Zagazig J. Agric. Res., Vol. 32 No. (5) 2005 1631 - 1647

TOXICITY OF IMIDACLOPRID AND CYANOPHOS INSECTICIDES IN PREGNANT WHITE ALBINO RATS DURING ORGANOGENESIS PERIOD

Sherif, R.M.[1], K.A. Gouhar[1], M.M. Farid[2] and A.A. Gharib[1]

[1] Plant Protection Dept., Fac. of, Agric., Zagazig Univ., Egypt.

[2] Mammalian and Aquatic Toxicology Dept., Central Agric. Pesticides Lab. (CAPL), Central Agriculture Research, Dokki, Giza, Egypt.

Accepted 6 / 7 / 2005

ABSTRACT: Maternal toxicity of imidacloprid (Admire 200 SC) and cyanophos (Cyanox EC 50 %) in pregnant female white albino rats (*Rattus norvegicus*, Bork.) was studied. The LD_{50} of the tested insecticides was 484.06 mg / kg body weight with confidence limit within range from 385.74 to 607.44 for imidacloprid, while, it was 807.60 with interval limit ranged between 671.58 - 971.18 mg cyanophos / kg b. wt. in this study.

The pregnant rats were daily orally administered 12.1, 24.2 and 48.4 mg / kg b. wt. of imidacloprid (i.e., 2.5, 5.0 and 10% of LD_{50} respectively) and 4, 6 and 8 mg cyanophos / kg b.wt./day (i.e., 0.56, 0.74 and 0.99% of LD_{50}) during organogenesis period (from the 6 *th* to 15 *th* day of gestation).

Cyanophos produced a significant decrease on maternal weight gain at the highest dose. No observed effects were recorded on maternal gravid uterine weight and pregnant weight gain with all doses of the two tested compounds.

Cyanophos was more effective than imidacloprid on organs weight ratios especially relative weight of kidney, heart and lung. According to histopathological alternations, cyanophos was more toxic than imidacloprid. On the other hand, the two tested compounds showed severe histopathological lesions in brain and kidney more than in liver.

Key words: Imidacloprid, cyanophos, maternal toxicity, pregnant rats, body weight gain, organ weight ratio, histopathology.

INTRODUCTION

The extensive use of pesticides is usually accompanied with serious problems of pollution and health hazards. It is now well established that many pesticides in common use can be toxic and have adverse effects on physiological function of some organs, reproductive system and offspring of experimental animals.

Imidacloprid is a widely used insecticide to control sucking insects, soil insects, termites and some chewing insects. It is also used as a flea control pests (Farm chemical hand book, 2000). Cyanophos is an organophosphorothiate insecticide, effective against different pests infesting fruits and vegetables. It is also used to control locusts and various sanitary pests.

Imidacloprid works by interfering with the transmission of stimuli in the nervous system. It causes a blockage in a type of neuronal pathway, nicotinergic, (Tomizawa *et al.*, 1995 a, b & Nagata *et al.*, 1998). On the other hand, cyanophos as organophosphorus compound acts as cholinesterase inhibitor (Aldridge, 1996).

Manson and Kang, 1989 & 1994; and Christian, 2001 illustrated the parameters of maternal toxicity. Several investigators e.g., Bhaumik & Gupta (1990); Mathur & Bhatnager (1991); Bitsi *et al.*, (1994); Narotsky & Kavlock (1995); Somlyay & Virgula (1995); Srivastava & Raizada (1995); Srivastava & Raizada (1996); Ema *et al.* (1997); Berlinska and Sitarek (1997); Singh & Sharma (1998);Varnagy *et. al.*,(2000) and Lawson & Luderer, (2004) studied maternal toxicity of pesticides on experimental animals.

The aim of the present work is to the maternal toxicity of these widely used insecticides in pregnant female white albino rats at different dosages starting from 6 *th* to 15 *th* day of gestation (GD 6 – GD 15).

MATERIALS AND METHODS

A- Insecticides Tested

1. **Imidacloprid** (Admire 200 SC), 1 – ((6 – chloro – 3 –pyridinyl) methyl) – N–nitro – 2 – imidazolidinimine, supplied by scientific office of Bayer, El Maadi City, Cairo, Egypt.
2. **Cyanophos** (Cyanox 50% EC), O– (4– Cyanophenyl) O,O–dimethyl phosphorothioate, supplied by Sumitomo and

repacked by Kafr El Zayat Pesticide and Chemical Company (KZ).

