J. Egypt. Soc. Toxicol.
(Vol. 34: 85-98 Jan. 2006)
WWW.estoxicology.org

COMPARATIVE HAEMATOLOGICAL AND HEPATORENAL TOXICITY OF IGR, LUFENURON AND PROFENOFOS INSECTICIDE ON ALBINO RATS

Shehata E. M. Shalby

Pests& Plant Protection Dept., National Research Centre, Dokki, Cairo, Egypt

ABSTRACT

The present investigation was conducted to compare the toxicity of the IGR, lufenuron and the organophosphorus insecticide, profenofos on blood content, liver and kidney functions of male albino rats. The tested compounds were orally administered to rats at $^1/_{20}$ and $^1/_{10}$ of their median lethal doses (LD_{50s}) for two months (day after another), then toxicants were withdrawn for 30 days to allow recovery of toxic effects.

Data indicated that $^1/_{10}$ LD_{50} of both compounds caused significant changes on blood contents and biochemical parameters of treated rats without return to normal levels at the end of recovery period, while, the smallest dose revealed negligible changes on some tested parameters with resumed normal values. The adverse effects reached its peak at 45 and 60 days of treatment (high dose treated rats) followed by decrease during recovery intervals without returned to normal, but at $^1/_{10}$ LD_{50}, lufenuron caused sever damage on kidney; urea and creatinine showed high levels at the end of recovery periods (92.0 and 220.0 % above normal level, respectively).

Data indicated that, $^1/_{10}$ LD_{50} of lufenuron treated rats exhibited changes in leucocytes, platelets counts, transaminases activities, creatinine and urea concentrations more than the organophosphorus insecticide. On the contrary, the same dose of profenofos mostly affected on erythrocytes counts, haemoglobin levels and alkaline phosphatase (ALP) activity. The obtained data would suggest that the two tested compounds at high dose have an inhibitory action on haemopiesis. In addition, both compounds proved to have comparable toxicity towards animals.

Keywords: IGR's, lufenuron - profenofos - haemato – hepatorenal – toxicity - rats.

INTERODUCTION

The wide use of insecticides in the agriculture, either individually or in different combinations, although improved the quantity of the harvests, its quality regarding the insecticides (residues) in fruits, leaves or any other part of the plant is really threatening the health of consumers (Zidan *et al.*, 1998). The adverse health effects are clearly minimized by selecting the right pesticide at proper time of application and using the right method. It is therefore, necessary to follow the international recommendations and enforce national legislation (Abdel-Megeed *et al.*, 2001).

Insect growth regulators IGR's are widely used to control pests infesting vegetables and field crops during the last few years. Large amounts of these compounds are used every year for control program of several pests. Lufenuron (antimoulting compound) is one of the most newly introduced synthetic insect growth regulators. IGR's have a large potential for becoming an environmentally and economically important group of chemicals, however, few toxicological studies have been carried out to evaluate the acute and chronic toxicity effects of lufenuron on the laboratory animals. Knowledge about various mechanisms of pesticide interaction should be utilized in predicting the human hazards of pesticides. Consequently, studies on laboratory animals have become the main source of toxicological data. A toxicant may induce several types' ofinjury and the severity of effects is usually related to the dose and duration of exposure to the chemical under a specified conditions (Frank and Sielkenzr, 1991).

Therefore, the present study aimed to compare the subchronic toxicity of IGR, lufenuron and the organophosphorus insecticide, profenofos on blood content as well as liver and kidney functions on male albino rat.

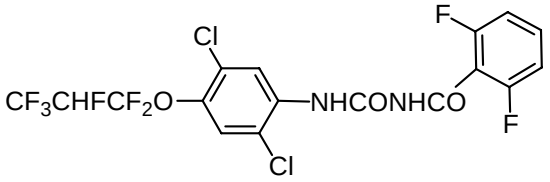
MATERIALS AND METHODS

I-Chemicals used:

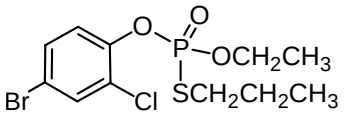
1- Lufenuron: (Match 5 % E.C). Uses: Insect growth regulator for control of Lepidoptera and Coleoptera larvae on cotton, maize and vegetables; and citrus

whitefly and rust mites on citrus fruit, at 10-50 g/ha. (Anonymous, 2004).

2- Profenofos: (Selecron 72 % E.C). Uses: Control of insects (particularly Lepidoptera) and mites on cotton, maize, sugar beet, Soya beans, potatoes, vegetables, tobacco, and other crops, at 250-1000 g/ha. (Anonymous, 2004).



Lufenuron



Profenofos

II- Treatments:

Male albino rats (80-100 g) were obtained from the Animals Laboratory at Helwan Farm, Ministry of Health. The animals were housed in standard environmental conditions and had free access to tap water and food.

To study the haematoand hepatorenal toxicity (toxic effect on blood content, liver and kidney functions) of, lufenuron and profenofos, the animals were divided into five groups (10 rats each). The 1st and 2nd groups were treated by one- twentieth of the median lethal dose ($^1/_{20}$ LD_{50}) of the tested compounds, while 3rd and 4th groups were treated by one- tenth of the median lethal dose ($^1/_{10}$ LD50) of these chemicals (LD_{50} of lufenuron is 2000 mg/kg b.w.; while profenofos is 380 mg/kg b.w.; Anonymous, 2004). The fifth group was control; toxicants were dissolved in corn oil and administered by convenient stomach tube day after anthor during two months.

At intervals of 15, 30, 45 and 60 days, blood samples were collected in two tubes, the first containing heparin (7.5 I.U./ml) according to Schalm (1986), for hematological investigations.

III- Haematological study: erythrocytes (RBCs) count, leucocytes (WBCs) count, hemoglobin (Hb), hematocrite, platelets count, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) were determined according to Schaim (1986) method.

IV - Biochemical determination:

Another tube without anticoagulant was kept to colt, then centrifuged and the serum was separated and kept at 4 ˚C till the biochemical analysis. The activities of aminotransferases (AST & ALT) and alkaline phosphatase (ALP) enzymes were determined colorimetrically (Reitman and Frankel, 1957; Kind and King, 1954), respectively. Serum urea and creatinine concentrations were measured according to Coulombe and Farreau (1963) and Henry (1974), respectively. The albumin level was determined according to the method of Dumas *et al.* (1971). Bilirubin concentration was determined according to Jendrassik (1983) method. The activities and concentrations of previous parameters were measured to evaluate the pathophysiological changes induced by such toxins.

The two tested compounds were withdrawn for 30 days to allow recovery the toxicant. All data obtained were statistically analyzed "F" test at 0.05 level according to Snedecor and Cachran, 1980 (a significant between different treatments).

RESULTS AND DISCUSSION

I- Haematological effects:

Data in Table (1) and Fig. (1) demonstrate significant decrease in erythrocytes counts (RBCs) in treated rats with both sublethal doses of antimoulting compound, lufenuron and organophosphorus, profenofos insecticides at the all experiment intervals, without recovery to the normal levels until the end of experiment, except in case of treated rats by low dose of lufenuron after 15 days of treatment. After 60 days of treatment the erythrocyte values were 3.4, 2.1 and 3.0, 2.5 X 10^6 in treated rats by $^1/_{20}$ and $^1/_{10}$ LD_{50} of lufenuron and profenofos, these values reached to 6.1, 5.0 and 4.0, 3.1 X 10^6 (1.6, 19.4 and 35.5, 50.0 % below the normal level, Fig. 1) at the end of recovery period, respectively.

At the same Table and Fig. results of, treated rats by $^1/_{20}$ of LD_{50} of lufenuron and profenofos caused significant decrease after 15 and 30 days in leucocytes counts (WBCs), while, after 45 and 60 days a significant increase (4.8 ,5.2 and 4.2, 5.9 X 10^3) as compared with untreated animals (4.15 and 4.0 X 10^3). These amounts, after 30 days of recovery in treated rats by $^1/_{20}$ LD_{50} of profenofos reached to 12.8 % above normal level, but in treated rats by the same dose of lufenuron become normal. Treated rats by one tenth of median lethal doses of tested chemicals caused increase in leucocytes counts as compared with the control after all the experimental periods, since leucocytes values were 5.1 and 4.1 X 10^3 after 15 days, these values reached 8.3 and 7.2 X 10^3 (80.0 and 107.5 % above normal) after 60 days of treatment. These amounts were decreased during the recovery periods (59.0 and 33.3 % above normal after 30 days for recovery, respectively.) but don't reach normal levels. The high increase of leucocytes may be due to the inflammatory response induced as defense mechanism. Also, both compounds may affect the leucocytic count by the stressogenic effect of these insecticides on the reticuloendothelial system (Gromysz, 1993).

