

Teratogenic Effects of Certain Insecticides on mice.

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ABSTRACT

Three different insecticides Carbaryl, methyl Parathion and Fenvalerate were given as a single oral dose to pregnant Swiss Albino female mice. The results showed the extra-rib; unossified proximal phalanges of foot and middle phalanges of hand which observed at 250 mg/kg of Carbaryl. Cervical-rib; unossified distal phalanges of hand and middle phalanges of foot observed at 24 mg/kg of methyl parathion. Otherwise cervical-rib was observed only at 200 mg/kg of fenvalerate. Tested insecticides had a detrimental effect on the activity of placental alkaline phosphatase in vitro. This study throws some light on the effect of the tested chemicals organization period and the activity of the placental alkaline phosphatase in vitro.

INTRODUCTION

Many organophosphate (OP) and alkyl-carbamate (AC) insecticides are potent teratogens (Eto *et al.*, 1980). Carbaryl is a broad spectrum carbamate insecticide which

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reversibly inhibits cholinesterase enzyme. Studies on the potential embryotoxicity of carbaryl have produced inconsistent findings. Smally *et al.* (1968) reported a low irregular incidence of malformation among the offsprings of beagle doses given were 6, 12, 25 or 50 mg/kg/day of carbaryl in the diet, no embryotoxicity or teratogenicity was observed in rabbits given up to 200 mg/kg/day in the diet (Robenes 1969). Organophosphate insecticides are more toxic to weavling and newborn rats than the adult (Lue *et al.*, 1965). Methyl parathion has recently been investigated in rats and mice but administration of the insecticide was only on a single day of gestation. High fetal mortality and incidence of cephth plate as well as suppression of fetal growth and ossification occurred with adult (Tanimura *et al.*, 1967).

Pyrethrum was not found to have any teratogenic activity at dose level of 90 mg/kg/day administered in capsule daily to 7 new zealand white female rabbits, dose from 8-15 of pregnancy, and of 5000 ppm added in the diet of 18 female rats in a litter and generation reproduction study (Weire-1965). Abbas *et al.* (1986) indicated that fenvalerate was the most persistent in all tissues of laying chickens followed by cypermethrin and deltamethrin. The present study investigates possible teratogenicities of carbaryl, methyl parathion and fenvalerate in Swiss-Albino mouse in an attempt to calrify the effects on early stages of mice pregnancy and the relation between the teratogenicity and the activity of placental alkaline phosphatase in vitro.

MATERIALS AND METHODS

- I - Insecticides : Technical grades of carbaryl (90%) methylparathion (95%) and fenvalerate (95%) were obtained from

Environmental Protection Agency (EPA).
Research Triangle park. N.C., U.S.A.

- II - Animals : Females mice were bred with males of the same strain of using one male per every two females. when a plug was present, the females were separated and housed in groups (Five pregnant females were used in each group). **Teratology** data sheet, Research Triangle, N.C. was used for tabulating the data.
- III- Treatment of animals : The dose levels of insecticides carbaryl, methyl parathion and fenvalerate were; 25, 50, 250; 2.4, 4.8, 24 and 20,40, 200 mg/kg respectively. Treatment and observations of animals were mentioned previously by (Komeil et al., 1991)
- V- Placental alkaline phosphatase in vitro: The method was described previously Bessy et al. (1946) and some modification was made by (Komeil et al., (1991). The concentration required to inhibit 50% of the enzyme activity (I_{50}) was calculated

RESULTS AND DISCUSSION

Unossified middle phalanges of the hand unossified proximal phalanges of foot and extra-rib were observed at the high dose of carbaryl (Figure 1a,b). These results are in agreement with Murray et al., (1979) who noted that treatment with carbaryl resulted in several minor skeletal variants among mice offspring. Robens (1969) found fused ribs short maxilla or mandible in the offspring Guinea pig treated with carbaryl of skeleton formation in the pups of Beagle dogs following treatment with carbaryl. Unossified distal phalanges of the hand, middle phalanges of foot and cervical rib (Figure 2a,b) were

observed at the high dose of methyl parathion as well as the unossified middle phalanges of the foot was observed at the middle dose of methyl-parathion. In spite of the high dose of methyl. parathion. the examination was considered only on the other hand the bifurcated rib (Figure 3a,b) appeared only in one litter of high dose of methyl-parathion but asymmetrical sternbrae (Figure 4a,b) was observed at the middle and high dose of methyl parathion. Skeletal malformations induced by the tested doses of methyl parathion in the present study are in agreement with those reported by Tanimura et al. (1967) in the offspring of ICR/JCL mice following treatment with methyl parathion as day 10 of gestation.

Complete unossification (Figure 5a,b) was observed at all tested doses of methyl parathion and the high dose of fenvalerate. Main observed skeletal malformations were extra-rib, cervical rib and unossified middle phalanges of foot.