B- Experimental Animals

Healthy and sexually mature, three months old males and primiparous females white albino rat (*Rattus norvegicus*. Bork), Wistar strain of 160 ±10g, body weight were obtained from Organization of Biological Products & Vaccine (Helwan Farm, Cairo, Egypt) and housed in plastic cages in groups of 5 animals / cage. The experimental animals were allowed to acclimatize under the laboratory conditions for 2 weeks at least prior the experiment at a temperature of 25 ± 5 °C and relative humidity of 50 ± 20 %. They were provided with balanced pelleted diet (23 % protein) and tap water *ad libitum*.

C- Experimental Design

The present study was carried out on 10 mature males, for mating only, and 130 virgin mature females. Females were divided into two main groups; the first group (60 females) was to determine the acute oral medium lethal dose (LD_{50}), and the second group to study the maternal toxicity.

1. Acute oral toxicity

Mature females were divided into two groups of 30 ones. Each group was intubated orally using stomach tube with different doses of the tested compounds. These doses were prepared in distilled water and gave to rats as mg / kg b.wt. of 6 females for each dose. The first group was dosing 0, 700, 770, 847, 931.7 mg of imidacloprid. Also, the second group was dosing 0, 400, 440, 484, 532.4 mg of cyanophos. Then the dosing rats were kept under observation for 24 hours and symptoms of toxicity and mortality were recorded.

The acute oral LD_{50} values were calculated according to the method of Weil (1952).

2. Maternal toxicity

Maternal toxicity was studied on the 2 nd group reveal the detrimental effects of tested compounds on pregnant females during organogenesis period (6 – 15 days of pregnancy).

a- Preparations of females

Three females were mated over night with a normal male (proven sire). Mating (copulation) is confirmed in the next morning by the presence of spermatozoa in the content of the vaginal smear and /

or the observation of the copulatory plug in situ; these findings designate day 0 of presumed gestation (Manson and Kang, 1989& 1994; Prakash and Arora, 1998 & Christian, 2001). In addition, the body weight was recoded daily for pregnant females that were proved to be in continuous oestrus and showed increased body weight.

b- Animal treatments

The dosage for maternal toxicity (i.e., teratogenicity testing) was decided by a preliminary range finding test with pregnant rats using limits of LD_{50} dose. The maximum dose that was not lethal to any female, but decreased the weight gain during the gestation period was selected as highest dose. The tested doses were prepared in distilled water and administered to animals as mg / kg b.wt. / day.

At the 5 *th* day of pregnancy, the seventy pregnant female rats were randomly divided into 7 groups of 10 females for each group. Each group was intubated orally using stomach tube with different doses from tested insecticides as following:

Group A: orally administered 0.5 ml distilled water and kept without any insecticidal treatment as a control.

Group B, C, and D: were given imidacloprid at the dosage levels of 12.1, 24.2 and 48.4 mg / kg b.wt. /day (i.e., 2.5, 5 and 10 % of LD_{50}, respectively).

Group E, F, and G: were dosed with 4, 6 and 8 mg cyanophos / kg b. wt. / day (as percent 0.56, 0.74 and 0.99 of LD_{50}).

The tested materials were dosed from day 6 to 15 of pregnancy to cover the whole period of organogenesis. Both control and treated groups were daily weighed and been under observation until the 20 *th* day of gestation at which they were weighed, sacrificed and dissected to investigate the effect of tested substances on dams. An estimation of whether maternal toxicity has occurred was made from maternal daily weight data, organ weight / body weight ratio, and histopathological changes in some vital maternal organs such as liver, kidney and brain.

D- Data Collection

1. Body weight and organ weights

Daily body weight of pregnant females was recorded. Then the pregnant body weight gains were calculated. On day 20 of gestation (GD 20), the pregnant females

were weighed and sacrificed then the gravid uterus was removed and weighed. Final maternal weight was calculated by minus of gravid uterus weight from weight of pregnant female on GD 20 also, final maternal weight minus initial pregnant weight (on GD 0) equal maternal weight gain throughout the treatment period as reported by Bhaumik & Gupta (1990); Teruel *et al.* (2003) and Lawson & Luderer (2004). Measurement of maternal organ weights percent was carried out at the term sacrifice. The percentage of organ weights (gm/ 100 gm body weight) was transformed to arcsine.