Data in Table (2) and Fig. (2) showed that, $^1/_{10}$ LD_{50} of lufenuron and profenofos caused significant decrease in hemoglobin content in treated animals compared with

normal level, without recovery to the normal levels until the end of experiment. The low dose ($^1/_{20}$ LD_{50}) of both tested chemicals caused negligible changes in hemoglobin content after 15 and 30 days of application. The prolongation of time exhibited significant reduction in hemoglobin content after 45 and 60 days from administration. After 30 days for recovery, recovery occurrence and hemoglobin content returned to the normal levels in treated animals by $^1/_{20}$ LD_{50} of profenofos (+ 2.89 %, Fig. 2). High percent of decrease was obtained at 15 days for recovery in case of $^1/_{10}$ LD_{50} of lufenuron (- 35.2 %) and 30 days for recovery in $^1/_{10}$ LD_{50} of profenofos treated rats (-38.4 %). The reduction of Hb content as well as RBCs counts may be attributed to the toxic effect of both compounds.

Platelets play an important role in homeostasis and coagulation process in the body and their origin in the bone marrow. Thrombocytopenia is a subnormal numbers of platelets in the circulating blood. It is the most common cause of abnormal bleeding in the living organisms. Obtained results (Table 2 and Fig. 2) indicated that, $^1/_{10}$ LD_{50} of lufenuron and profenofos treated rats caused significant decrease in platelets counts during the experimental course, reached its maximum on 60 days(48.8 and 43.0 % below normal level, respectively).

On the other hand, treated rats by $^1/_{20}$ LD_{50} of profenofos caused increase in platelets counts, while the same dose of IGR induced the similar effects after 15 and 30 days for treatment, and decrease at 45 and 60 days and during recovery intervals. The reduction of platelets (thrombocytopenia) in treated rats was also reported by Siegelman *et al.*. (1984). The present findings revealed reduction in numbers of both RBCs and platelets probably due to suppressive and toxic effect on bone marrow and subsequently on haematopoiesis. Since platelets are synthesized in bone marrow, so the double suppressing effect on RBCs and platelets would be explained (Jamel Al-Layl, 2004).

As shown in Table (3) and Fig. (3) the mean corpuscular hemoglobin (MCH) values in treated animals by $^1/_{20}$ LD_{50} of tested compounds showed no significant differences from that of control rats. On the contrary, $^1/_{10}$ LD_{50} of lufenuron caused significant increase at 30, 45 and 60 days of treatment (8.8, 14.8 and 22.8 % above normal level, respectively), , also the same trend was noticed in case of $^1/_{10}$ LD_{50} of the organophosphorus insecticide after 30 and 60 days of treatment (31.0 and 34.0 pg). The prolongation of time indicate recovery occurrence and mean corpuscular hemoglobin (MCH) values returned to the normal levels.

Data in Table (3) and Fig. (3) also indicated that the tested doses did not induce, in general, significant differences in mean corpuscular hemoglobin concentration (MCHC) in treated animals compared with normal level after 15, 30 and 45 days from treatment. The $^1/_{20}$ LD_{50} of profenofos treated rats induced significant decrease in this parameter at 60 days (12.5 % bellow the normal, Fig. 3) from treatment, while treated rats by the highest dose of IGR, lufenuron induced significant increase (+ 10.0 %) at the same period. All treated animals recovered and reached to the normal level during the recovery period.

The data in Table (4) and Fig. (4) show a gradual decrease in the level of heamatocrit in treated rats which reached its maximum after 60 days in case of $^1/_{10}$ LD_{50} of lufenuron and profenofos (30.0 and 34.3 % below normal). $^1/_{20}$ LD_{50} doses treated rats recovered and reached to the normal level during the recovery period. None of the treated rats with $^1/_{10}$ LD_{50} dose returned to the normal at the end of experiment (– 17.5 and -15.0 %).

Data in the same table and fig., indicated that treated rats by $^1/_{20}$ LD_{50} of profenofos induced significant increase in the mean corpuscular volume (MCV) level at 60 days from treatment (+11.9 %), while, $^1/_{10}$ LD_{50} of the same toxicant caused significant decrease at 45, 60 days for treatment and 15 days for recovery (-22.2, -28.0 and -25.4 %, respectively) and reached the normal level at the end of recovery period. Generally, the insect growth regulator treated rat's induced significant increase in this parameter, except at 30 and 45 days in case of $^1/_{20}$ LD_{50} (0.84 and 7.7 % below the normal level). The highest changes were observed at 60 days from application in treated rats by $^1/_{10}$ LD_{50} of lufenuron and profenofos (+32.1 and -28.0 %, respectively).

So we can conclude that the increase of WBCs count may be related to the response of toxic agents and other foreign materials in the host environment. Reduction in Hb concentration was due to reduction in total number of RBCs. The decrease in HCT and increase in MCV are characteristic of an anemic condition (Seirverd, 1972). The obtained results coincide with those reported by Said *et al.*. (1986), who found that diflubenzuron (IGR) caused bad effects on blood content of treated rats more than cylfoxylate, methomyl and fenvalerate. They noticed also, that the changes in blood content to recovery cannot be preceded in poisoned animals with diflubenzuron till 30 days after treatment. Also, Shalby (2002) reported that organophosphorus, fenitrothion; chlorpyrifos-methyl and pirimiphos-methyl insecticides caused a significant effect in WBCs, RBCs counts and haemoglobin levels in treated rats. Also, Carp and Bashamohideen (1989), observed an increase in RBCs counts after fenvalerate and cypermethrin administrated. On the contrary, Roe *et al.*., (1979) reported that a single spray of monocrotophos insecticide (Nuvacron 40) did not affect significantly the count of erythrocytes (RBCs) and leucocytes count (WBCs) and haematocrite values in volunteers. Radwan *et al.* (2001a), recorded no or slight changes in RBCs counts and haemoglobin content, but a different response occurred with WBCs after fenitrothion, cyphenothrin, azadirachtin and pyriproxyfen treatment.

II- Effect on liver functions:

Animals in their living environments, ingest, inhale, and absorb many chemicals that can impose stress on the organism and trigger tissue damage by numerous biochemical mechanisms. Since the liver is a primary site of biotransformation of foreign compounds, it is particularly

vulnerable. The obtained results indicated that, one-tenth of median lethal doses of both tested compounds induced the significant increase in aspartate aminotransferase (AST), Table (5) and Fig. (5) the elevated levels in the enzyme activity was observed at 60 days of treatment (124.1 and 100.3 % above normal level in lufenuron and profenofos treated rats, respectively), followed by slight less values until the recovery period (+ 56.8 and +44.9). $^{1}/_{20}$ LD_{50} of IGR compound induced reduction in this enzyme activity at all of experiment intervals, while, the same dose of profenofos treated rats caused decrease in the activity of AST enzyme at 15 and 30 days, and then gradual significant increase at 45, 60 days and for recovery period.

At the same Table, data clearly indicated that alanine aminotransferase (ALT) activity have the same trend of activity of previously mentioned in case of AST, except in $^{1}/_{20}$ LD_{50} lufenuron treated rats induced abnormal rates of increase during the period of 15 and 30 days (+ 11.4 and + 13.0 %) after oral administration, then this increase gradual less at 45 and 60 days and reached the normal level at 30 days for recovery. Transaminases are important enzymes in biological process. They play an important role in amino acid catabolism and biosynthesis. ALT and AST transfers the amino group of alanine and aspartate amino acids to alpha ketoglutaric acid forming glutamic and pyruvic acids. AST and ALT activities were activated in liver of treated animals. The disruption of transaminases from the normal values denote biochemical important and lesions of tissues and cellular function because they are involved in the detoxification process, metabolism and biosynthesis of energetic macromolecules for different essential functions (Tordior and Van Heem Stra-Lequin, 1980)

Data in Table (6) and Fig. (6) indicated that the one-tenth of LD_{50} of both tested chemicals caused significant increase in alkaline phosphatase activity in treated rats, and reached its maximum at 45 days in lufenuron (12.3 u/L) and at 60 days in profenofos treated rats (14.56 u/L), without return to normal. After 15 days, $^{1}/_{20}$ LD_{50} of profenofos treated rats induced decrease in activity of this enzyme, followed by gradual increase and reached its maximum at 15 days for recovery (57.53 % above normal, Fig.6). $^{1}/_{20}$ LD_{50} of antimoulting compound (lufenuron) showed very low negative values than normal and didn't return to normal till the end of experiment, i.e. – 2.19 %. Similar results were obtained by Abdel-Gawad *et al.* (2005), reported that AST, ALT and alkaline phosphatase activities were significantly increased of treated hens with chlorpyrifos without returned to control level after one month recovery period.

Also, the data in Table (6) and Fig. (6) show a gradual increase in the level of albumin in $^{1}/_{10}$ LD_{50} of lufenuron and profenofos treated animals which reached its maximum after 60 days (73.0 and 90.8 % above normal), but treated rats didn't return to normal level by the end of recovery period (+ 54.0 and + 39.2%). Treated rats by $^{1}/_{20}$ LD_{50} of Organophosphorus insecticide caused significant increase in albumin concentration after 15 and 30 days of treatment (+12.5 and + 17.8 %), followed by slight reduction with the lapse of time (- 21.7 %, after 30 days for recovery). The contrary was obtained with the $^{1}/_{20}$ LD_{50} of IGR, showing reduction in albumin concentration at 15 and 30 days, the prolongation of time revealed different trend of changes than the normal level without recovery.

