

¹H NMR-based metabonomic analysis of the serum and urine of rats following subchronic exposure to dichlorvos, deltamethrin, or a combination of these two pesticides



Hui-Ping Wang^{a,b,1}, Yu-Jie Liang^{a,1}, Ying-Jian Sun^c, Jia-Xiang Chen^a, Wei-Yuan Hou^a, Ding-Xin Long^a, Yi-Jun Wu^{a,*}

^a Laboratory of Molecular Toxicology, State Key Laboratory of Integrated Management of Pest Insects and Rodents, Institute of Zoology, Chinese Academy of Sciences, Beichenxi Road, Beijing 100101, PR China

^b Beijing Chaoyang District Center for Disease Control and Prevention, Beijing 100021, PR China

^c Department of Veterinary Medicine and Animal Science, Beijing University of Agriculture, Beijing 102206, PR China

ARTICLE INFO

Article history:

Received 21 October 2012

Received in revised form 25 March 2013

Accepted 28 March 2013

Available online 6 April 2013

Keywords:

Organophosphorus pesticide

Pyrethroid

Metabonomic analysis

¹H NMR spectra

Combined toxicity

Subchronic effect

ABSTRACT

Metabonomic analysis, clinical chemical analysis and histopathology were used to investigate the toxic effects of subchronic exposure to dichlorvos, deltamethrin, and a combination of these two pesticides, in rats. Weight loss, hind limb weakness and histopathological changes in kidney tissue were only observed in rats exposed to high doses of deltamethrin, or a combination of deltamethrin and dichlorvos. Urinary metabonomic analysis indicated that exposure to a mixture of dichlorvos and deltamethrin was followed by increases in urinary lactate, dimethylamine, N-glycoprotein (NAC) and glycine similar to those observed in rats treated with either dichlorvos or deltamethrin alone. Serum metabonomic analysis suggests that dichlorvos induced an increase in lactate and alanine and a decrease in dimethylglycine (DMG), NAC and very low- and low-density lipoprotein (VLDL/LDL). High levels of lactate and low levels of NAC and VLDL/LDL were observed in the deltamethrin treatment group. Treating rats with a mixture of dichlorvos and deltamethrin caused an increase in serum lactate, trimethylamine-N-oxide (TMAO), choline and alanine, with the highest levels of these metabolites observed in those that received the highest dose. Exposure to a mixture of dichlorvos and deltamethrin also resulted in a decrease in serum acetone, DMG, NAC, and VLDL/LDL. Changes in serum TMAO, alanine, choline and acetone in this treatment group were higher than in rats treated with either dichlorvos or deltamethrin. These results suggest that exposing rats to subchronic doses of dichlorvos, deltamethrin, or a combination of these pesticides, disrupted the energy metabolism of the liver and reduced kidney function.

© 2013 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Dichlorvos (DDVP), an organophosphorus pesticide, and deltamethrin (DM), a photostable pyrethroid, are widely used in agriculture, industry and medicine. Large-scale and long-term use of these chemicals inevitably pollutes the environment thereby posing a serious threat to human health.

Early research on DDVP toxicity in rats mainly focused on general toxicity, such as lethality, reproductive toxicity, teratogenesis

and carcinogenesis. More recent studies have investigated the effects of DDVP on the cholinergic system [1], brain development [2] and behavior [3,4]. In addition, DDVP has been found to impair antioxidant defense systems, increase lipid peroxidation [5] and induce hepatotoxicity in rats [6]. Previous research on DM has been mainly on its cumulative toxicity, genotoxicity, carcinogenesis, and neurotoxicity. More recent research has concentrated on its toxicity to the brain and liver [7,8]. Although there has been some work on the effects of long-term chronic exposure to low

Abbreviations: ALB, albumin; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CHE, cholinesterase; CRE, creatinine; DDVP, dichlorvos; DM, deltamethrin; DMA, dimethylamine; DMG, dimethylglycine; FIDs, free induction decays; ¹H NMR, ¹H nuclear magnetic resonance; LD₅₀, half-lethal doses; LDL/VLDL, low- and very low- density lipoprotein; MIX, mixture of dichlorvos and deltamethrin; NAC, N-acetylglycoprotein; PCA, principal components analysis; SIMCA, soft independent modeling of class analogy; TMAO, trimethylamine-N-oxide; TSP, 2,2',3,3'-deuterio-trimethylsilylpropionic acid.