2. Histopathological studies

The treated pregnant females were sacrificed at the 20 *th* day of gestation. Liver, kidney and brain were examined grossly, then specimens were taken and fixed in 15% formalin saline for the histopathological alternations. Routine histopathological procedure was done and stained by Hematoxilen and Eosin stain (H & E) for histopathological examinations (Humason, 1979).

E. Statistical Analysis Procedures

One – way ANOVA test (Gad and Weil, 1989& 1994; Gad, 1999 & 2001) using SPSS software for Windows version 10 was used to analyse the data. LSD carried significant statistitical differences between all treatments.

RESULTS AND DISCUSSION

A- Acute Oral Toxicity (LD_{50} s) of Imidacloprid and Cyanophos to Females of *Rattus norvegicus*

The acute oral toxicity of imidacloprid and cyanophos were found to be 484.06 for imidacloprid and 807.6 mg / kg b. wt. for cyanophos Table (1).

B- Maternal Toxicity of Imidacloprid and Cyanophos Insecticides

1. Maternal body weight gain and pregnant weight gain

Results in Table (2) indicate that, no significant changes in gravid uterine weight and maternal weight gain of treated dams at treatments, except, a significant decrease in maternal weight gain at the high dose of cyanophos was observed. Similarly, pregnant weight gains during the dosing period (GD 6–GD16) and after administration period (GD 16 – GD 20) as noted in Table (2). Our results are computable to findings

Table 1: LD_{50} and confidence limits (C.L) of imidacloprid and cyanophos on female white albino rats

Pesticide	No. of group	Dose (mg / kg b.wt.)	No. of animals / group	No. of dead animal	LD 50 value	C.L (95 %) Lower	C.L (95 %) Upper
Imidacloprid (Admire 200 SC)	1	0.0	6	0			
	2	400.0	6	2			
	3	440.0	6	2	*484.06*	*385.74*	*607.44*
	4	484.0	6	3			
	5	532.4	6	4			
Cyanophos (Cyanox 50 EC)	1	0.0	6	0			
	2	700.0	6	1			
	3	770.0	6	2	*807.60*	*671.58*	*971.18*
	4	847.0	6	5			
	5	931.7	6	3			

Table 2: Effect of imidacloprid (Admire - 200 SC) and cyanophos (Cyanox - 50 EC) on body weight and body weight gain of dam rats treated orally daily during organogenesis period

	Parameters	Control	Pesticide Doses (mg / kg b.wt. / day) Imidacloprid 12.1	Imidacloprid 24.2	Imidacloprid 48.4	Cyanophos 4	Cyanophos 6	Cyanophos 8
Maternal weight (M.wt.)	Initial wt.	155.0 ^{bc} ± 8.3666	155.9 ^{bc} ± 4.8636	162.0 ^{bc} ± 3.8355	166.6 ^{c} ± 4.9826	129.4 ^{a} ± 2.0613 **	146.5 ^{b} ± 7.6757	164.5 ^{c} ± 4.4378
	Finial pregnant wt.	223.1 ± 11.49729	215.4 ± 10.60943	231.0 ± 8.3240	221.0 ± 9.7457	204.5 ± 6.5375	219.5 ± 12.348	220.0 ± 9.1894
	Gravid uterine wt.	41.7 ±2.8521	44.1 ± 4.2386	46.9 ± 4.4158	37.5 ± 3.9391	43.9 ± 1.4564	45.7 ± 3.8932	47.8 ± 4.8735
	Finial maternal wt.	181.4 ±9.8491	171.3 ±7.6754	184.1 ± 6.5497	183.5 ± 9.4083	160.6 ± 6.8867	173.8 ± 9.8768	172.2 ± 6.2695
	Maternal wt. Gain	26.4 ^{b} ± 3.8158	15.4 ^{ab} ± 6.7102	22.1 ^{ab} ± 3.7990	16.9 ^{ab} ± 5.1065	31.2 ^{b} ± 6.9439	27.3 ^{b} ± 3.9386	7.7 ^{a} ± 6.1175 *
Pregnant weight gain (P.wt.G.)	0 – 6 th day	14.8 ^{a} ± 1.5041	15.1 ^{a} ± 2.2333	21.5 ^{b} ± 2.4777 **	15.8 ^{a} ± 1.1813	23.2 ^{b} ± 1.3064 **	20.0 ^{ab} ± 1.2910 *	19.0 ^{ab} ± 1.7951
	6 – 16 th day	29.5 ± 2.9107	23.1 ± 4.5054	28.7 ± 2.8908	18.6 ± 3.0521	30.6 ± 3.4839	32.0 ± 5.1747	22.0 ± 6.1554
	16 – 20 th day	23.8 ± 3.3126	21.3 ± 4.1421	18.8 ± 2.9280	20.0 ± 3.6878	21.3 ± 3.3534	21.0 ± 3.0551	14.5 ± 3.7601
	0 – 20 th day	68.1 ± 5.4435	59.5 ± 10.1042	69.0 ± 5.9870	54.4 ± 6.5544	75.1 ± 6.6674	73.0 ± 6.2893	55.5 ± 9.1120