Table (7) and Fig. (7) shows that $^{1}/_{20}$ LD_{50} of IGR, lufenuron and organophosphorus insecticide didn't cause any adverse effects on the bilirubin concentration in rats. One-tenth of median lethal dose of pervious compounds showed slightly increase of bilirubin activity at 15, 30 and 45 days from treatment. The highest increase occurred within 60 days (+62.2 and +35.1 % in lufenuron and profenofos treated rats, respectively) then decreased sharply at 30 days for recovery (37.5 and 45.0 % bellow the normal level).

The present work proved an increase in AST, ALT, ALP activities, albumin and bilirubin levels as a result of pesticide administration. Such an increase in serum enzymatic activities could be the end of degenerative changes in hepatic cells. The obtained results coincide with those obtained by Abdel-megeed *et al.* (2001), who found significant increase in GOT and GPT activities, and negligible changes in the activity of ALP as well as a high increase in bilirubin level in $^{1}/_{10}$ LD_{50} of juvenile hormone mimic, Pyriproxyfen and azadirachtin treated rats. The marked increase in serum bilirubin and GPT activity in response to pesticides manifests their potential hepatotoxic actions as hepatic necrosis in accompanied by abnormal increase in serum level of transaminase (El-Garawany *et al.*., 1990)

III- Effect on kidney functions:

As presented in Table (8) and Fig. (8) data clearly showed that the highest dose of both tested chemicals induced significant increase in blood urea content, reached its peak at 60 days of treatment (98.4 and 83.6 %, for lufenuron and profenofos, respectively). This value in case of organophosphorus insecticide followed by gradual less without return to normal level (+ 29.1 %, after 30 days for recovery) while, in lufenuron treated rats continued in high levels at the end of recovery period (+ 92.0 %). $^{1}/_{20}$ LD_{50} treated rats caused significant increase in urea content at 30 days of treatment (11.7 and 14.8 % above normal level), the progression of time this dose induced gradual increase in this vital biochemical parameter in rats, followed by recovery to normal level at the end of experiment.

At the same trend, the data also revealed that the effect of the highest dose of the two tested chemicals induced significant increase of creatinine levels in treated rats as compared with control. Non significant changes were noticed in this biochemical parameter in $^{1}/_{20}$ LD_{50} of lufenuron treated rats, while, $^{1}/_{20}$ LD_{50} of profenofos induced slight changes with lapse of time than normal, then returned to the normal level within 30 days for recovery. $^{1}/_{10}$ LD_{50} of insect growth regulator, lufenuron caused gradual increase in creatinine level and reached its maximum at the end of

experiment (+220.0%). Surprisingly, the value was increase by more two times compared with that of the untreated animals. On the other hand, $^{1}/_{10}$ LD_{50} of profenofos treated rats caused sharp increase of creatinine levels and reached its peak at 15 days for recovery (+ 192.3 %), followed by reduction at the end of recovery period (73.3 % above untreated animals, Fig.8). Generally, high increasing of creatinine and urea concentrations in $^{1}/_{10}$ LD_{50} of lufenuron treated rats more than in case of profenofos may be due to the decreasing role of IGR on glomeular filtration, which subsequently raised the level of serum creatinine uremia. Such finding suggests the induction of renal damage or renal toxicity and probably would lead to renal failure by this compound.

The changes occurred in kidney function parameters (urea and creatinine) with the tested pesticides were in form of highly significant increase of urea and creatinine; especially in $^{1}/_{10}$ LD_{50} treated rats after 45 and 60 days from administration. These changes may be due to epithelial necrosis to the renal tubules with nuclear and chromatin changes in the epithelium of cortical tubules (Janssen, 1984).The failure of kidney functions as a result of exposure to pesticides were reported by many investigators. El-Maghraby (2004), noticed that significant differences in blood urea and creatinine levels after 3 months of feeding mice on faba and soybean treated with carbaryl. Also, Abdel-Gawad *et al.* (2005) observed that, creatinine and urea concentration were significantly increased in laying hens fed on diet contaminated with chlorpyrifos, but these parameters returned to normal values after one month recovery period.

CONCLUSION

Generally, the present results and former literatures or pervious studies showed clearly that all chemicals, unfortunately, are toxic or caused bad effects on human, animals and environment, particularity it's used in pest control field without exception. Accordingly, the extensive and unwise use of synthetic chemicals in the control programs against agricultural pests of creates in major deleterious side effects. This result is in agreement with those found by Murphy, 1975, who reported that most of the chemicals that are used as pesticides are not highly selective but are generally toxic to many non target species including man, and other desirable forms of life. Also, in accordance with Radwan *et. al.* (2001a), Radwan *et. al.* (2001b) and Abdel-Mageed *et. al.* (2001), Shalby (2002) and Jamel Al-Layl (2004), these unwise changes may be due to the metabolic fates of the tested insecticides and interference of their metabolites with vital compounds of the cells (El-Nabaraway *et al.*., 2005).

From these aforementioned results it was concluded that IGR, lufenuron and organophosphorus, profenofos insecticide caused nearly the same lesions and have potential harmful effects. For all that, the adverse health effects are clearly minimized by selecting the right pesticide at proper time of application and using the right way.

REFERENCES

Abdel-Gawad, H.; H. Taha and B. Hegazi (2005): Toxicological potential and fate of the insecticide chlorpyrifos in laying hens. Bull. NRC, Egypt, 30(2): 179-193.

Abdel-Megeed M.I.; U.M.Radwan; A.Z. Hindy and A. Zrook (2001): Liver functions under stress of certain common pesticides residue used on fruits and vegetables orally administrated. Annals Agric. Sci., Ain Shams Univ., Cairo, Egypt, 46(1): 383-404.

Anonymous (2004): The Pesticide Manual, version 3.1, 2004-05, Thirteen Ed. Editor: C D S Tomlin.

Coulombe, J.J. and L. Farreau (1963): A new simple semi-micro method for colourimetric determination of urea. Clin. Chem. 9: 102-108.

Carp, P.M. and M. Bashamohideen (1989): Fenvalerate and Cypermethrin induced changes in the haematological parameters of cyprinus carpio. Acta. Hydrochimica, et. Hydrobiolgica. 17(1): 101-107.

Dumas, B.T.; Watson, W.A. and Biggs, H.G. (1971): Quantitative colorimetric determination of albumin in serum or plasma. Clin. Chem. Acta., 31: 87.

El-Garawany, A.A.; H.A. Samaan and M. Sadek (1990): Comparative hepatorenal toxicity of some commonly used chemical environmental pollutants. Egypt J. Pharm. Sci., 30(4): 331-336.

El-Maghraby, S. (2004): Toxicological potential to mice of ^{14}carbaryl bound residues in faba and soybeans. . Bull. NRC, Egypt, 29(6): 681-690.

El-Nabaraway, I.M.; A.A. Saleh; M.M. Kady; S.E. Negm and Sh.E.M. Shalby (2005): Toxicity and fate of subacute and minimal doses of certain organophosphorus insecticides in white albino rat. 3rd Conf. Agric. and Biol. Res. Dev., National Research Centre, Dokki, Cairo, Egypt, April 23-24, 2005 , Egypt J. Agric. Res., Sp. Issue, 2(2): 841-853.

Frank, C.L. and R. Sielkenzr (1991): Assessment of safety / risk of chemicals: inception and evolution of ADI and dose- response modeling procedures. J. Toxicology Letters, 59: 5-40.

Gromysz (1993): Substrate specificity of mouse-liver microsomal enzymes in S-fenvalerate metabolism *ACS* Symposium series No. 42, synthetic S-envalerate. American Chemical Society, Washington, D.C.

Henry, R.J. (1974): Clinical chemistry, Principles and Technics, Harber and Row Publ., NY, pp. 197.

Jamel Al-Layl, K.M.S. (2004): Toxicological and histopathological effects of the Cyanobacterium *Oscillatoria rubescens* on blood and liver of the white albino rats. Arab Univ. J. Agric. Sci., Ain Shams Univ., Cairo, Egypt, 12(2): 821-837.

Janssen, W. (1984): Forensic Histopathology. Spring-Verlag, Berlin, NY, pp. 314-315.

Jendrassik, L. (1983): Method of enzymatic analysis. Verlag Chem. pp. 1196-1199, Associated Press, N.Y.

Kind, P.R.N. and King, E.J. (1954): Determination of serum alkaline and acid phosphatases. J. Clin. Path., 7: 322.

Murphy, S.D.; (1975): Toxicology, the basic science of poisons. Macmillan publishing Co., Inc., N.Y., p. 408.

Radwan, M.U.; Z.A. Hindy; M. Abdel-Megeed and A. Zrook (2001a): Residual activity of orally administrated pesticides used on fruits and vegetables on rat blood parameters behavior. Annals Agric. Sci., Ain Shams Univ., Cairo, Egypt, 46(1): 365-382.

Radwan, M.U.; M.A. Abdel-Megeed; Z.A. Hindy and A. Zrook (2001b): Kidney functions under stress of residual activity of some pesticides commonly used on fruits and vegetables orally administrated. Annals Agric. Sci., Ain Shams Univ., Cairo, Egypt, 46(1): 405-421.

Reitman, S. and Frankel, S. (1957): A colourimetric method for determination of serum glutamic oxaloacetic and glutamic pyruvate transaminases. Amer. J. Clin. Path., 28: 26-33.

Roe, R.R.; M.R. Merathe and S.D. Gangoli (1979): Effect of exposure of human volunteers to aerial spray of monocrotophos. Ecotoxicol. Environ. Safety 3: 325-334.

