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# EVALUATION OF THE DEVELOPMENTAL TOXICITY OF ALDICARB IN THE RAT

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## ABSTRACT

Aldicarb, 2-methyl -2-(methylthio)- propionaldehyde O- methylcarbamoyloxime, is currently manufactured in the US by Rhone-Poulenc Company and sold under the trade name Temik. In the present study, aldicarb was evaluated for potential developmental toxicity. Groups of 30 bred females Fischer 344 rats were given 0, 0.1, 0.3, and 0.5 mg/kg per day by gavage on gestation days 6-15; the fetuses were evaluated on gestational day 21. Clinical signs of toxicity attributed to aldicarb were noted in dams receiving 0.3 and 0.5 mg/kg per day. Maternal and fetal brain acetylcholinesterase activities were reduced in treated groups of 0.3 and 0.5 mg/kg per day. Maternal effects in the treated group of 0.5 mg/kg per day included depressed body weight. Fetal weight and viability were decreased, and fetal death, early, and late resorption were increased at the 0.5 mg/kg per day maternal dose. Skeletal abnormalities were also increased in this group. Aldicarb showed fetotoxic effects at a maternal dose of 0.5 mg/kg per day, a dose that also produced maternal toxicity.

**Key words:** Aldicarb; Developmental toxicity; malformations, fetotoxicity; maternal toxicity; rat

## INTRODUCTION

Aldicarb, 2-methyl -2- (methylthio)propionaldehyde -O- methylcarbamoyloxime, is an oxime carbamate insecticide and soil- systemic pesticide used against certain insects, mites, and nematodes (Risher *et al*., 1987). It is one of the most acutely toxic pesticides registered according to EPA (EPA, 1988). The acceptable daily intake value (ADI) for aldicarb is 0.003 mg/kg/day (Kidd and James, 1991) and the oral reference dose (RfD) is equal 0.001 mg/kg/day in humans following repeated exposures (EPA, 1994). Like all members of this chemical family, it inhibits the action of an enzyme that is an essential component of both insect and mammal nervous systems. The enzyme, acetylcholinesterase (AChE), controls the chemical reaction that transforms acetylcholine, a neurotransmitter, into choline (Cremlyn, 1991). Without functioning AChE, acetylcholine accumulates and prevents the smooth transmission of nerve impulses across the junctions between nerves. This causes loss of muscular coordination, convulsions, and ultimately death (Cremlyn, 1991). However, unlike the relatively irreversible anticholinesterase activity of the organophosphate pesticides, the carbamylation process which produces the anti-AChE action is quickly reversible even if death has occurred (Morgan, 1989). Extensive oral toxicological testing of aldicarb has been conducted. The acute oral toxicity of aldicarb is high, with oral $LD_{50}$ values in rats, mice, guinea pigs, and rabbits ranges from 0.5 mg/kg to 1.5 mg/kg when administered in a liquid or oil form (Hays and Laws, 1991; EPA, 1987). The highest dose at which no adverse effects for humans were observed (NOEL) was 0.02 mg/kg/d (EPA, 1991). Although aldicarb is acutely highly toxic to humans and laboratory animals, there is no substantial evidence of carcinogenicity, mutagenicity, teratogenicity, or immunotoxicity. After reviewing the available genotoxicity data, it concluded that aldicarb was not genotoxic (EPA, 1987; WHO, 2003; Blevins *et al*., 1988; Godek *et al*.,1984). In mammal cells, no evidence was found linking aldicarb exposure to the three types of genetic damage: mutation frequency of Chinese hamster ovary cells, chromosome aberrations in mouse bone marrow cells, and unscheduled DNA synthesis in rat liver cells (California Department of Pesticide Regulation, 1991). Furthermore, aldicarb exposure has not been associated with an increase in cancer incidence in tests conducted by the National Toxicology Program (Haseman, 1987). Two dietary carcinogenicity studies had been conducted with aldicarb in rats and three in mice produced no significant effects in either species (WHO, 2003). Furthermore, in a study conducted by the National Cancer Institute (NCI) to determine a possible carcinogenic effects in rats and mice at dose levels of 2 or 6 ppm in the diet, concluded that none of the tumors could be clearly attributed to the administration of aldicarb in the either species (National Cancer Institute, 1979). A three generation study in rats at doses of 0.05 and 0.10 mg/kg/day produced no significant toxic effects and in another reproductive study, a dose of 0.70 mg/kg/day produced no adverse reproductive health effects in rats (Union Carbide Corporation, 1974). In another 3- generation reproductive toxicity study, rats were fed with doses of 0, 0.04, 0.20, and 1.0 mg aldicarb per kg body weight per day. Although