Values represent means ± SEM (n = 10).

Significance level: * $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$ compared with control.

of Bitsi *et al.* (1994) who showed that, no significant effect on body weight was observed in the mothers which feeding on wheat material freshly spiked with malathion during gestation.

Similar results were recoded by Srivastava and Raizada (1995) who reported that, isoproturon herbicide administered orally at 45, 90 and 180 mg / kg b. wt. / day to dams during day 6 – 20 of pregnancy did not produce maternal toxicity at 45 or 90 mg of tested compound.

Body weight is frequently the most sensitive parameter to indicate and adverse effect (Gad and weil, 1989, 1994 and Gad, 2001). A significant reduction in maternal weight gain in treated dams could be due to an effect on the uterine compartment rather than on the maternal weight, since average final maternal weights minus uterine weight was not statistically different from that of control. Factors contributing to decrease uterine weight might be due to intrauterine growth retardation of the offspring as fetal weights and lengths were decreased by treatment (Bhaumik and Gupta, 1990). Also, Elsaieed and Nada (2002) stated that, reduction in body weight gain is mainly attributed to the fetal retarded growth and resorption recoded in the treated animals.

2. Effect of tested compounds on internal organ weights

Changes in body and organ weights are considered as a good indicator for intoxicification effects of pesticides. Absolute and relative (adjusted for body weight of mother) organ weights should be considered, because a decrease in absolute weight may occur that is not necessarily related to a reduction in body weight gain (Hess, 1990; Nakia *et al.*, 1993).

The data presented in Table (3) demonstrate the influence of different doses of imidacloprid and cyanophos on internal organ weights in treated dams during organogenesis period. The data showed that, the relative weights of liver and brain were not affected at all doses of the two insecticides. The weights of kidney in case of cyanophos treatments at three doses were reduced. The relative spleen weights were significantly reduced at the three tested doses for imidacloprid and the highest dose of cyanophos (8 mg) comparing with untreated group. On contrast, heart weights of treated dams were altered at the

Table 3: Effect of imidacloprid (Admire - 200 SC) and cyanophos (Cyanox - 50 EC) on maternal organ weight ratio of pregnant rats treated orally daily during organogenesis period