Said. A.A.; S.E. Negm; A.A. Saleh and A.A. Abdel-Ghany (1986): Studies on histopathological changes of certain insecticides and antimoulting compounds: I-Haematological studies on rats treated with these toxicants. J. Agric., Sci., Mansoura Univ., 11(4): 1597-1604.

Schalm, O.W. (1986): Veterinary Hematology. 4th Ed., Loa and Fibiger, Philadelphia, pp.21-86.

Seirverd, C.E. (1972): Hematology for medical technology, 4th Ed. Lee and Febiger Philadelphia, 300-363.

Shalby, Sh.E.M. (2002): Determination of pesticide residues in and on tomato fruits and their effects on experimental rats. Ph.D. Thesis, Fac. Agric., Mansoura Univ., Mansoura, Egypt.

Siegelman, H.W.; W.H. Adams; R.D. Stoner and D.N. Xlathen (1984): Toxins of microcystis aeruginosa and their haematological and histopathological effects. ACS Symposium on Seafood Toxins. Series No. 262: 407-413.

Snedecor, G.W. and W.G. Cochran (1980): Statistical Methods. 7th (Ed). State university press, Ames, Iowa.

Tordior, W.F. and E.A. Van Heem Stra-Lequin (1980): Field studies monitoring exposure and effects in the deffelopment of pesticides. Elsevier, Amsterdam, Oxford, New York: 207.

Zidan, Z.H.; A.K. Mashhour; A.A. Zidan; A.A. Fawzy and Y.A. Okasha (1998): Toxicological effect of long term administration of minimal doses of certain insecticides on white albino rats. 7th Conf. Agric. Dev. Res., Annals Agric. Sci., Ain Shams Univ., Cairo, Egypt, 15-17 Dec., 1998, Sp. Issue 3, 1085-1101.

Table (1): Effect of IGR, lufenuron and profenofos insecticide on erythrocytes and leucocytes counts of male albino rats

Treatments \ Periods		15 days	30 days	45 days	60 days	Recovery for 15 days	Recovery for 30 days
Erythrocytes (RBCs) counts (1 x 10^6)							
Lufenuron	$^1/_{20}$ LD_{50}	5.7 a	4.3 b	3.8 b	3.4 b	5.3 a	6.1 a
	$^1/_{10}$ LD_{50}	4.7 c	3.6 c	3.2cd	2.1 d	3.1 b	5.0 b
Profenofos	$^1/_{20}$ LD_{50}	5.2 b	4.5 b	3.5bc	3.0bc	3.3 b	4.0 c
	$^1/_{10}$ LD_{50}	5.0 b	4.0 bc	3.0 d	2.5cd	2.6 b	3.1 c
Control		5.5 a	6.0 a	5.1 a	5.5 a	5.0 a	6.2 a
LSD 5 %		0.253	0.587	0.357	0.702	0.846	0.933
Leucocytes (WBCs) counts (1 x 10^3)							
Lufenuron	$^1/_{20}$ LD_{50}	3.7 b	4.0 c	4.8 c	4.2 d	4.8 d	3.5 e
	$^1/_{10}$ LD_{50}	5.1 a	6.2 a	5.3 b	8.3 a	7.65 a	6.2 a
Profenofos	$^1/_{20}$ LD_{50}	3.5 b	3.6 c	5.2 b	5.9 c	6.1 c	4.4 c
	$^1/_{10}$ LD_{50}	4.1 b	5.7 b	6.8 a	7.2 b	6.9 b	5.2 b
Control		3.8 b	4.1 c	4.15d	4.0 d	4.8 d	3.9 d
LSD 5 %		0.623	0.476	0.233	0.422	0.287	0.315

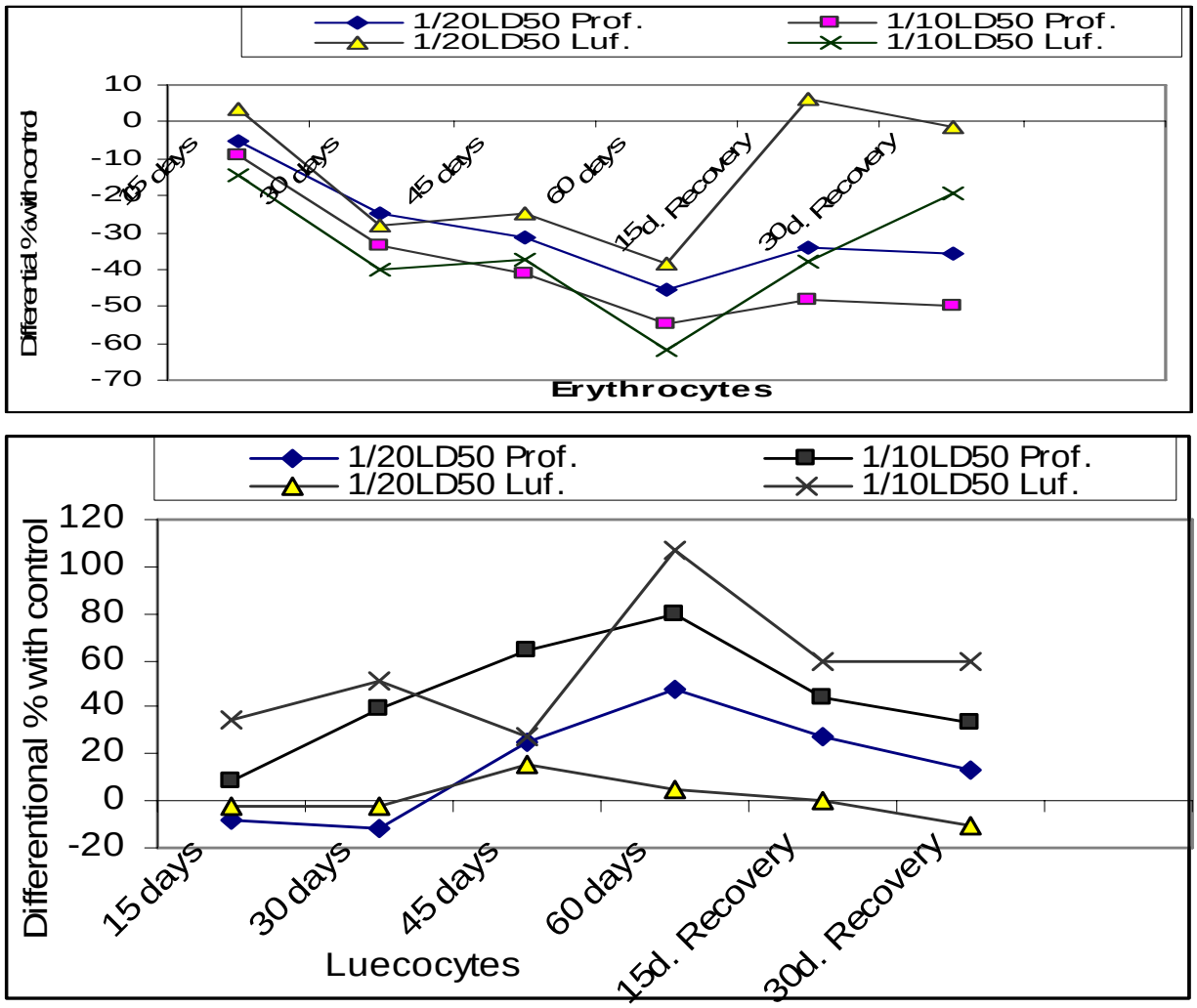
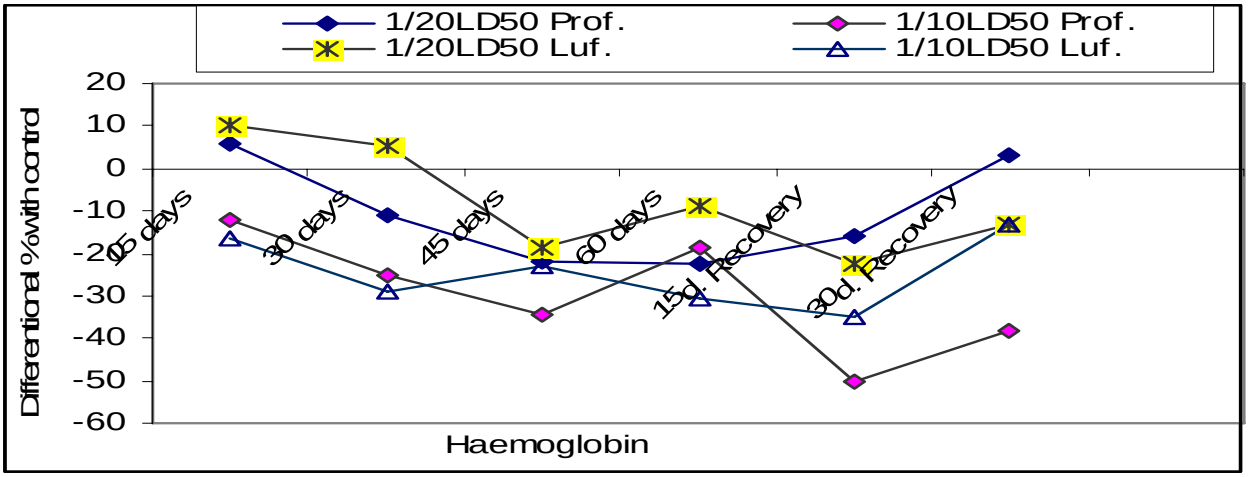


