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Short Communication

Effect of dichlorvos on tissue esterases in rats

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Abstract

The effect of dichlorvos was investigated on various tissue esterases in rats after single oral administration (60 mg/kg). It produced significant ($P < 0.05$) inhibition of cholinesterase and carboxylesterase enzymes in all tissues within 30 min after administration. At 3 h, maximum inhibition in cholinesterase and carboxylesterase enzyme levels was recorded in blood (45%) and liver (58%), respectively. The present investigation reveals dichlorvos to be a potent inhibitor of tissue esterases, *in vivo*, and its exposure may impair biotransformation of xenobiotics that are mainly biodegraded by carboxylesterase enzyme.

Key words: Dichlorvos, cholinesterase, carboxylesterase.

1. Introduction

Dichlorvos, an organophosphate insecticide, has wide application in agriculture and veterinary practices[1]. It is also used to control a variety of pests[2,3]. Extensive use of this insecticide raises questions on health hazards to man and domestic animals. Estimation of esterases as a tool for organophosphate insecticide poisoning has been reported[4,5]; however, such studies are lacking for dichlorvos. The present investigation aims to study the effect of single oral administration of dichlorvos on tissue esterases in rats.

2. Materials and methods

Insecticide and chemicals: Nuvan® (76%) of Hindustan Ciba-Geigy, Ltd., Bombay was the source of dichlorvos. Indophenyl acetate and acetylthiocholine were obtained from Eastman Organic Chemicals, Rochester, New York and Sigma Chemical Co., St. Louis, Missouri, respectively.

Animals and treatment: Adult male albino rats (Winstan strain, 200–350 g) were used in the present study. The animals, maintained on standard diet, were acclimatized in the

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Table I
Effect of single oral administration of dichlorvos (60 mg/kg) on tissue esterases in rats

Tissue	Time after administration (min)							
	0	15	30	60	180	360	540	720
Cholinesterase (nmol acetylthiocholine hydrolysed/min/g protein)								
Blood	675.5±3.6	606.3±5.3[b]	525.5±1.5[b]	494.4±2.2[a]	368.8±3.4[a]	436.4±4.4[a]	583.4±2.7[b]	695.6±1.5
Liver	569.3±16	503.3±20[b]	457.9±11[b]	362.4±8.9[a]	388.8±14[a]	395.5±13[a]	466.4±12[b]	543.6±8.6[b]
Lung	125.7±2.2	120.5±1.6	110.5±3.1[b]	96.4±1.5[b]	82.8±3.2[a]	91.6±3.5[b]	112.3±3.5	128.3±4.9
Testes	85.1±1.5	84.6±1.4	78.6±2.8	69.5±2.3[b]	54.8±1.6[a]	65.2±3.1[b]	72.3±4.9[b]	81.5±2.2
Muscles	39.5±1.1	37.6±0.6	30.5±0.8[b]	26.1±0.6[a]	24.8±0.2[a]	29.2±0.3[b]	34.3±0.6	37.5±1.8
Carboxylesterase (nmol indophenol formed/min/g protein)								
Blood	109.6±1.6	95.9±1.6[b]	63.6±1.3[a]	48.5±1.8[a]	51.2±1.8[a]	69.6±2.1[a]	87.3±1.5[b]	99.5±3.2
Liver	398.6±1.8	380.8±6.3	330.7±9.8[b]	224.1±6.2[a]	169.4±9.5[a]	265.3±11[a]	321.1±1.12[b]	343.7±6.9
Lung	67.5±1.6	62.5±0.9	53.9±0.2[b]	43.8±0.4[a]	39.5±0.9[a]	46.4±0.7[a]	59.5±1.1[b]	70.8±0.5
Testes	28.6±2.2	27.4±1.6	22.5±1.3[b]	19.7±2.15[a]	14.1±1.84[a]	12.8±2.2[a]	18.4±2.5[a]	26.3±3.6
Muscles	43.9±1.6	42.5±1.1	38.4±2.2	22.8±3.8[a]	22.8±3.8[a]	20.6±0.9[a]	35.4±0.5[b]	40.3±1.3

