney functions as well as their histopathological changes in male albino rats were evaluated.

2. Materials and methods

2.1. Materials

Fenitrothion insecticide in the formulated form, Sumithion 50, which contains fenitrothion 50%, was purchased from Kafr Elzayat Co. for Insecticide Ind., Kafr Elzayat, Egypt.

2.2. Antioxidant used

Green tea extract contains 98% polyphenols purchased from Hunan Changsha Yuanhang Biology Product Co., Ltd., China.

2.3. Animals and experimental design

Male albino rats *Rattus norvegicus (3–4) months age,* weighing between 150–180 g were used. Animals were supplied by the breeding unit of the Egyptian Organization for the Biology and Vaccine Production, Egypt. The animals were housed in plastic cages, fed *ad libitum* and allowed to adjust to the new environment for two weeks before starting the experiment. The rats were housed at 23 ± 2 °C dark/light cycle. All animals were treated according to the standard procedures laid down by OECD guidelines 407 (1992) repeated dose 28 days oral toxicity study in rodents [17].

Animals were randomly divided into six experimental groups five animals each as follows:

(1) *Group I (control group):* Each animal in this group was given distilled water (1 ml/animal) by gastric intubation every day for 28 days.
(2) *Group II; green tea (GT):* Rats were orally given 60 mg green tea extract/animal dissolved in distilled water every day for 28 days.
(3) *Group III; fenitrothion high dose (FnH):* Rats were orally given 1/30 LD_{50} (20 mg/kg bw) of fenitrothion daily *via* gastric tube for 28 days.
(4) *Group IV; fenitrothion low dose (FnL):* Rats were orally given 1/60 LD_{50} (10 mg/kg bw) daily *via* gastric tube daily for 28 days.
(5) *Group V; fenitrothion high dose with green tea extract (GTFnH):* Rats were orally given green tea extract (60 mg/animal) 1 h prior administration of 1/30 LD_{50} (20 mg/kg bw) of fenitrothion daily for 28 days.
(6) *Group VI; fenitrothion low dose with green tea extract (GTFnL):* Rats were orally given green tea extract (60 mg/animal) 1 h prior administration of 1/60 LD_{50} (10 mg/kg bw) of fenitrothion daily for 28 days.

2.4. Sampling

Blood collected from the retro-orbital plexus vein according to Schermer [18], on heparinized tubes at 14 days and 28 days of treatment periods. Plasma samples were separated by centrifugation of the blood samples at 3600 rpm for 15 min. Plasma samples were kept at −20 °C for subsequent use. At the end of the experiment, animals were sacrificed and samples of the liver and kidney were excised for histopathological studies.

2.5. Histopathology

Histopathological examination was carried out according to Drury and Wallington [19]. The liver and kidney tissues were dissected and the tissue samples were fixed in 10% formalin solution for 14–18 h, passed in a series of graded ethanol and embedded in paraffin. Paraffin sections were cut with at 5 μm thickness and stained with