Organs	Control	Pesticide Doses (mg / kg b.wt. / day) Imidacloprid			Cyanophos		
		12.1	24.2	48.4	4	6	8
Liver	12.2447 ^{bcd} ± 0.2063	11.486 8 ^{ab} ± 0.3514	12.0132 ^{abc} ± 0.3622	11.1559 ^{a} ± 0.3571 *	13.0050 ^{d} ± 0.3422	12.5565 ^{cd} ± 0.2623	11.8580 ^{abc} ± 0.1289
Kidney	4.3898 ^{a} ± 0.0003	4.4458 ^{ab} ± 0.0825	4.5546 ^{ab} ± 0.0905	4.5342 ^{ab} ± 0.1363	4.7885 ^{b} ± 0.1392 *	4.7545 ^{b} ± 0.0713 *	4.7751 ^{b} ± 0.1273 *
Brain	4.9586 ± 0.2929	5.4903 ± 0.1339	5.3715 ± 0.1003	5.1897 ± 0.1288	5.6049 ± 0.1482	5.4513 ± 0.1225	5.5041 ± 0.1130
Spleen	4.0812 ^{c} ± 0.1538	3.2497 ^{a} ± 0.2357 **	3.3863 ^{ab} ± 0.3003 *	3.1403 ^{a} ± 0.1704 **	4.0098 ^{c} ± 0.2031	3.9326 ^{bc} ± 0.1806	3.3299 ^{ab} ± 0.1561 *
Heart	3.3295 ^{a} ± 0.0584	3.5530 ^{bc} ± 0.0738 *	3.3681 ^{ab} ± 0.0669	3.3332 ^{a} ± 0.0314	3.6636 ^{c} ± 0.0960 ***	3.5491 ^{bc} ± 0.0502 *	3.5850 ^{c} ± 0.0492 ***
Lung	4.7850 ^{ab} ± 0.1783	5.1246 ^{abc} ± 0.2767	4.5568 ^{a} ± 0.1435	5.2592 ^{abc} ± 0.1855	5.4833 ^{bc} ± 0.1684 *	5.0643 abc ± 0.1991	5.6807 ^{c} ± 0 .3499 **
Gravid Uterus	28.6793 ± 0.9143	30.2537 ± 1.3993	30.1886 ± 1.7119	26.8209 ± 1.7939	31.8235 ± 1.1591	30.7931 ± 1.2815	31.4870 ± 1.8755

Values represent means ± SEM (n = 10).

Significance level: * $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$ compared with control.

all-experimental doses and the lowest dosing with cyanophos and imidacloprid, respectively. The low and high doses (4 & 8 mg) of cyanophos produced significant increases in weight ratios of lung compared to control group (Table, 3). While, no significant changes were noticed in the relative weight of gravid uterus in all cases of treatments of the two insecticides (Table, 3). The present data agree with the pervious studies conducted on fenitrothion at dose 30 mg (Berlinska and Sitarek 1997) and on monocrotophos - treated female rats (Singh and Sharma, 1998).

3. Histopathological changes of experimental compounds in internal organs

a- Liver

Liver tissue of the animals treated with 48.4 mg imidacloprid showed focal area of necrosis, foamy cells, macrophages and kuffer cells activation. In additional, degenerative changes, haemosiderin pigments and Kuffer cells activation were found at 8 mg cyanophos (Fig. 1). Also, at 6 mg there were vacuolar degenerations and haemosiderin pigments depositions in hepatocytes were found. Animals treated with 24.2 and 12.1, mg imidacloprid and 4 mg cyanophos showed marked improvement of histological changes. The normal histological structure of liver was listed in Figure (2).

b- Kidney

Pathological examination of the kidney females treated with the highest dose of imidacloprid demonstrated that, glomerular hypercellularity and cytosiderosis in renal tubular epithelium. Degenerative changes in tubular epithelium were seemed in groups treated with 42.2 mg of imidacloprid. As shown in Figure (3), the kidneys of imidacloprid – treated females (at 12.1 mg) were severely affected where the blood vessels were congested and hemorrhages were noticed in the interstitial tissue together with cytosiderosis.

Concerning the animals dosing with cyanophos at three doses, toxic nophrosis were noticed with severe degenerative changes in epithelial cells of renal tubules, absences of tubular lemon, separation of cells from basement membrane, different stages of necrosis of the cells and accumulation of proteinaceous substance in Bowman's capsule of glomerulus (Fig. 4). The

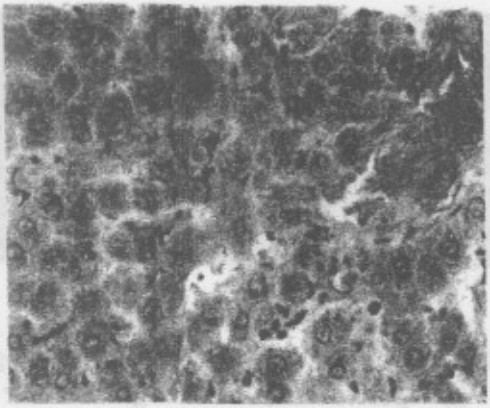

Fig. 1: Liver of pregnant female given 8mg of cyanophos during organogenesis period, showing degenerative changes, haemosiderin pigments and Kuffer cells activation (H & E X 400)