Values given are mean ±SE of the results obtained from 5–8 animals. [a]Significantly different at $P < 0.01$ when compared with 0 min value. [b]Significantly different at $P < 0.05$ when compared with 0 min value

departmental laboratory for 15 days before commencement of the experiments. The rats were randomly divided into eight groups of ten animals each. Dichlorvos, dissolved in 0.8–1.0 ml of propylene glycol, was given in a single oral dose of 60 mg/kg body weight (75% LD_{50}). Animals of group 1, served as controls, received an equal volume of propylene glycol. Animals of group 1, 2, 3, 4, 5, 6, 7 and 8 were decapitated at 0, 15, 30, 60, 180, 360, 540 and 720 min after oral administration of insecticide. The study was carried out only in survivors and rats that died before the pre-determined time were not taken into account.

Collection of samples and assay of enzymes: At the time of sacrifice, blood was collected into heparinized test tubes and plasma separated. The organs *viz.*, liver, lung, testes and skeletal muscle were removed and 5–10% of tissue homogenates were prepared in chilled distilled water, using a Potter Elvehjem type glass homogenizer[6]. Cholinesterase enzyme was assayed, using acetylthiocholine as substrate[7,8] and the enzyme activity was expressed as nmol acetylthiocholine hydrolysed/min/g protein. Carboxylesterase level was assayed by using indophenyl acetate as substrate[9]. The significant difference between two means was determined at $P < 0.05$ and $P < 0.01$ levels.

3. Results and discussion

The oral administration of 3/4 LD_{50} dose of dichlorvos produced clinical symptoms of organophosphate insecticide poisoning in all animals[6,10]. The typical signs were hypersalivation, urination, defecation, miosis, lacrimation, restlessness, abdominal cramps, tremors and convulsions. Three animals showing severe toxic signs, died between 6 and 7 h of dichlorvos administration. The quick appearance of toxic symptoms following dichlorvos administration suggests that this insecticide is rapidly absorbed after oral administration. The toxic symptoms appeared after 6–10 min of administration and persisted up to 7 h.

Table I shows the effect of dichlorvos on tissue levels of cholinesterase and carboxylesterase enzymes. At 3 h, maximum inhibition in cholinesterase levels was noted in blood (45%) followed by testes (36%) and lung (34%). The present observations are in agreement with the results of other workers, who demonstrated that organophosphate insecticides caused marked inactivation of tissue cholinesterase[6]. Our observations tend to indicate that inhibition of tissue cholinesterase was maximum between 1 and 3 h after administration of insecticide when the animals also showed peak toxic symptoms. Further, among various tissue cholinesterases, determination of blood cholinesterase activity may be regarded as a better index to assess the exposure of dichlorvos in animals.

There was significant ($P < 0.01$) inhibition in the levels of carboxylesterase enzyme. The extent of carboxylesterase inhibition in various organs declined in the following order: liver (58%), blood (56%), testes (55%), muscle (51%), lung (41%). Ecobichon and Zelt[11] also observed marked inhibition in renal and hepatic carboxylesterases following acute doses of fenitrothion in rats. Inhibition of carboxylesterase enzyme may have

profound effect on toxicity of other organophosphorus insecticides that are selectively inactivated by this enzyme system[12]. The inhibitory effect of dichlorvos on carboxylesterase activity observed in the present study may enhance the toxicity of malathion, another organophosphate insecticide. Several carboxylesterase inhibitors have been demonstrated to potentiate the toxicity of malathion in man and animals[14,15].

4. Conclusions

The present results suggest that dichlorvos is a potent inhibitor of tissue esterases, *in vivo*. In addition to its inherent toxic effects, exposure of dichlorvos may diminish carboxylesterase-dependent detoxification of xenobiotics.

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