Fig. (1): The differential percentages of erythrocytes and leucocytes counts in treated rats as compared with control

Table (2): Effect of IGR, lufenuron and profenofos insecticide on hemoglobin values and platelets counts of male albino rats

Treatments \ Periods		15 days	30 days	45 days	60 days	Recovery for 15 days	Recovery for 30 days
Hemoglobin values %							
Lufenuron	$^1/_{20}$ LD_{50}	14.53 a	13.3 a	11.6 b	10.0 b	11.3 c	11.96 b
	$^1/_{10}$ LD_{50}	11.03 d	8.93 c	11.03 b	7.63 c	9.46 d	11.96 b
Profenofos	$^1/_{20}$ LD_{50}	14.0 a	11.2 b	11.2 b	8.53 c	12.26 b	14.2 a
	$^1/_{10}$ LD_{50}	11.6 c	9.43 c	9.4 c	7.86 c	7.3 e	8.5 c
Control		13.2 b	12.6 a	14.3 a	11.0 a	14.6 a	13.8 a
LSD 5 %		0.563	0.788	1.184	0.83	0.674	1.407
Platelets counts (10^3)							
Lufenuron	$^1/_{20}$ LD_{50}	201.33ab	201.67b	198.0 c	201.0 c	196.33 c	187.67 b
	$^1/_{10}$ LD_{50}	197.0 ab	175.67c	148.33e	108.0 e	125.67 e	205.0 a
Profenofos	$^1/_{20}$ LD_{50}	207.0 a	210.0 a	219.0 a	224.0 a	214.33 a	193.0 b
	$^1/_{10}$ LD_{50}	188.33 b	171.0 c	157.67d	120.33d	160.33 d	175.67 c
Control		200.0 ab	195.33b	205.0 b	211.0 b	203.0 b	193.0 b
LSD 5 %		12.195	7.016	6.935	9.787	4.769	7.52



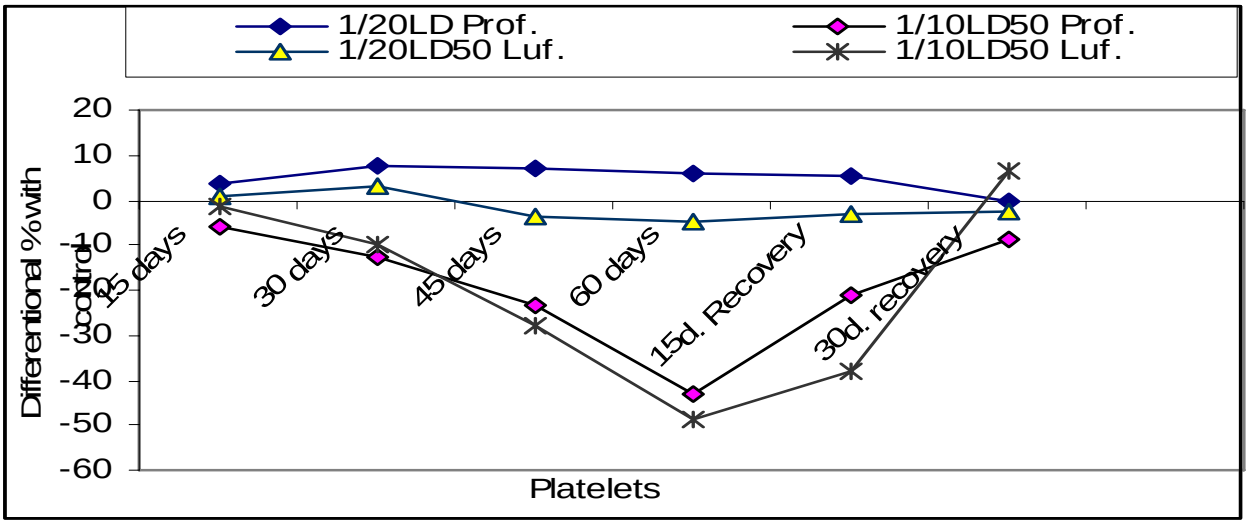


Fig. (2): The differential percentages of haemoglobin level and platelets count in treated rats as compared with control

Table (3): Effect of IGR, lufenuron and profenofos insecticide on MCH and MCHC of male albino rats

Treatments \ Periods		15 days	30 days	45 days	60 days	Recovery for 15 days	Recovery for 30 days
Mean corpuscular haemoglobin (MCH) Pg							
Lufenuron	$^1/_{20}$ LD_{50}	29.5 a	28.5b	28.0 b	29.5 b	29.0 a	28.0 a
	$^1/_{10}$ LD_{50}	29.0 a	31.0a	31.0 a	35.0 a	30.0 a	28.0 a
Profenofos	$^1/_{20}$ LD_{50}	28.5 a	29.0b	27.0 b	30.0 b	28.5 a	28.2 a
	$^1/_{10}$ LD_{50}	28.0 a	31.0a	30.0ab	34.0 a	28.5 a	27.5 a
Control		28.0 a	28.5b	27.0 b	28.5 b	29.0 a	27.5 a
LSD 5 %		1.031	1.474	2.228	3.179	2.136	1.824
Mean corpuscular haemoglobin concentration (MCHC) g/dl							
Lufenuron	$^1/_{20}$ LD_{50}	33.6 a	34.5 a	32.0 a	28.0 c	28.0 c	32.0 a
	$^1/_{10}$ LD_{50}	31.4 a	29.5 b	32.0 a	34.5ab	33.8 ab	33.0 a
Profenofos	$^1/_{20}$ LD_{50}	33.6 a	34.5 a	32.0 a	28.0 c	28.0 c	32.0 a
	$^1/_{10}$ LD_{50}	31.4 a	29.5 b	32.0 a	34.5ab	33.8 ab	33.0 a
Control		33.0 a	32.5ab	33.5 a	32.0 b	33.0 ab	32.0 a
LSD 5 %		1.971	2.363	2.763	2.083	1.713	1.985

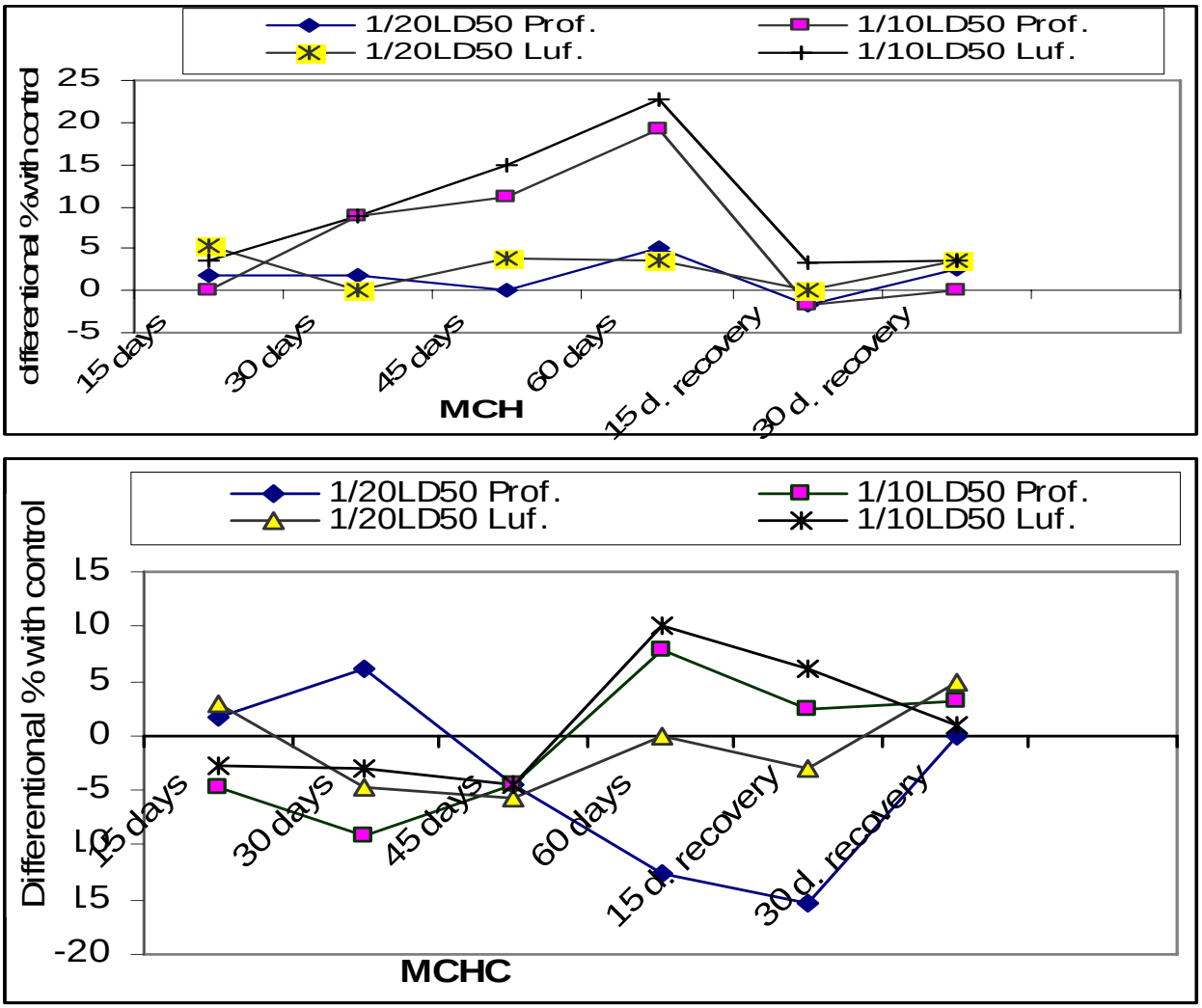


Fig. (3): The differential percentages of MCH and MCHC levels in treated rats as compared with control

