Egypt. J. Vet. Sci. **Vol. 39**, pp. 1-9 (2005)

Pharmacokinetics Effects of some Insecticides on White Albino Rats

I.M. El-Nabaraway*, A.A.Saleh, M.M.I.Kady**, A.S.M. Fouzy*** and Sh.E.M. Shalby***

**Plant Protection Dept., National Research Center, **Pesticides Department, Faculty of Agriculture, Mansoura Univ. and ***Food Toxicology and Contaminant Dept., National Research Center, Cairo, Egypt.*

THE TREATMENT of adults' female albino rats with Maximum Residue Limit (MRL) to tomato fruits of the three organophosphorus insecticides namely, primiphos-methyl, chloriphos-methyl and fenitrothion (1, 0.5 and 0.5 ppm) respectively on different periods (from 1, 6, 12, 24, 48, 96 hours and 7 days) to indicate and follow-up the effect of these insecticides on liver and kidney functions. A significant increasing activities of Aspartate Amino Transferase (AST) were found. No changes in Alanine Amino Transferase (ALT) and Alkaline phosphatase activities were observed in treated rats by the MRLs of the tested insecticides as compared with control. The data gathered showed that there were no significant changes in creatinine levels and urea concentrations of the treated rats at the different periods after dosing by the MRL of the tested insecticides. The data also clearly indicated an insignificant decrease in total protein levels, observed in rats treated by MRL of the tested insecticides after 1, 6, 12, 24, 48, 96 hrs and 7 days of treatment. Cholesterol level displayed slight or insignificant increasing in rats which were treated with the aforementioned insecticides. Generally treating rats by MRL of the prementioned insecticides resulted in a small (deleterious) effect on some biochemical parameters after 7 days of treatment. No effects have been detected at the first hours of the experiments.

Pesticides are chemical substances that are used regularly in agriculture. It is vital to farmers to protect crops against pests and to enhance crop yields. On the other hand, the same pesticides are capable of causing diseases (David Lawrence, 2003).

The three organophosphorus insecticides that were object of this research effort, namely primiphos-methyl, chloriphos-methyl and fenitrothion, are widely used to control some insects with economic impact on vegetable crops (Shalby, 2002). These pesticides may be the cause of death both through either accidental or intentional ingestion, mainly due to the uncontrolled use and less regulated

application of these pesticides in agricultural practices. From this point of view, the research effort entertained here in aimed to study the effects of maximum residue level of insecticides on some biochemical parameters for white albino rats.

Material and Methods

Insecticides used

The following insecticides were used:

A- Primiphos-methyl:O-(2-diethylamino-6-methyl-pyrmidine-4-yl).

B- Chlorpyrifos–methyl: o,o-dimethyl o-(3,5,6-trichloro-2-pyridinyl) phosphorothioate.

C- Fenitrothion: o,o-dimethyl o-(3-methyl-4-nitrophenyl) phosphorothioate.

Experimental animals

Seventy adult female rats with an average weight of 70-85 gm were obtained from the farm of experimental animals at Helwan. Rats were divided into seven groups, each of which contained ten rats. These rats were treated with a single oral dose of the maximum residue limit (MRL) of each insecticide, as follows: 1, 0.5 and 0.5 ppm for primiphos - methyl, Chlorpyrifos – methyl, Fenitrothion respectively, (Codex, 1997).

Samples

Blood samples were collected after 1, 6, 12, 24, 48, 96 and 7 days of treatment to follow the effect of MRL of insecticides after these periods on albino rats.

Kits

Standard kits for the enzymes (AST), (ALT), (ALK-PH), urea, creatinine total protein and total cholesterol were obtained from Biomérieux Laboratory Instruments Co., France.

Blood analysis

Activity of serum (AST) and (ALT) were determined via utilization of aforementioned analytical kits according to the method of Reitman and Frankel (1957), serum ALK.PH was determined according to the method of Kind and King (1954), serum urea was determined according to Patton and Cruoch (1977), creatinine was determined according to the method described by Husdan (1968), serum cholesterol was determined according to the method of Siedel (1983) and total protein was determined according to the method of Henry *et al* (1974).

Statistical analysis

The data of liver and kidney functions were statistically analyzed via F-test at the 0.05 level of significance, according to Snedecor and Cochran (1982).