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the highest dose administered was near the reported $LD_{50}$ for rats, no significant effects on fertility, viability of offspring, lactation or other parameters were observed (Union Carbide Corporation, 1966). By contrast, in human cells, aldicarb causes an increase in the number of three different kinds of chromosome abnormalities: sister-chromatid exchanges, chromatid breaks, and chromosome breaks (Cid and Matos, 1984, 1987). Aldicarb exhibited immunomodulatory capability in mice at low concentration up to 1000 ppb in drinking water (Olsen *et al*., 1987). Furthermore, aldicarb selectively affected macrophage- mediated cytotoxicity of tumor target cells without affecting the cytotoxicity mediated by natural killer cells (Dean *et al*., 1990). Aldicarb has also caused reproductive problems in laboratory rats. In an oral developmental toxicity study, pregnant rats given the dose levels of 0.125, 0.25 or 0.5 mg/kg/day from aldicarb from gestation day 6 to 15 showed a positive effect including decreased maternal body weight, food consumption, and skeletal abnormalities (Rhone-Poulenc Ag Company, 1988). In addition, aldicarb exposure of rats during pregnancy decreases maternal food consumption and body weights. The weight of their offspring was also reduced, and the babies suffered from skeletal abnormalities, delayed bone formation, and ruptured blood vessels (WHO, 1991). Similar kinds of effects have been noted in birds. In ducks, application of aldicarb to eggshells during incubation caused shortening of a foot bone and the middle toe (Chambers *et al*., 1989). Treatment of young chicks for one week with aldicarb reduced their growth for forty days after treatment had ended (Farage- Elawar, 1990). On the other hand, aldicarb administered to pregnant rats at very low levels (0.001 to 0.1 mg/kg/day) depressed acetylcholinesterase activity more in the fetuses than in the mothers. Furthermore, it was also retained in the mother's body for longer periods than in nonpregnant rats (Cambon *et al*., 1979). Although adldicarb has been classified as extremely hazardous (EPA, 1988), no recent information regarding the developmental toxicity effects was found. The study reported herein was conducted to further evaluate the developmental toxicity of aldicarb at doses considerably lower than those reported to cause no developmental toxicity in rats following oral exposure .

## MATERIALS AND METHODS

### Chemical

Aldicarb was obtained from the Chem. Service, Inc. The purity of the test material was 99.4%.

### Animals and conditions

Male and female Fischer 344 rats, approximately 10 weeks old, were obtained from the High Institute of Public Health, Alexandria University, Alexandria, Egypt. All rats were examined for health status and acclimated to the laboratory environment for 2 weeks prior to use. Temperature was maintained at 23 ± 2 ºC, and relative humidity at approximately 50%, with a 12 h: 12 h light: dark photoperiod. Animals were housed in stainless – steel cages and given standard diet and water *ad libitum* throughout the study. Adult virgin female rats were mated with adult males (one male/two females). Sperm –positive females were considered to be in Day 0 of pregnancy. Pregnant rats (28 – 29 per group) were treated by oral gavage starting at Day 6 through Day 15 of gestation with 0, 0.1, 0.3, 0.5 mg/kg/d aldicarb and distilled water served as the vehicle control. The administered volume of each dose was 4 ml/kg body weight per day, adjusted for recorded body weight changes during the study.

### Maternal effects

Females were examined daily throughout the experimental period for signs of toxicity. Maternal body weight was recorded on days 6, 9, 12, 15, and 20 of gestation. Feed consumption was recorded on days 6, 9, 12, 15, and 20 of gestation. Weights of maternal liver, kidneys, and brain were recorded at the time of Cesarean section on day 21 of gestation.

### Fetal effects

Pregnant females anaesthetized using diethyl ether on day 21 of gestation. The uterine horns were examined for the number and location of fetuses and resorption sites. Fetuses were removed, weighed, sexed, and evaluated for external abnormalities. The uteri of apparently non-pregnant rats were stained with 10 % sodium sulfide (Salewski, 1964) and examined for evidence of implantation sites. One – third of the fetuses were fixed in Boiun's solution for razer blade sectioning (Wilson and Warkany, 1965). The remaining fetuses were fixed in alcohol, double stained with alizarin red S for ossified bone and alcian blue for cartilage, and cleared in 2 % KOH and glycerin (Wilson and Warkany, 1965).