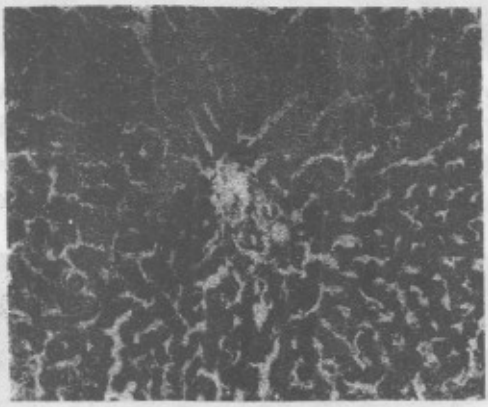

Fig. 2: Liver of pregnant female control, showing normal histological structure, H & E X200

Fig. 3: Kidney of imidacloprid-treated female rat at 12.1 mg/kg b.wt./ day from GD 6 to GD 15, showing congestion of blood vessels in peritubular and glomerular region with cytosiderosis (H & E X 200)

Fig. 4: Showing, toxic nophrosis in treated female kidneys at three doses of cyanophos noticed by degenerative changes in epithelial liming of renal tubules and accumulation of proteinaceous substances in Bowman's capsule, H & E X 400

Fig. 5: Kidney of female rat represented as control showing normal histological pattern (H & E X 200)

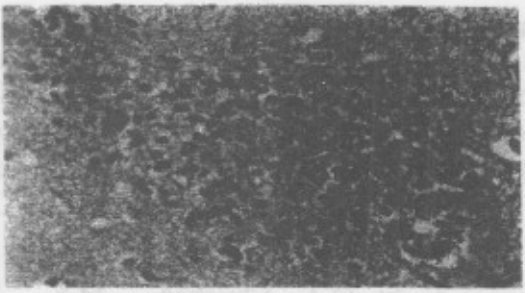

Fig. 6: Brain of dosed pregnant female at 48.4mg imidacloprid throughout organogenesis period, showing oedema and focal gliosis, H & E X.400

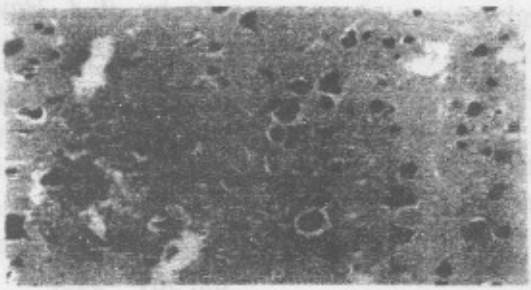

Fig. 7: Brain of pregnant female after dosing period (6^{th} – 15^{th} day of pregnancy) with 8 and 6 mg/kg b. wt./ day of cyanophos showing, neuronal degeneration and neuronophagia, H & E X 400

Fig. 8: Brain of untreated pregnant female rat (H & E X 400)

pathological findings at cyanophos – treated females were evidenced by dose – related alterations in lesions. The kidney of the control group was apparently normal (Fig., 5).

c- Brain

In the animal treated with 48.4 mg of imidacloprid, the examined brain tissue showed oedema and focal gliosis (Fig., 6). With 8 and 6 mg of cyanophos, neuronal degeneration and neuronophagia were found Figure (7). Also, oedema, neuronal degeneration and focal area of necrosis were noticed in animal groups dosing the lowest dose of cyanophos (4 mg). Figure (8) represent a normal histological pattern of the brain.

REFERENCES

Aldridge, W.N. 1996. Mechanisms and concepts in toxicology. CRC Press, Inc., Ed. by Taylor & Francis, USA: 77 – 114.

Berlinska, B. and K. Sitarek. 1997. Disturbances of prenatal development in rats exposed to fenitrothion. Rocz Panstw Zaki Hig, 48 (3): 217 – 228.

Bhaumik, A. and P. K. Gupta. 1990. Teratogenicity of decamethrin in rats. Indian Vet. J., 67: 213 – 219.

Bitsi, G. A., S.V. Khan, M.H. Akhtar, S. Kacew, N.D.G. White, Kamal – Singh and K. Singh. 1994. Fate of wheat bound malathion residue in rats during gestation. Chemosphere, 29 (3): 451 – 455.

Christian, M.S. 2001. Test methods for assessing female reproductive development toxicology. In.: *Principles & methods of toxicology.* 4th ed., edit by *W.A Hayes* Taylor & Francis, USA: 1301- 1382.