Results and Discussion

Effects on some biochemical parameters in the blood of female white albino rat

I- Effect on liver function test

A- Aspartate amino transferase (AST):

As shown in Table 1, activities of AST were significantly increased ($p < 0.05$) in treated rats by MRL of all tested insecticides, except for treated rats by the MRL of pirimiphos-methyl and chlorpyriphos-methyl after 12, 24 hrs and 7 days (52.5, 53.0, 52.3 and 52.0, 52.3, 53.0 u/L, respectively), as well as in treated rats by MRL of fenitrothion after 12, 24, 48 hrs and 7 days (52.2, 52.9, 51.9 and 52.5 u/L, respectively) of treatments.

TABLE 1. Effect of single oral dose of pirimiphos-methyl, chlorpyriphos-methyl and fenitrothion on Aspartate Amino Transferase activity in white albino rat.

Treatments / Period	Average Untreated µ/L	Pirimipho-methyl MRL µ/L	Chlorpyriphos-methyl MRL µ/L	Fenitrothion MRL µ/L	LSD 5 %
Zero *	52.0 a	53.0 b	52.5 b	53.1 b	0.771
6 hours		53.4 b	53.0 b	53.0 b	0.896
12 hours		52.5 a	52.0 a	52.2 a	1.245
24 hours		53.0 a	52.3 a	52.9 a	1.132
48 hours		52.9 b	53.1 b	51.9 a	0.678
96 hours		53.1 b	52.9 b	53.1 b	0.616
7 days		52.3 a	53.0 a	52.5 a	0.949

* = One hour after application. a,b show signifigance (LSD 5%).

B- Alanine amino transferase (ALT):

Data obtained in Table 2 indicated that Alanine Amino Transferase (ALT) activities in the treated rats were going through the same trend as previously mentioned in case of AST activities.

TABLE 2. Effect of single oral dose of pirimiphos-methyl, chlorpyriphos-methyl and fenitrothion on Alanine Amino Transferase activity in white albino rat.

Treatments / Period	Average Untreated µ/L	Pirimiphos-methyl MRL µ/L	Chlorpyriphos-methyl MRL µ/L	Fenitrothion MRL µ/L	LSD 5 %
Zero *	36.0 a	35.0 a	36.5 a	37.1 a	0.293
6 hours		36.2 b	35.0 a	36.2 b	0.606
12 hours		36.9 b	36.1 a	35.9 a	0.516
24 hours		37.1 b	35.6 a	36.2 a	1.015
48 hours		36.7 b	36.4 a	36.3 a	0.380
96 hours		36.4 b	35.7 a	35.3 a	0.481
7 days		36.1 a	36.2 a	36.3 a	0.561

* = One hour after application.

C- Alkaline phosphatase:

As shown in Table 3, no significant changes were observed in alkaline phosphatase activity in rats treated with the MRL of the tested insecticides, except in case of dosing rats by the MRL of pirimiphos-methyl and chlorpyriphos-methyl after 96 and 24 hrs (134.1 and 135.2 u/L), respectively .

These results are in agreement with those found by Kandil *et al.* (1991), who reported that a significant increase in the activity of plasma alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase was observed after dosing mice by subchronic dose of cyanofos. Similar effects were obtained by Saleh (1997), who recorded that, a significant increase in AST and ALT activities were happened in treated rats by $^1/_{20}$ of the LD_{50} of technical and formulated chlorpyriphos-methyl. Zidan *et al.* (1998) studied the effect of the oral $^1/_{20}$ of the LD_{50} dose of fenvalerate, profenofos and methomyl on the liver functions of white albino rats. The author demonstrated that AST showed highly significant increase with the three tested insecticides, as well as the ALT levels were significantly increased by the same trend. Changes occurred in alkaline phosphatase were not significant except in case of fenvalerate, which led to a significant decrease.

TABLE 3. Effect of single oral dose of pirimiphos-methyl, chlorpyriphos-methyl and fenitrothion on alkaline phosphatase activity in white albino rat.

Treatments / Period	Average Untreated µ/L	Pirimiphos-methyl MRL µ/L	Chlorpyriphos-methyl MRL µ/L	Fenitrothion MRL µ/L	LSD 5 %
Zero *	133.0 a	133.5 a	134.0 a	132.8 a	1.985
6 hours		133.0 a	132.5 a	133.2 a	1.273
12 hours		134.0 a	133.0 a	134.2 a	1.280
24 hours		133.2 a	135.2 b	133.5 a	0.675
48 hours		133.8 a	136.2 a	135.0 a	6.35
96 hours		134.1 b	133.8 a	133.9 a	0.954
7 days		134.0 a	133.1 a	136.0 a	3.64

* = One hour after application.

II- Effects on kidney function tests

A- Creatinine concentration:

As shown in Table 4, no significant changes ($P < 0.05$) in creatinine levels were detected in all dosed group except for those treated rats by chlorpyriphos-methyl after 1 and 6 hrs (0.78 and 0.77 mg/dL) and after 48 hrs of dosing by fenitrothion (0.76 mg/dL).