### Acetyl cholinesterase assay

### Sample collection and preparation

After anesthesia with diethyl ethyl, dams brains were quickly isolated on ice. The uterus was removed and placed on wet ice. Four fetuses were removed: upper right horn, lower right horn, upper left horn, and lower left horn. The fetal brains were collected individually and frozen on dry ice. Maternal and fetal brains were homogenized with a
Potter- Elvehjem type homogenizer using a glass mortar and Teflon pestle. Brain was homogenized in 20 volumes (w/v) ice-cold 50 mM sodium phosphate buffer (pH 8) (Lassiter *et al*., 1998).

**Determination of protein and acetylcholinesterase activity**

Protein was determined according to the protein – dye binding method of Bradford (Bradford, 1976). The dye solution was made by dissolving 100 mg of Coomassie Brilliant Blue G-250 in 50 ml 95% ethanol and 100 ml 85 % (w/v) phosphoric acid. To 5 ml of this solution was added 0.1 ml brain preparation, and the contents were mixed by vortexing. Absorbance was measured at 595 nm at least 2 min but not more than 50 min after mixing, in 3- ml cuvettes against a reagent blank using a Spectronic 21D Spectrophotometer. The concentration was estimated from a standard curve of concentrations of bovine serum albumin (BSA). Acetylcholinesterase activity was determined by measuring the rate of hydrolysis of acetylcholine iodide (3 x 10-3 M) in 0.1 M sodium phosphate buffer (pH 8) according to a published method (Ellman *et al*., 1961). Substrate was incubated with brain (2.5 mg wet tissue) in a total volume of 3.2 ml. The absorbance (412 nm) was recorded using a Spectronic 21D Spectrophotometer. Correction was made for nonenzymatic hydrolysis of substrate.

**Statistical evaluation**

An estimation of maternal toxicity was made from maternal body weights, feed consumption, and absolute and relative organ weights and the dose groups were compared to the control group utilizing the one- way analysis of variance procedure (ANOVA) followed by Tukey's multiple comparisons. The maternal body weight on day 6 of gestation was used as a covariant (ANCOVA) for comparing weights of the treatment groups with those of the control. Fetal weights analyzed with a nested ANOVA followed by Tukey's multiple comparisons (Winer, 1971). Percentage of resorptions and fetuses with abnormalities were evaluated with pairwise Mann- Whitney tests with a modified Bonferroni correction to compare each treatment to the control ((Lehmann, 1975). Sex ratio and litter size data were compared with the Kruskal – Wallis test (Lehmann, 1975; Norusis, 1994). The Student's t-test and ANOVA were used to compare mean acetylcholinesterase activity among groups. Cholinesterase activity of aldicarb –treated dams was expressed as a percent of the control. Parameter values were compared at the 5 % level of significance.

**RESULTS**

**Maternal Observations**

**Clinical signs of toxicity and acetyl cholinesterase activity**

There were no deaths or abortions during the course of the present study. Signs of cholinergic toxicity including tremors, diarrhea, and salivation were noted in dams at 0.3 and 0.5 mg/kg/d compared to the control and the other treated groups. These signs appeared on days 10 and 9 of gestation (days 5 and 4 of treatment) in the dose groups of 0.3 and 0.5 mg/kg/d, respectively and progressed throughout the period of the treatment. These signs were shown in 60% and 80% in dose groups of 0.3 and 0.5 mg/kg/d, respectively. The effects on the cholinesterase activity are presented in table 1. At 0.1 mg/kg/d aldicarb, maternal and fetal brain cholinesterase activities were 95 and 99 % of 10 control, respectively. Maternal and fetal brain cholinesterase activities were markedly reduced in the treated groups 0.3 and 0.5 mg /kg/d compared to the control group (66, 40 %, and 61, 36%, respectively). In both treated groups, the reduction of fetal brain cholinesterase activity was higher than those in maternal brain.

**Maternal body and organ weights**

Maternal body changes and organ weights are presented in table 1. Early in the treatment period from day 9 through 12 of gestation, the maternal body weights and weight gains of dams in the 0.5 mg/kg/d treated group were reduced compared to the control group and the other treated groups. No significant differences in the absolute and relative organ weights in any of the treated groups compared to the control.

**Feed Consumption**

There was no significant change in feed consumption in any of the treated groups compared to the control group.