Table (4): Effect of IGR, lufenuron and profenofos insecticide on heamatocrit and mean corpuscular volume of male albino rats

Treatments \ Periods		15 days	30 days	45 days	60 days	Recovery for 15 days	Recovery for 30 days
Heamatocrit %							
Lufenuron	$^1/_{20}$ LD_{50}	38.0 a	33.7 c	37.3 b	32.7 bc	32.3 a	37.7 ab
	$^1/_{10}$ LD_{50}	33.3 bc	29.0 d	33.0 bc	28.0 bc	28.0 b	33.0 b
Profenofos	$^1/_{20}$ LD_{50}	36.8 ab	38.7 a	36.3 b	34.7 ab	30.0 a	37.3 ab
	$^1/_{10}$ LD_{50}	31.2 c	27.2 e	32.3 c	26.3. c	26.7 b	34.0 b
Control		36.0 ab	37.0 b	43.0 a	40.0 a	35.7 a	40.0 a
LSD 5 %		3.353	1.043	4.034	5.628	6.082	4.987
Mean Corpuscular Volume (MCV) fl							
Lufenuron	$^1/_{20}$ LD_{50}	88.2 a	82.3bc	82.2 c	90.7 c	95.7 a	92.7 a
	$^1/_{10}$ LD_{50}	88.0 a	92.3 a	103.0 a	112.4 a	94.1 a	92.4 a
Profenofos	$^1/_{20}$ LD_{50}	87.3 a	87.7 ab	91.3 b	95.2 b	85.3 b	87.7 b
	$^1/_{10}$ LD_{50}	88.8 a	77.1 c	69.3 d	61.3 e	62.1 c	84.2 b
Control		87.0 a	83.0bc	89.1 b	85.1 d	83.2 b	87.3 b
LSD 5 %		3.974	6.142	3.658	3.018	5.617	3.586

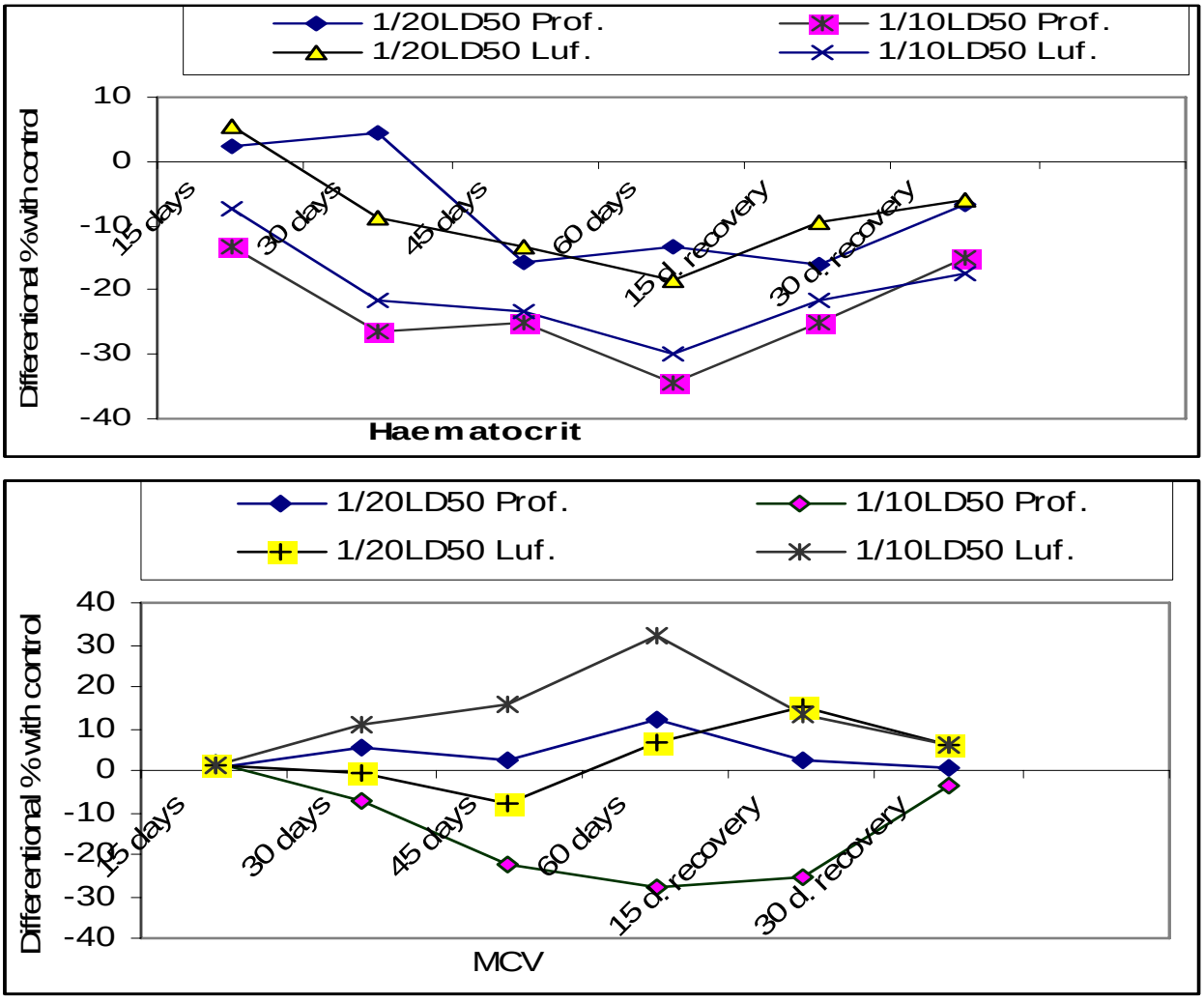


Fig. (4): Te differential percentages of haematocrit and MCV levels in treated rats as compared with control

Table (5): Effect of IGR, lufenuron and profenofos insecticide on transaminase (AST and ALT) enzymes activities of male albino rats

Treatments \ Periods		15 days	30 days	45 days	60 days	Recovery for 15 days	Recovery for 30 days
Aspartate aminotransaminase activity (AST) U / L							
Lufenuron	1/20 LD50	26.1 b	24.3bc	23.2 d	20.3 e	24.7 e	27.2 d
	1/10 LD50	33.0 a	40.3 a	44.2 b	65.0 a	55.1 a	45.8 a
Profenofos	1/20 LD50	25.3 b	23.1 c	29.3 c	33.3 c	35.2 c	33.6 c
	1/10 LD50	32.2 a	40.3 a	52.2 a	58.1 b	44.1 b	42.3 b
Control		27.0 b	26.2 b	27.5cd	29.0 d	28.5 d	29.2 d
LSD 5 %		2.06	2.477	4.689	3.33	2.9	3.128
Alanin aminotransaminase activity (ALT) U/ L							
Lufenuron	1/20 LD50	40.1 b	42.7 b	36.3 c	37.5 c	32.2 e	35.4 d
	1/10 LD50	44.3 a	49.0 a	62.5 a	73.1 a	67.0 a	61.3 a
Profenofos	1/20 LD50	32.8 c	34.7 c	34.3 d	40.2 c	40.2 c	42.7 c
	1/10 LD50	35.5 c	47.3 a	56.8 b	61.9 b	52.2 b	49.3 b
Control		36.0 c	37.8 c	34.3 d	36.5 c	35.2 d	36.3 d
LSD 5 %		3.569	4.508	1.531	3.171	2.485	3.357