B-Urea concentration :

As shown in Table 5, no significant changes were observed in urea concentrations at the different periods after dosing rats by the MRL of the tested insecticides, except after 1, 6 hrs and 7 days in treated rats by MRL of chlorpyriphos-methyl (13.2, 13.4 and 13.2 mg/dL) and after 6 hr in treated rats by the same dose of fenitrothion (13.3 mg/dL).

TABLE 4. Effect of single oral dose pirimiphos - methyl, chlorpyriphos - methyl and fenitrothion on creatinine concentration in white albino rat.

Treatments / Period	Average Untreated mg/dL	Pirimiphos-methyl MRL mg/dL	Chlorpyriphos-methyl MRL mg/dL	Fenitrothion MRL mg/dL	LSD 5 %
Zero *	0.75 a	0.76 ab	0.78 b	0.74 a	0.016
6 hours		0.74 a	0.77 b	0.75 a	0.014
12 hours		0.76 a	0.76 a	0.76 a	0.016
24 hours		0.75 a	0.75 a	0.74 a	0.016
48 hours		0.74 a	0.75 a	0.76 b	0.014
96 hours		0.76 a	0.74 a	0.75 a	0.016
7 days		0.75 a	0.76 a	0.76 a	0.018

*= One hour after application.

TABLE 5. Effect of single oral dose pirimiphos - methyl, chlorpyriphos - methyl and fenitrothion on urea concentration in white albino rat.

Treatments / Period	Average Untreated mg/dL	Pirimiphos-methyl MRL mg/dL	Chlorpyriphos-methyl MRL mg/dL	Fenitrothion MRL mg/dL	LSD 5 %
Zero *	13.11 a	13.14 ab	13.2 b	13.0 a	0.104
6 hours		13.08 a	13.4 c	13.3 b	0.097
12 hours		13.2 a	13.3 a	13.4 a	0.333
24 hours		13.22 a	13.16 a	13.2 a	0.110
48 hours		13.4 a	13.0 a	12.9 a	2.276
96 hours		12.9 a	13.4 a	13.25 a	0.869
7 days		13.09 a	13.2 c	13.09 b	0.043

* = One hour after application.

The same trend was observed by Asghar *et al.* (1994), who reported that urea and creatinine concentrations were significantly increased in male rabbits which were daily fed on 1 mg methyl parathion per body weight for twelve weeks.

On the other hand, Saleh and Zidan (1995) found that a single acute dose at level of LD_{50} of pirimiphos-methyl significantly increased creatinine level after one day, while insignificant increasing was seen after the third and seventh days Similar effects were obtained by Zidan *et al.* (1998), who recorded that a high significant increase in the blood urea and creatinine levels in treated rats by $^1/_{20}$ of the LD_{50} of fenvalerate, profenofos and methomyl. They also, noticed that a high significant increase in the blood urea and creatinine concentrations were achieved in treated rats by oral residue dose estimated after 7 days from foliage application of the three tested insecticides. Data obtained by Aioub and Hegab (2000) indicated that creatinine concentrations significantly increased after one day of treating rats by $^1/_{20}$ and $^1/_{10}$ of the LD_{50} of methomyl.

C- Total protein:

As shown in Table 6, the obtained data indicated that a rather significant decrease in total protein levels was observed in treated rats after 1, 6, 12, 24, 48, 96 hrs and 7 days of treatments.

TABLE 6. Effect of single oral dose pirimiphos-methyl, chlorpyriphos-methyl and fenitrothion on total protein in white albino rat.

Treatments / Period	Average Untreated g/dL	Pirimiphos-methyl MRL g/dL	Chlorpyriphos-methyl MRL g/dL	Fenitrothion MRL g/dL	LSD 5 %
Zero *	2.9	2.85 a	2.9 a	2.9 a	0.067
6 hours		2.95 b	2.92 a	2.91 a	0.123
12 hours		2.97 b	2.89 b	2.89 b	0.098
24 hours		3.0	2.91	2.95	0.087
48 hours		2.92	2.87	2.91	0.071
96 hours		2.9	2.93	3.0	0.053
7 days		3.0	2.95	2.9	0.055

* = One hour after application.

D- Cholesterol levels:

Results in Table 7 clearly indicated that the total cholesterol levels in blood were going through the same trend as previously mentioned in case of AST, ALT, alkaline phosphatase activities, creatinine and urea concentration. Data obtained showed slight or no significant changes in cholesterol levels.