Elsaieed, M.E. and A.S. Nada. 2002. Teratogenicity of hexavalent chromium in rats and the beneficial role of ginseng. Bull. Environ. Contam. Toxicol., 68: 361 – 368.

Ema, M., A. Harazono, E. Miyawaki and Y. Ogawa. 1997. Effect of the day of administration on the developmental toxicity of tributyltinchloride in rats. Arch. Environ. Contamin. Toxicol., 33 (1): 90 – 96.

Farm Chemical Hand Book. 2000. Meister publishing company. Vol. Gad, S. C. (1999): Statistics and experiment design for toxicologist. 3 rd ed., Edit by CRC Press, LLC, New York, USA: 175 – 200.

Gad, S. C. 1999. Statistics and experimental design for toxicologist. 3 rd ed., Edit by CRC Press, LLC, New York, USA: 175 – 200.

Gad, S. C. 2001. Statistics for toxicologist. In.: *Principles & methods of,* 83. *toxicology.* 4th ed., edit by *W.A Hayes* Taylor & Francis, USA: 285 – 364.

Gad, S.C. and C.S. Weil. 1989. Statistics for toxicologist. In.: *Principles & methods of toxicology.* 2nd ed., edit by *W.A Hayes* Taylor & Francis, USA: 221 – 274.

Gad, S.C. and C.S. Weil. 1994. Statistics for toxicologist. In.: *Principles & methods of toxicology.* 3ed ed., edit by *W.A Hayes* Taylor & Francis, USA: 435 – 485.

Hess, R.A. 1990. Quantitative and qualitative characteristics of the stages and transitions in the cycle of the rat seminiferous epithelium: light microscopic observations of perfusion-fixed and plastic-embedded testes. Biol. Reprod., 43: 525–542.

Humason, G.L. 1979. Animal tissue techniques. 4 *th* ed. Freeman, W. H. and Company, San Francisco, USA.

Lawson, G. and U. Luderer. 2004. Gestational and lactational exposure to heptachlor does not alter reproductive system development in rats. Vet. Human Toxicol., 224, 46 (3): 113 – 118.

Manson, J.M. and Y.J. Kang. 1989. Test methods for assessing female reproductive and development toxicology. In.: *Principles & methods of toxicology.* 2ed ed., edit by *W.A Hayes* Taylor & Francis, USA: 311 - 359.

Manson, J.M. and Y.J. Kang. 1994. Test methods for assessing female reproductive and development toxicology. In.: *Principles & methods of toxicology.* 3rd ed., edit by *W.A Hayes* Taylor & Francis, USA: 989 - 1037.

Mathur, A. and P. Bhatnager. 1991. A teratogenic study of carbaryl in Swiss mice. Food Chem. Toxicol., 29 (9): 629 – 632.

Nagata, K., J. H. Song, T. Shono and T. Narahashi. 1998. Modulation of the neuronal nicotinic acetylcholine receptor – channel by the nitro – methylene heterocycle imidacloprid. J. Pharmacol. Exp. Ther., 285: 731 – 738.

Nakai, M., B.J. Moore and R.A. Hess. 1993. Epithelial reorganization and irregular growth following carbendazim-induced injury of the efferent ductules of the rat testis. Anat. Rec., 235: 51–60.

Narotsky, M.G. and R.J. Kavlock.1995. A multidisciplinary approach to toxicological screening: II – Developmental toxicity. J. Toxicol. & Environ. Health., 45 (2): 145 – 171.

Prakash, M. and C.K. Arora. 1998 Breeding in laboratory animals. Anmol published PVT. LTD, New Delhi (India): 215-261.

Singh, S.P. and L.D. Sharma. 1998. Monocrotophos induced embryotoxicity and teratogenicity in rats. Indian J. Toxicol., 5 (2): 47 – 52.

Somlyay, I.M. and A. Virgula. 1995 Study of Mancozeb + ethanol interaction during a model teratogenicity test in rats. Mededeling, Faculteit Landbouwkundige en Toegepaste, Biologische Wetenschappen, Uiversitiet, Gent: 119 – 125.

Srivastava, M.K. and D.R.B. Raizada. 1995. Developmental Toxicity of the substituted phenyl urea herbicide Isoproturon in rats. Vet. & Human, Toxicol, 37 (3): 220-223.