Table 1. Materanl parameters in rats after exposure to aldicarb on days 6-15 of gestation.

| | | Aldicarb (mg/kg/d) | | | |
|---|---|---|---|---|---|
| | Days | 0.0 | 0.1 | 0.3 | 0.5 |
| No. of dams | | 29 | 26 | 28 | 26 |
| Body weights a | 6 | 190+6 | 186+7 | 189+7 | 187+6 |
| | 9 | 194+10 | 191+9 | 193+9 | 191+7 |
| | 12 | 202+11 | 201+8 | 203+8 | 195+10* |
| | 16 | 217+10 | 217+9 | 220+9 | 200+9* |
| | 21 | 257+13 | 255+8 | 260+8 | 223+12** |
| Body weight gaim a | 6-9 | 4+2 | 5+4 | 4+5 | 4+2 |
| | 9-12 | 8+3 | 10+3 | 10+7 | 4+5** |
| | 12-16 | 15+4 | 16+9 | 17+8 | 5+7** |
| | 16-21 | 40+6 | 38+6 | 40+5 | 23+9** |
| | 6-21 | 67+11 | 69+15 | 71+16 | 36+21 |
| Organ weights | | | | | |
| Absolute a | | | | | |
| Brain | | 1.45+0.77 | 1.40+1.55 | 1.39+0.25 | 1.42+0.52 |
| Liver | | 8.90+0.32 | 7.89+0.25 | 8.88+0.15 | 7.80+0.15 |
| Kidneys | | 0.45+0.25 | 0.42+0.33 | 0.43+0.35 | 0.39+0.10 |
| Relative b | | | | | |
| Brain | | 0.01+0.42 | 0.01+0.91 | 0.01+0.51 | 0.01+0.77 |
| Liver | | 0.03+0.03 | 0.03+0.11 | 0.03+0.63 | 0.03+0.75 |
| Kidneys | | 0.002+0.59 | 0.002+0.47 | 0.002+0.87 | 0.002+0.88 |
| Means brain acetylcholinesterase (mg protein/min) | | 30.70+1.90 | 29.30+0.90 | 20.17+0.77* | 12.31+1.11** |
| Fetal brain acetylcholinesterase (mg protein/min) | 29.28+1.50 | 29.11+0.99 | 17.80+0.55** | 10.50+0.11**. | |

Data are presented as mean +SD; a Body and organ weights in grams; b Organ weight/ body weight;
*Significantly different from control at p<0.05; ** Significantly different from control at p<0.01.

Table 2. Materanl parameters in rats after exposure to aldicarb on days 6-15 of gestation.

| | Aldicarb (mg/kg/d) | | | |
|---|---|---|---|---|
| | 0.0 | 0.1 | 0.3 | 0.5 |
| Number of females | 30 | 30 | 30 | 30 |
| Number of pregnant | 29 | 26 | 28 | 26 |
| Pregnant (%) | 97 | 87 | 93 | 87 |
| Number of litters | 29 | 26 | 28 | 26 |
| Implantation sites / litter | 11.4+2 | 11.1+2 | 11.2+2 | 11.6+1 |
| Liver fetuses / litter (% of implantation) | 10.6+3 (93) | 10.3+3 (93) | 10.6+3 (95) | 7.4+3 (64)** |
| % of implantation loss | 7+10 | 7+13 | 5+8 | 36+9 |
| Dead fetuses / litter (% of implantation) | 0+0 | 0+0 | 0+0 | 1.1+5 (10)* |
| Early resorption / litter (% of implantation) | 0.2+1 (2) | 0.1+0.7 (1) | 0.2+0.6 (2) | 1.3+2 (11)* |
| Late resorption / litter (% of implantation) | 0+0 | 0+0 | 0+0 | 1.8+3 (16)* |
| % litters with resorptions | 17 (5/29) | 8 (2/26) | 14 (4/28) | 77 (20/26)** |
| % litters totally resorpted | 0+0 | 0+0 | 0+0 | 19 (5/26)** |
| Sex ratio M : F (%) | 5.0:5.6 | 4.9:5.4 | 4.8:5.8 | 3.5:3.9 |
| Fetal body weight (g)/litter | 5.30+0.15 | 5.45+0.20 | 5.66+0.14 | 3.90+0.25** |

Data are presented as mean +SD; a Body and organ weights in grams; b Organ weight/ body weight;
*Significantly different from control at p<0.05; ** Significantly different from control at p<0.01.