TABLE 7. Effect of single oral dose pirimiphos-methyl, chlorpyriphos-methyl and fenitrothion on total cholesterol in white albino rat.

Treatments / Period	Average Untreated mg/dL	Pirimiphos-methyl MRL mg/dL	Chlorpyriphos-methyl MRL mg/dL	Fenitrothion MRL mg/dL	LSD 5 %
Zero *	29.1 a	28.9 a	28.7 a	28.5 a	0.565
6 hours		30.0 a	29.3 a	30.0 b	0.533
12 hours		29.1 a	30.2 ab	31.2 b	1.233
24 hours		29.0 a	30.0 a	30.8 a	3.889
48 hours		31.0 a	29.0 a	29.6 a	1.010
96 hours		30.5 b	31.1 b	28.7 a	0.549
7 days		30.0 b	28.8 a	29.5 ab	0.875

* = One hour after application.

The obtained results are in agreement with those found by, Asghar *et al.* (1994), who reported that blood cholesterol levels were increased in rats which daily treated by 1 mg methyl parathion per kg body weight for twelve weeks.

On the other hand, data obtained by Saleh and Zidan (1995) indicated that total protein values were increased in rats, which treated, by acute and subchronic doses of pirimiphos-methyl.

Data obtained by Zidan *et al.* (1998) indicated that a high significant increase was observed in the total protein levels in treated rats by oral $^{1}/_{20}$ LD_{50} of fenvalerate, profenofos and methomyl. Profenofos caused the highest increase followed by methomyl then fenvalerate. Also, the authors reported that the oral residue dose estimated after 7 days of foliage application of the tested insecticides affecting the total protein levels. These levels showed a very high significant increase with prementioned insecticide residues. Results obtained by Eissa (1999), indicated that, total plasma protein concentrations were decreased in treated rats by malathion, pirimiphos-methyl, chlorpyriphos-methyl, carbosulfan and methomyl, as well as their extracted residues from different parts of watermelon 48 hrs after treatments. The author also, showed that, plasma cholesterol concentrations were decreased with malathion, pirimiphos-methyl, carbosulfan and methomyl, while chlorpyriphos- methyl increased cholesterol concentrations.

Conclusion

Treating rats by Maximum residue level (MRL) for tomatoes fruits of primiphos-methyl, chloriphos-methyl and fenitrothion insecticides have a slight effect (non significant) on liver and kidney function through different periods (through 1, 6, 12, 24,48, 96 hours and 7 days).

References

Aiaoub, A.A.A. and Hagab, A.M.I. (2000) Fate and toxicity of methomyl in albino rats. *Zagazig J. Agric. Res.* 27 (2), 581.

Asghar, M., Sheikh, M.A. and Hashmi, A. (1994) Effects of orally fed methyl parathion on some haematochemical parameters of rabbits. *Pakistan J.Vet Sci.* **14** (1), 54.

Codex Alimentration commission (1997) Codex maximum limits for pesticide residues. *Joint FAO/WHO Food Standards Programme.*

David Lawrence (2003) Pesticides Exacerbate Dermetosis in Porphyria Patients *Porphyria Educational Services* June 2003 Newsleiter.

Eissa, F.I. (1999) Studies on the determination of some pesticides residues and their toxic effect against some pests. *M.Sc. Thesis,* Fac. Agric., Kafer El-Sheikh, Tanta Univ., Egypt.

El-Gendy, Kawther, Aly, Nagat, Rashwaan, Eiman and El-Sebae, A.H. (1999) Biochemical targets affected by sublethal doses of cypermethrin in mice. *Egypt. J. Agric. Res.*, **77** (2), 701.

Henry, R.J., Cannon, D.C. and Winkelman, J.W. (1974) *Clin Chem., Principles and Technics,* Harper and Row, Publ., p. 415.

Husdan, H. (1968) Creatinine enzymatic colorimetic methods. *Clin. Chem.* **14**, 222.

Kandil, M.A., El-Nattar, F.M., Mohamed, M.U. and Gad, M.M.E. (1991) Effect of cyanophos on certain enzyme activity and thyroid function of mice. *Fourth Arab Conf. of Plant Protection, Cairo,* 1-5 Dec. p. 279.

Kind, P.R.N. and King, E.G. (1954) Colrimetric method for determination of serum alkaline phosphatase. *J.Clin. Path.***7**, 322.

Patton, J. and Crouch, S.R. (1977) Urea enzymatic colorimtric method. *Anal Chem.* **49**, 464.

Reitmans, S. and Frankel, S. (1957) Colorimetric method for determination of serum (AST) and (ALT) activity. *Am. J. Clin. Path.* **28**, 56.