* Corresponding author. Address: Chinese Academy of Sciences, Institute of Zoology, 1-5 Beichenxi Road, Beijing 100101, PR China. Tel.: +86 10 64807251; fax: +86 10 64807099.

E-mail address: wuyj@ioz.ac.cn (Y.-J. Wu).

¹ Equal contributions to this paper.

Table 1

Doses of dichlorvos (DDVP), deltamethrin (DM) and a mixture of these two pesticides (MIX), administered to rats in this study.

Groups	Doses (mg/kg/day)		
	Low (1/125 LD ₅₀)	Middle (1/50 LD ₅₀)	High (1/20 LD ₅₀)
DDVP	0.64	1.60	4.00
DM	1.02	2.56	6.40
MIX	0.64 (DDVP) + 1.02 (DM)	1.60 (DDVP) + 2.56 (DM)	4.00 (DDVP) + 6.40 (DM)

Abbreviations: DDVP, dichlorvos; DM, deltamethrin; MIX, a mixture of DDVP and DM; LD₅₀, half-lethal dose.

levels of DDVP [9–11] and DM [7,12,13], no model was established to evaluate the long-term consequences of repeated oral exposure to low doses of a mixture of DDVP and DM, which may give us some clues to understanding the mechanisms of the combined toxicity of the two pesticides at their lower concentrations.

Endogenous metabolites are important factors in cellular regulatory and metabolic processes that respond to toxicological insults. Metabolomics, the multi-targeted analysis of endogenous metabolites from biological samples, using high-resolution ¹H nuclear magnetic resonance (NMR) spectroscopy combined with computer-based pattern recognition methods, such as principle