The inhibitory effect of tested insecticides on placental alkaline phasphatase was studied in vitro. the results showed that fenvalerate was the Most **potent** inhibitor to the enzyme with **I₅₀** value of 2.3 U mole followed by methyl parathion and carbaryl with **I₅₀** values of 5.8 and 70 U mole **respectively** (table I).

Table (1) effect of carbaryl, methyl parathion and fenvalerate on placental alkaline phosphatase in vitro.

Compound	I ₅₀ um
Carbaryl	70.00
Methyl parathion	5.80
Fen valerate	2.30

These results are in agreement with Murphy (1965) who showed a relationship between organophosphorus insecticides and



Fig. (1a):Control 1st lumbar vertebra

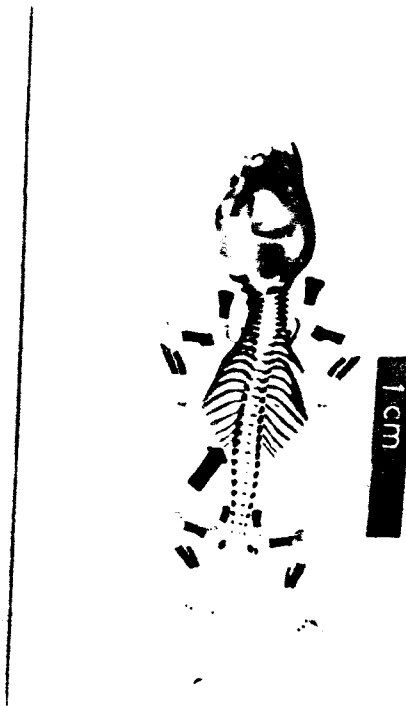


Fig. (1b) :Extra-rib at the 1st lumbar vertebra



Fig. (2a) :Control 6th cervical vertebra.



Fig. (2b):Cervical rib at the 6th cervical vertebra.



Fig. (3a): Control 2 nd thoracic rib .

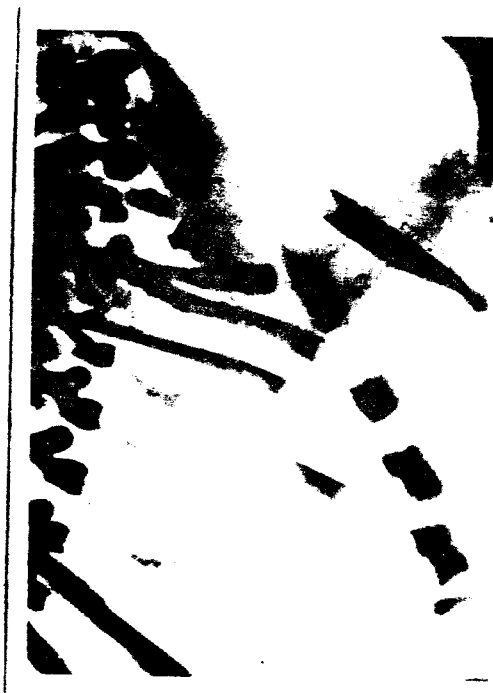


Fig.(3b) :Bifurcated rib at the 2nd thoracic rib.



Fig.(4a): Control symmetric sternbrae.

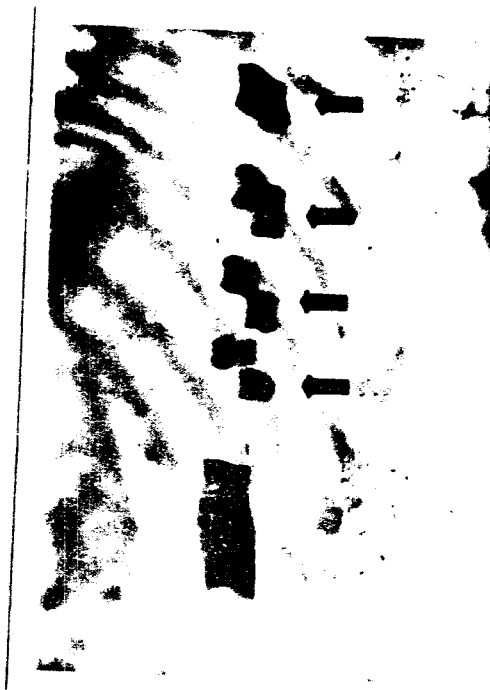


Fig.(4b): symmetric sternbrae.



Fig. (5a):Control complete ossification.



Fig. (5b):complete unossification.

alkaline phosphatase in rats in vivo. Komeil et al. (1991), revealed that there was a relationship between the systemic fungicides benomyl and carbenazim and placental alkaline phosphatase of mice in vitro. These results explained that all the tested insecticides which showed skeletal malformation showed also inhibitory effect on the placental alkaline phosphatase in vitro. for that reason the alkaline phosphatase can be considered to be as an indicator for teratogenicity examination.

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