Saleh, A.A. (1997) Experimental studies on the effects of Gesapax herbicides on the mothers and their fetuses. *J. Agric. Sci. Mansoura Univ.*, **22** (7) 2451.

Saleh, A.A. and Zedan, H.A. (1995) Acute and subchronic toxicity of pirmiphos-methyl for white rat. *1st Int. Conf. Pest Control, Mansoura, Egypt*, 429.

Shalby, Sh.E.M. (2002) Determination of pesticides residues in and on tomato fruits and their effects on experimental rats. *Ph. D. Thesis. Agric. Sci. of Pesticides.* Fac. Agric., Mansoura University, Egypt.

Siedel, J., *et al.* (1983) Cholesterol CHOD-POP. *Clin. Chem.* **29,** 1075.

Snedecor, G.W. and Cochran, W.G. (1982) "*Statistical Methods*", 7th ed. Iows State Univ. Press, Ame. Iowa, USA.

Zidan, Z.H., Mashhour, A.K., Zidan, A.A., Fawzy, A.A. and Okasha, Y.A. (1998) Toxicological effect of long terms administration of minimal doses of certain insecticides on white albino rats. 7th *Conf. Agric. Dev. Res.*, Fac. Agric. Ain Shams Univ. Cairo, 1085-1101.

(*Received* 31 / 1 / 2005;
accepted 26 / 6 / 2005)

تأثير المبيدات على بعض مكونات الدم فى إناث الفار الأبيض

إبـــراهيـــم منـــولـــى النبـــراوى* ، عـــادل صـــلاح** ، محمـــــود القاضـــــى**،
أحمد سيد مرسى فوزى*** و شحاته شلبى*
* قسم وقاية النبات – المركز القومى للبحوث، ** قسم المبيدات – كلية الزراعـــة– جـــامعة المنصورة و *** قسم سموم وملوثات الغذاء -المركـــز القـــومى للبحـــوث– القاهرة – مصر .

تم فى هذه التجربة معاملة الفئران بجرعة واحدة من الحد الأقصى لمتبقى المبيدات لثمار الطماطم (MRL) بالمبيدات البريميفوس – ميثيل ، الكلوربيريفوس ميثيل والفنتروثيـــون ومقدارها(١، ٠,٥ و ٠,٥ و جزء فى المليون) على التوالى من كل مبيد ثم ذبحت هـــذه الفئران بعد ١ ، ٦ ، ١٢ ، ٢٤ ، ٤٨ و ٩٦ ساعة و ٧ أيام من المعاملة وذلك لقيـــاس نشاط بعض المعايير البيوكيميائية فى دم وسيرم الحيوانات المعاملة ، وجد أن تأثير جرعة المبيدات المختبرة أدت إلى حدوث تأثيرات طفيفة على نشاط إنزيم الGOT حيـــث لـــم يحدث تغيير معنوى فى معظم فئران التجربة عند مقارنتها بالكنترول ،كما لم يحـــدث أى تغيير معنوى فى نشاط إنزيم الـــ GPT بـــعد ١ ، ٦ ، ١٢ ، ٢٤ ، ٤٨ ، ٩٦ ســـــاعة و٧ أيام من المعاملة بجرعة واحدة من الـــ MRL ، بينما حدث تغيير معنوى فى مستوى إنزيم الفوسفاتيز القاعدى بعد ٢٤ ، ٩٦ ساعة فى الفئران المعاملة بالكلوربيريفوس–ميثيل والبريميفوس ميثيل على الترتيب. فى حالة وظائف الكلية لم يحدث أي تغيير معنوي فى قيم الكرياتنين فى الفئران المعاملة بالحد الأقصى للمتبقي من المبيدات المختبرة فيما عدا بعد ١ ، ٦ ساعة فى الفئران المعاملة بالكلوربيريفوس – ميثيل وبعـــد ٤٨ ســـاعة فـــى الفئران المعاملة بالفنتروثيون. أوضحت النتائج وجود فروق معنوية فى تركيز اليوريا بعد ١ ، ٦ ساعة و ٧ أيام فى الفئران المعاملة بالكلوربيريفوس – ميثيل وبعد ٦ ساعات فـــى الفئران المعاملة بالـــ MRL لمبيد الفنتروثيون ، كما حدث تغير طفيف فى قيمة البروتين الكلى و لم تتغير قيمة الكوليسترول الكلى كثيرا فى الفئران المعاملة بالحد الأقصى للمتبقى من مبيدات البريميفوس ميثيل والكلوربيريفوس ميثيل والفنتروثيون.