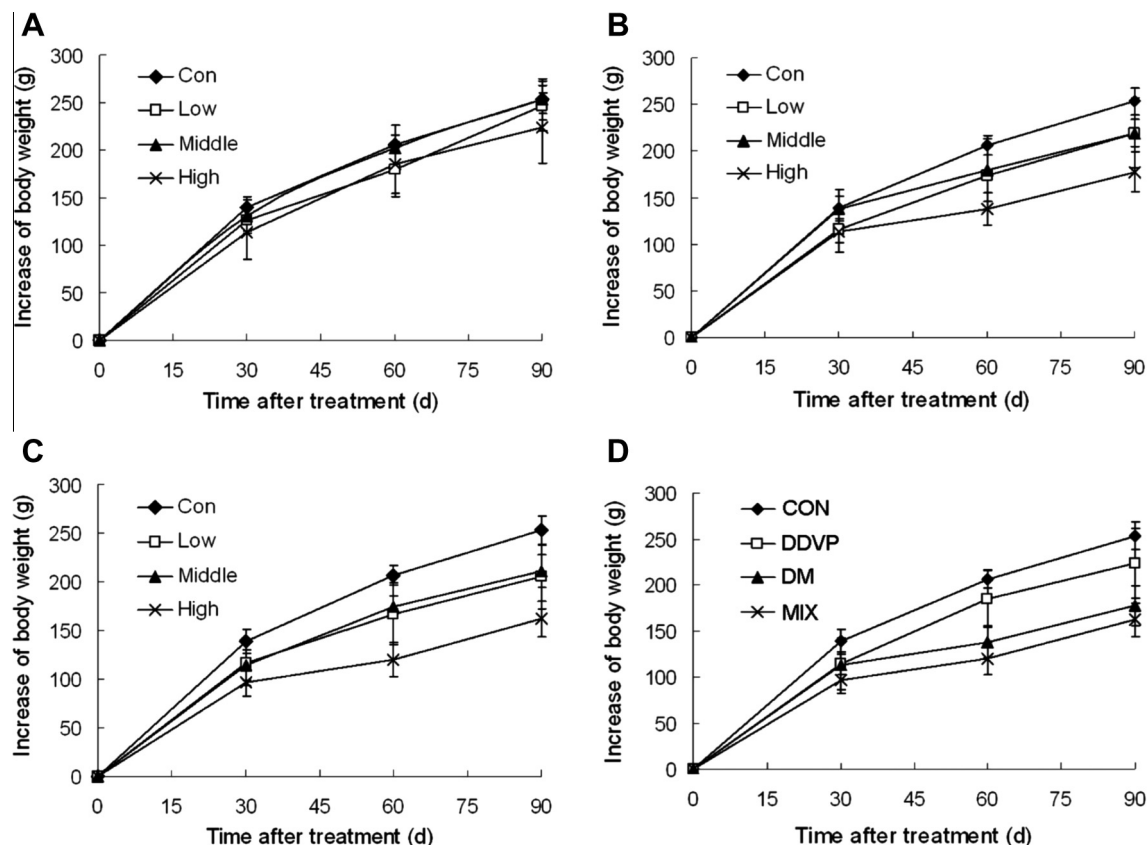


Fig. 1. Body weights of control (CON) and rats orally treated with dichlorvos, deltamethrin, or a combination (MIX) of these chemicals, for consecutive 90 days. (A) DDVP, (B) deltamethrin, (C) MIX and (D) high dose group.

Table 2

Selected clinical chemistry parameters of the rats treated with different doses of dichlorvos (DDVP), or deltamethrin (DM), or a combination of these pesticides (MIX).

Pesticides	Dose groups	Parameters					
		AST (U/L)	ALT (U/L)	ALP (U/L)	CRE (mol/L)	BUN (mg/dL)	CHE (U/L)
DDVP	Control	101.75 ± 22.21	46.50 ± 8.38	53.25 ± 8.67	45.00 ± 4.95	6.57 ± 1.70	325.75 ± 27.33
	Low	102.75 ± 13.88	49.25 ± 4.82	56.00 ± 6.67	48.50 ± 4.82	6.52 ± 0.66	197.75 ± 4.97 ^a
	Middle	107.00 ± 10.75	48.25 ± 5.76	48.75 ± 6.50	47.50 ± 3.28	5.97 ± 0.84	163.00 ± 12.19 ^a
	High	114.00 ± 14.28	48.00 ± 3.94	48.75 ± 4.66	43.00 ± 3.08	5.61 ± 0.67	130.50 ± 10.21 ^a
DM	Low	92.00 ± 17.83	48.75 ± 7.82	52.50 ± 6.80	43.25 ± 4.49	6.68 ± 1.18	238.25 ± 31.02 ^a
	Middle	95.25 ± 8.38	54.00 ± 8.25	72.25 ± 6.80	42.25 ± 7.73	5.10 ± 0.28	237.50 ± 23.77 ^a
	High	108.25 ± 14.91	52.50 ± 6.80	77.25 ± 7.22	44.25 ± 7.73	5.81 ± 0.48	242.25 ± 28.63 ^a
MIX	Low	106.75 ± 16.50	43.00 ± 6.89	46.50 ± 4.15	44.50 ± 9.18	5.86 ± 0.57	196.25 ± 41.66 ^a
	Middle	95.00 ± 13.06	46.25 ± 2.59	52.00 ± 8.58	42.25 ± 2.59	6.12 ± 1.02	157.75 ± 26.41 ^{a,b}
	High	117.50 ± 10.31	50.25 ± 4.49	92.75 ± 8.70 ^a	45.25 ± 7.22	6.57 ± 1.11	121.75 ± 11.21 ^{a,b}

Data were presented as mean ± SD of *n* = 5 animals per groups. Statistical analysis was performed by ANOVA followed by Dunnett's test. Abbreviations: ALB, albumin; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CHE, cholinesterase; CRE, creatinine; MIX, mixture of dichlorvos and deltamethrin

^a *p* < 0.05 for significant difference from control group.

^b *p* < 0.05 for significant difference from either dichlorvos (DDVP) or deltamethrin (DM).

Download English Version:

<https://daneshyari.com/en/article/5848166>

Download Persian Version:

<https://daneshyari.com/article/5848166>

[Daneshyari.com](https://daneshyari.com)