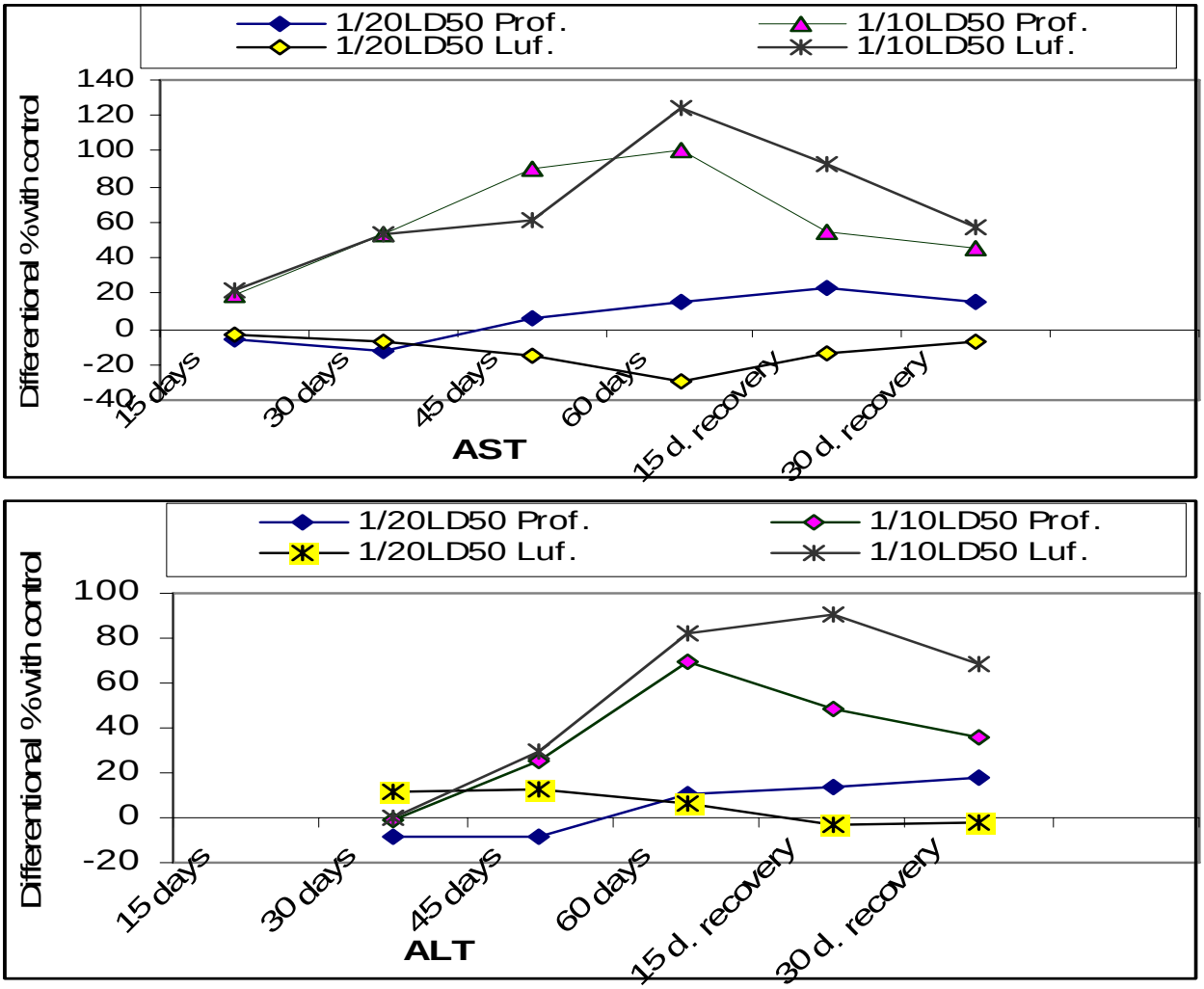
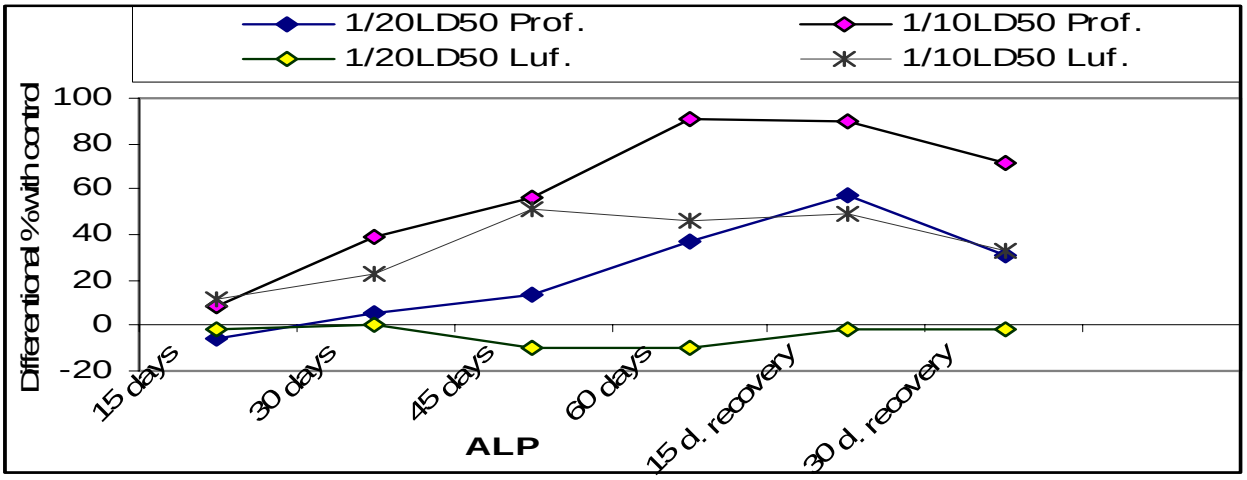


Fig. (5): The differential percentages of AST and ALT activities in treated rats as compared with control

Table (6): Effect of IGR, lufenuron and profenofos insecticide on alkaline phosphatase activity and albumin levels of male albino rats

Treatments \ Periods		15 days	30 days	45 days	60 days	Recovery for 15 days	Recovery for 30 days
Alkaline phosphatase activity (ALP) U/ ml							
Lufenuron	$^1/_{20}$ LD_{50}	7.6 b	7.8 c	7.36 c	6.87 c	6.77 c	7.6 c
	$^1/_{10}$ LD_{50}	8.36 a	9.56 b	12.3 a	11.13b	10.3 b	10.33 b
Profenofos	$^1/_{20}$ LD_{50}	7.1 c	8.2 c	9.26 b	10.43b	10.87 b	10.2 b
	$^1/_{10}$ LD_{50}	8.16 a	10.83a	12.73a	14.56a	13.13 a	13.33 a
Control		7.5 b	7.8 c	8.13 c	7.6 c	6.9 c	7.77 c
LSD 5 %		0.378	0.705	0.906	0.837	1.198	1.085
Albumin concentration (mg / dl)							
Lufenuron	$^1/_{20}$ LD_{50}	3.8 c	3.5 d	4.8 b	4.3 c	5.6 b	4.1 b
	$^1/_{10}$ LD_{50}	4.0 c	5.4 a	7.1 a	6.4 b	7.16 a	5.9 a
Profenofos	$^1/_{20}$ LD_{50}	4.5 b	4.83 b	4.2 c	3.2 d	3.8 d	3.0 c
	$^1/_{10}$ LD_{50}	5.0 a	5.56 a	7.06 a	7.06 a	5.6 b	5.33 a
Control		4.0 c	4.1 c	4.6 bc	3.7 d	4.9 c	3.83 b
LSD 5 %		0.392	0.332	0.444	0.555	0.446	0.584



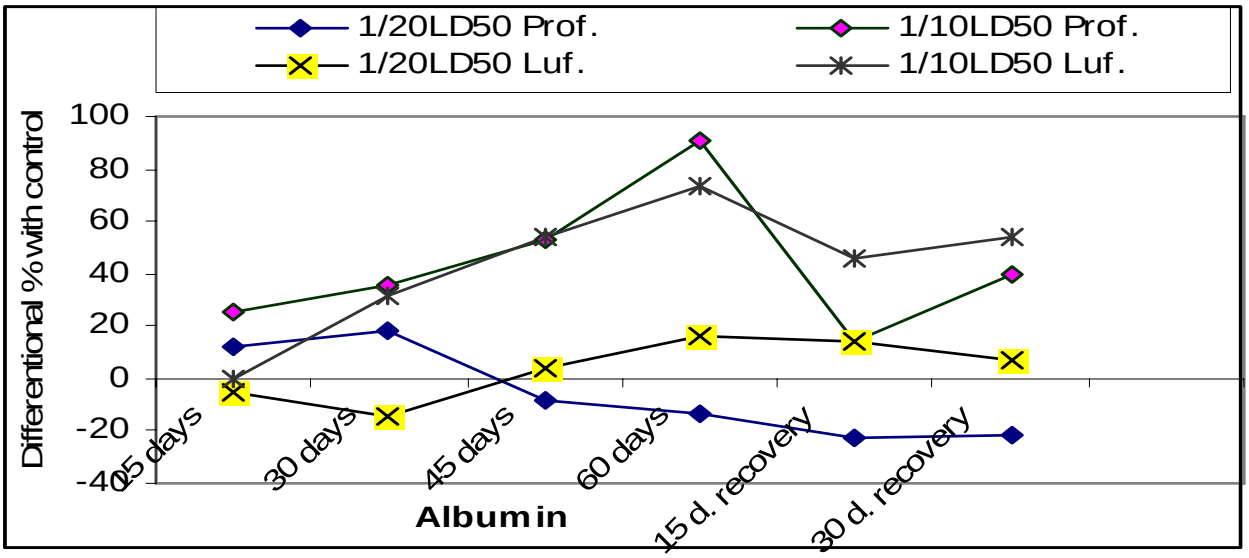


Fig. (6): The differential percentages of alkaline phosphatase activity and albumin level in treated rats as compared with control

Table (7): Effect of IGR, lufenuron and profenofos insecticide on bilirubin levels of male albino rats