**Fetal observations**

Developmental parameters and fetal weights are summarized in table 2. The number of implants per litter was not significantly altered in the aldicarb treated groups. Aldicarb produced a significant increase in the embryolethality in the 0.5 mg/kg/d treated group with approximately 36 % of the implants resorbed compared to the control and the other treated groups. Total resorption of litters was significantly increased in the treated group of 0.5 mg/kg/d compared to the control group. A significant decrease was observed in the number of live fetuses in the 0.5 mg/kg/d group compared to the control and the other aldicarb treated groups. While no significant difference was observed in the sex ratio of the fetuses in any of the treatment groups, a statistically significant increase in the number of dead fetuses, late and early resorptions was shown in the group treated with 0.5 mg/kg/d aldicarb. Fetal weights for rat fetuses were significantly lower than those in the control group at the 0.5 mg/kg/d treated group. Table 3 depicts the frequencies of abnormalities in the surviving fetuses from dams exposed to aldicarb. There is no significant value of external and visceral abnormalities in any of the treated groups compared to the control. Skeletal abnormalities were increased and these increases were statistically significant at the highest treated group 0.5

mg/kg/d, as compared to the control and the other treated groups. Skeletal abnormalities, principally were in the form of delayed ossification of Centrum, fused and absence of ribs, and absence of phalanges.

Table 3. Materanl parameters in rats after exposure to aldicarb on days 6-15 of gestation.

| | | Aldicarb (mg/kg/d) | | | |
|---|---|---|---|---|---|
| | | 0.0 | 0.1 | 0.3 | 0.5 |
| Number of fetuses (Number of litters) examined | | | | | |
| External examinationsa | | 308 (29) | 268 (26) | 297 (28) | 193 (26) |
| Visceral examinations | | 103 (29) | 89 (26) | 99 (28) | 64 (260 |
| Skeletal examination | | 205 (29) | 179 (26) | 198 (28) | 129 (26) |
| Number affected (% affected) | | | | | |
| External observations | | | | | |
| Polydactyly | F b | 1 (0.3) | 0 (0) | 1 (0.3) | 1 (0.5) |
| | L | 1 (3) | 0 (0) | 1 (4) | 1 (4) |
| Microphthalmia | F | 1 (0.3) | 0 (0) | 1 (0.3) | 1 (0.5) |
| | L | 1 (3) | | | |
| Soft cleft plate | F | 0 (0) | 0 (0) | 0 (0) | 1 (0.5) |
| | L | 0 (0) | 0 (0) | 0 (0) | |
| Visceral examinations | | | | | |
| Hemorrhage in the liver | F | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| | L | 0 (0) | 0 (0) | 0 (0) | 1 (4) |
| Convoluted dilated renal pelvis | F | 0 (0) | 1 (1) | 0 (0) | 0 (0) |
| | L | 0 (0) | 1 (4) | 0 (0) | 0 (0) |
| Severely dilated renal pelvis | F | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| | L | 0 (0) | 0 (0) | 0 (0) | 1 (4) |
| Skeletal observations | | | | | |
| Delayed ossification of centrum | F | 6 (3) | 5 (3) | 3 (2) | 25 (19)* |
| | L | 4 (14) | 4 (15) | 2 (7) | 20 (80)** |
| Fused ribs | F | 0 (0) | 1 (0.6) | 0 (0) | 17 (13)** |
| | L | 0 (0) | 1 (4) | 0 (0) | 11 (42)** |
| Absence ribs | F | 0 (0) | 0 (0) | 0 (0) | 2 (2) |
| | L | 0 (0) | 0 (0) | 0 (0) | 1 (4) |
| Absence of phalanges | F | 3 (2) | 0 (0) | 1 (0.5) | 50 (39)** |
| | L | 2 (7) | 0 (0) | 1 (4) | 26 (100)** |

a Only live fetuses were examined; b F=feuses; L=litters;
*Significantly different from control at $p<0.05$; ** Significantly different from control at $p<0.01$.