Srivastava, M.K. and R.B. Raizada. 1996. Developmental effect of technical Dimethoate in rats: Maternal and fetal toxicity evaluation. Indian J. Experim. Biol., 34 (4): 329 – 333.

Teruel, M.T., A.E. Felipe and H.D. Solana. 2003. Placental and fetal toxicity of albendazole sulphoxide in Wistar rats. Vet. Human Toxicol., 45 (3): 131 – 136.

Tomizawa, M., H. Otsuka, T. Miyamoto, M.E. Eldefrawi and I. Yamamoto. 1995a. Pharmacological characteristics of insect nicotinic acetylcholine receptor with its ion channel and the comparison of the effect of nicotiniods and neonicotiniods. J. Pesticide Sci., 20: 57 - 64.

Tomizawa, M., H. Otsuka, T. Miyamoto and I. Yamamoto. 1995 b. Pharmacological effects of imidacloprid and its related compounds on the nicotinic acetylcholine receptor with its ion channel from torpedoelectric organ. J. Pesticide Sci., 20: 49 – 56.

Varnagy, L., P. Buda, E. Molnar, I. Takacs and A. Karpati. 2000. Interaction of Dithane M – 45 (Mancozeb) and lead acetate during a teratogenicity test in rats. Acta, Vet. Hung., 48 (1): 113 – 124.

Weil, C.S. 1952. Tables for convenient calculation of median effective dose (LD_{50} or ED_{50}) and instructions in their use. Biometrics: 249-263.

سمية مبيدى الإميداكلوبريد و السياتوفوس فى الإناث الحوامل للفأر الأبيض الألبينو أثناء فترة تكوين الأعضاء الجنينية

رفعت مصطفى شريف[1] – كمال عبد الرازق جوهر[1] –

محمد محمود فريد[2] – أحمد عبدالله غريب[1]

[1] قسم وقاية النبات – كلية الزراعة – جامعة الزقازيق – مصر.

[2] قسم بحوث سمية المبيدات للثدييات و الأحياء المائية – المعمل المركزى للمبيدات– مركز البحوث الزراعية – الجيزة – مصر.

يهدف هذا البحث الى دراسة سمية مبيدى الإميداكلوبريد (أدمير ٢٠٠ معلق مركز) و السياتوفوس (سياتوكس ٥٠% مركز قابل للإستحلاب) على الإناث الحوامل للفأر الأبيض الألبينو (راتس نورفيجيكس، بورك). وأتضح أن قيمة ال LD_{50} كانت ٤٨٤,٠٦ مجم/ كجم من وزن الجسم بحد ثقة يتراوح من ٣٨٥,٧٤ الى ٦٠٧,٤٤ للإميداكلوبريد، فى حين كانت ٨٠٧,٦ وبمدى يتراوح من ٦٧١,٥٨ – ٩٧١,١٨ مجم من السياتوفوس/ كجم من وزن الجسم.

و عند حقن الإناث الحوامل يوميا بجرعات ١٢,١، ٢٤,٢، ٤٨,٤ مجم/كجم من وزن الجسم/ يوم من الإميداكلوبريد وهى تمثل ٢,٥، ٥، ١٠% من قيمة الجرعة القاتلة ل ٥٠% من الحيوانات المختبرة (LD_{50}) على التوالى و جرعات ٤، ٦، ٨ مجم سياتوفوس/ كجم من وزن الجسم/ يوم ممثلة ٠,٥٦، ٠,٧٤، ٠,٩٩% من قيمة ال LD_{50} أثناء فترة تكوين الأعضاء الجنينية (من اليوم السادس الى اليوم الخامس عشر من الحمل). أوضحت النتائج المتحصل عليها أن مبيد السياتوفوس بجرعته العالية أحدث انخفاضا معنويا فى معدل التغير فى وزن الأم. بينما لم يلاحظ أى تأثير يذكر على وزن الرحم الحامل و معدل التغير فى وزن الحوامل مع كل جرعات المختبرة من المبيدين.

وكان مبيد السياتوفوس أكثر تأثيراً من الإميداكلوبريد خاصة على وزن كل من الكلية والقلب و الرئة، وأكثر خطورة بالنسبة للتغيرات النسيجية فى بعض الأعضاء الداخلية للام (مثل الكبد والكلية والمخ). وقد كانت هذه التغيرات النسيجية واضحة فى الكلية والمخ عنها فى الكبد.