Periods / Treatments		15 days (mg/dl)	30 days (mg/dl)	45 days (mg/dl)	60 days (mg/dl)	Recovery for 15 days (mg/dl)	Recovery for 30 days (mg/dl)
Lufenuron	$^1/_{20}$ LD_{50}	0.28 a	0.35 b	0.33 a	0.4 b	0.35 a	0.43 a
	$^1/_{10}$ LD_{50}	0.4 a	0.5 a	0.47 a	0.6 a	0.3 a	0.25 b
Profenofos	$^1/_{20}$ LD_{50}	0.3 a	0.3 b	0.35 a	0.4 b	0.3 a	0.4 a
	$^1/_{10}$ LD_{50}	0.35 a	0.37 b	0.4 a	0.5 ab	0.28 a	0.22 b
Control		0.3 a	0.35 b	0.3 a	0.37 b	0.3 a	0.4 a
LSD 5 %		0.1197	0.1101	0.1537	0.1807	0.118	0.066

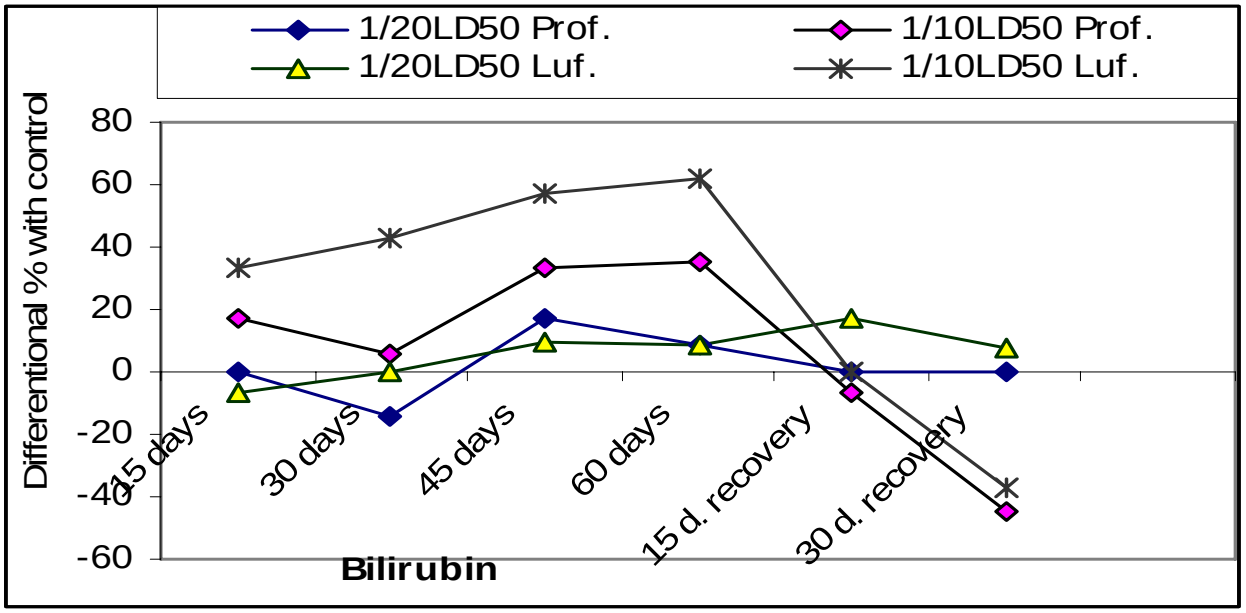


Fig. (7): The differential percentages of bilirubin level of treated rats as compared with control

Table (8): Effect of IGR, lufenuron and profenofos insecticide on creatinine and urea concentration of male albino rats

Treatments \ Periods		15 days	30 days	45 days	60 days	Recovery for 15 days	Recovery for 30 days
Urea concentration (mg /dl)							
Lufenuron	$^1/_{20}$ LD_{50}	33.2 b	36.3 b	38.0b	34.2 d	30.3 c	31.0 c
	$^1/_{10}$ LD_{50}	38.3 a	43.3 a	53.0 a	63.0 a	49.3 a	61.1 a
Profenofos	$^1/_{20}$ LD_{50}	35.3 b	37.3 b	40.3b	46.2 c	39.2 b	31.0 c
	$^1/_{10}$ LD_{50}	39.3 a	45.2 a	50.6 a	58.3 b	49.5 a	41.1 b
Control		33.0 b	32.5 c	32.0 c	31.75 e	31.67 c	31.83 c
LSD 5 %		2.185	2.436	2.561	1.433	2.818	1.617
Creatinine concentration (mg / dl)							
Lufenuron	$^1/_{20}$ LD_{50}	0.86abc	0.83 c	0.82b	0.85 b	0.75 bc	0.75 c
	$^1/_{10}$ LD_{50}	0.88 ab	1.01 b	1.4 a	2.1 a	2.0 a	2.4 a
Profenofos	$^1/_{20}$ LD_{50}	0.79 c	0.8 c	0.86b	0.9 b	0.83 b	0.75 c
	$^1/_{10}$ LD_{50}	0.9 a	1.2 a	1.7 a	2.3 a	1.9 a	1.3 b
Control		0.81 bc	0.78 c	0.78b	0.85 b	0.65 c	0.75 c
LSD 5 %		0.059	0.111	0.376	0.216	0.142	0.198

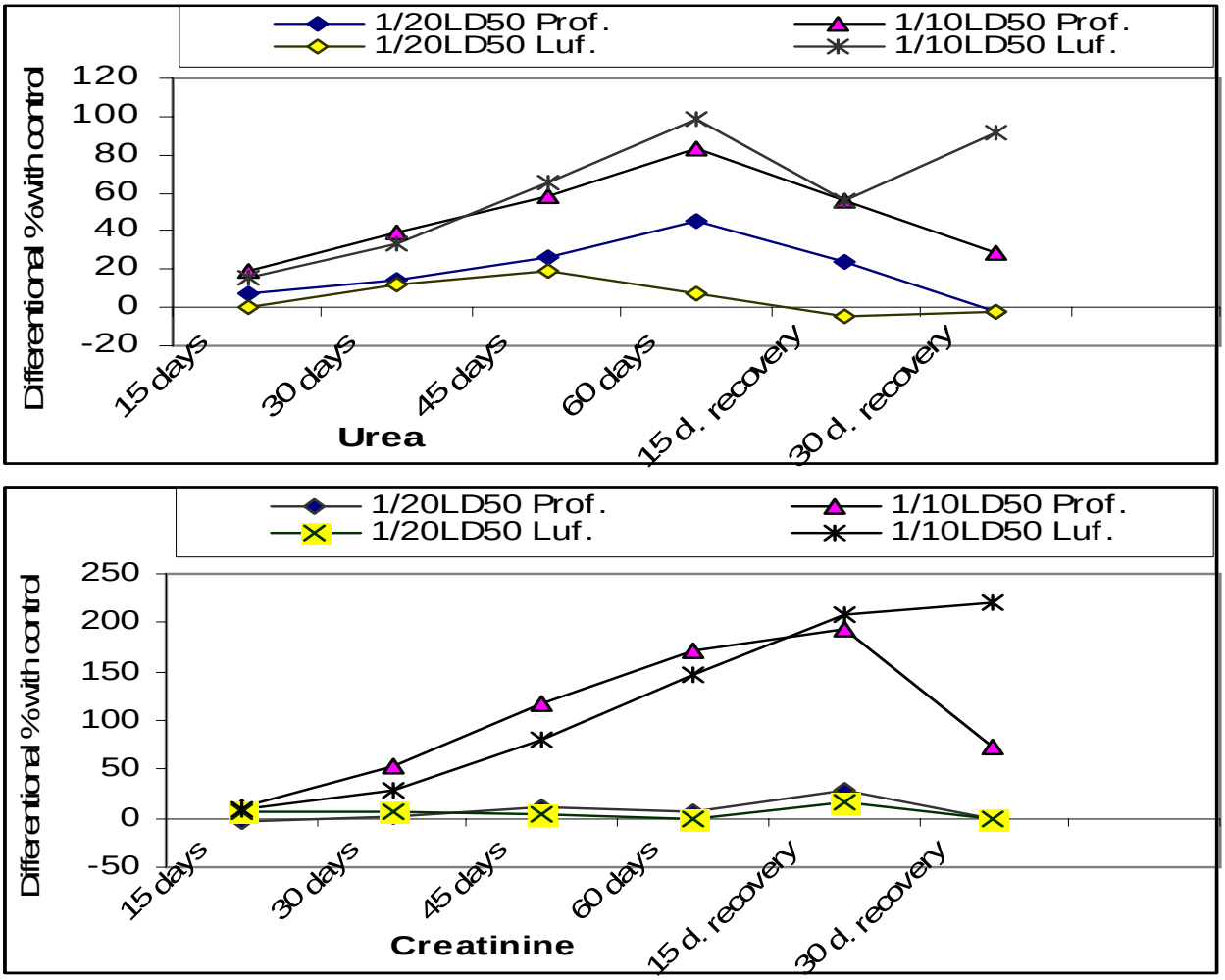


Fig.(8): The differential percentages of urea and creatinine levels in treated rats as compared with control.