## DISCUSSION

In the present developmental toxicity study, administration of 0.1 mg/kg/d aldicarb to pregnant rats by gavage did not produce maternal or embryo toxicity. Therefore, the NOEL of aldicarb for maternal and developmental toxicity in this study is equal 0.1 mg/kg/d. This result was in consistent with the data from the developmental study indicated that the NOEL for developmental effects was 0.125 mg/kg/d (WHO, 1991). Maternal effects in the 0.3 mg/kg/day treated group included chlolinergic signs and significant acetylcholinesterase activity depression without developmental toxicity. These results indicate that fetotoxic effects of aldicarb are not attributable to maternal acetylcholinesterase activity depression. Maternal and developmental toxicity were observed in the dams treated with 0.5 mg/kg/d aldicarb. These results are in agreement with the data indicated that aldicarb induced malformations in the female rats at the 0.5 mg/kg/d dose level (WHO,.1991), and the previous published studies (Farag *et al*., 2000, 2003; Clemens *et al*., 1990; Ballantyne and Marrs, 1992; Lachner and Abdel- Rahman, 1984). These studies suggest that dosages of the anticholinesterases that are maternally toxic can produce embryotoxicity or teratogenicity. On the other hand, these data are in contrast with the developmental toxicity studies suggested that aldicarb did not display any teratogenic potential effects in rats up to 0.7 mg/kg/day (Hays and Laws, 1991) and the NOAEL for systemic and developmental effects was equal to or greater than 1 mg/kg/d (Union Carbide Corporation, 1966). Our results indicated that brain cholinesterase activities were decreased at 0.3 and 0.5 mg/kg/d for both maternal and fetal brain cholinesterase. The inhibition of fetal AChE activity at both dose levels 0.3 and 0.5 mg/kg/d was more than those in maternal acetycholinesterase activity. These results are in agreement with the data indicated that aldicarb is a potent cholinesterase inhibitor and the rats showed overt signs of depression of cholinesterase activity = 5 min after they were given single oral doses of aldicarb ranging from 0.001 to 0.10 mg/kg (Cambon *et al*., 1979). Furthermore, doses of aldicarb as low as 0.001 mg/kg caused inhibition of AChE in fetal brains and livers. This dose is a thousand times lower than the adult LD50 (Caroline, 1992). Fetuses were more sensitive than their mothers to aldicarb's effects. The rapid depression of acetylcholinesterase activity in fetal and maternal blood

and tissues observed after the oral administration of aldicarb to pregnant rats demonstrated that aldicarb or its toxic metabolites (the sulfoxide and sulfone) are distributed to the tissues by the systemic circulation (Cambon *et al*., 1979, 1980). Pregnant females showed significant reduction of maternal body weights in dose group of 0.5 mg/kg/day. An explanation for the weight reduction in the absence of changes in feed consumption is the systemic maternal toxicity of aldicarb. On the other hand, the systemic maternal toxicity can trigger of the embryotoxicity at dose group of 0.5 mg/kg/day. The increase in dead fetuses and resorptions at the 0.5 mg/kg per day likely accounts for the decrease in the number of live fetuses/litter in this treatment group. The metabolic pathways for aldicarb in rats usually results in the formation of the sulfoxide, sulfone, oxime sulfone, nitrile sulfoxide, nitrile sulfone, and at least five other metabolites (Risher *et al*., 1987; United Nations Food and Agriculture Organization, 1980). The two major metabolites of aldicarb are aldicarb sulfoxide (ASO) and aldicarb sulfone (AS). ASO has the same LD50 as aldicarb; AS has an LD50 27 times higher; and the other metabolites have LD50 600 to 8500 times higher (Lynn *et al*., 1990). The sulfoxide and the sulfone have a mechanism of toxicity similar to that of aldicarb itself.

Of interest is that all of these metabolites have involved the fruits of members of the cucurbitaceous family, which includes cucumbers, melons, squash, and pumpkins. Aldicarb when dissolved in water, is taken up by the roots and deposited in the fruit of plants in this family (Lynn *et al*., 1990). Aldicarb has also been found in the groundwater in areas where it was applied. Widespread use of aldicarb and its ability to persist in the groundwater and to be taken up by plant make it important to assess the adverse health effects, especially on the pregnant women. In laboratory animals, it causes chronic damage to the nervous system, suppresses the immune system, and adversely effects fetuses. In human cells, aldicarb causes genetic damage. In conclusion, the present data demonstrate that aldicarb can produce adverse effects on maternal and rat fetuses at 0.5 mg/kg/d treated group. No adverse effects in the present study were observed in the 0.1 mg/kg/d treated group. This dose is about 33 times the acceptable daily intake for human (ADI = 0.003 mg/kg/d) (Kidd and James, 1991). Aldicarb caused embryotoxicity at 0.5 mg/kg/d, which is equal 1/3 of LD50 for rats (Hays and Laws, 1991; EPA, 1987), and about 165 times of ADI. We are concerned that exposures of this magnitude might occur through the systemic natural of aldicrb (absorbed into roots, stems, leaves, and fruit), via the residues which can contaminate the edible portion of the food crops.

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