Journal

J. Biol. Chem. Environ. Sci., 2009, Vol. 4(4): 187-205 www.acepsag.org

THE TOXICITY INFLUENCES OF ABAMECTIN AND ITS FORMULATIONS ON BODY WEIGHT GAIN AND BLOOD CONSTITUENTS OF MALE ALBINO RATS.

Ibrahim, N. M.[1], Eweies, E. A.[1], Kobisy, M. I.[2] and Abdel-Mobdy, Y. E. [1]

[1-]Department of Entomology and Pesticide, Faculty of Agriculture, Cairo University.

[2-]Department of Biochemistry, Faculty of Agriculture, Cairo University.

ABSTRACT

The present investigation to be reported was focused on the toxicity of abamectin and its formulation (Vertimec 1.8% and vapcomic 1.8%) administered at 1/20 and 1/40 LD50 sublethal doses for 12 consecutive weeks on body growth rate and blood constituents of male albino rats. The treatments the pesticides were applied orally after every two consecutive days. The effects of the both forms of abamectin (technical and formulation) on body weight gain, RBCs and WBCs counts, blood hemoglobin, plasma soluble protein profile (total protein, albumin and globulin), thyroid hormones (T4 and T3) liver function (AST and ALT activity as well as bilirubin content) and plasma acetylcholinesterase, acid and alkaline phosphatases and lactate dehydrogenases activities were evaluated and determinated, also blood glucose levels were estimated under the present experimental treatments.

Body weight gains of the experimental animals ingested technical or formulation of abamectin either with low dose (1/40 LD50) or high dose (1/20 LD50) were significantly lower than that of normal health control rats. In connection, the values of feed efficiency were decreased significantly, the percentages of the gain in body weight were around those of percentages of feed efficiency. Moreover, the both forms of the studied pesticide treatments significantly decreased blood contents of hemoglobin and RBCs count, but the contents of T4 and T3 of plasma as well as WBCs count of blood were insignificantly changed. The abamectin treatments showed considerable and highly significant stimulation in plasma

transaminases activity (AST and ALT) and bilirubin content. In addition, total soluble protein and albumin levels of plasma were significantly decreased but the value of globulin was unchanged under the same conditions. In case of sugar and some enzymes activity of plasma. The abamectin and its formulation treatments elevated the blood contents of glucose. The activity of cholinesterase was inhibited by the pesticide treatments, but the activity of acid and alkaline phosphatase as well as lactate dehydrogenases was stimulated under the same treatments condition. These increases or stimulations and decreases or inhibitions were higher in case of abamectin formulation than the technical form, also the high dose (1/20 LD50) ingestions were more effective than that of the low dose (1/40 LD50) treatments relative to the normal health control.

It means that abamectin and its formulation 1.8% (vertimec and vapcomic) produced disturbance in animal metabolism. The effect of abamectin formulation on male albino rats is pronounced than that of pure abamectin treatment. The present studies advice to prevent exposure of any people to these compounds to avoid their injurious hazard risk.

INTRODUCTION

Abamectin (avermectin B1) is a natural fermentation product derived from the soil bacterium *Streptomycens avermitilis*. Ivermectin is a synthetic derivative of abamectin. Anthelmintic and acaricidal activity of a group of chemically related compounds, the avermectins as reported by Lankas and Gordon (1989) are complex macrocyclic disaccharides made up of a member lactone rings. Abamectin, an analog of ivermectin, is a mixture of avermetins containing at least 80% of avermectin, B1a and less than 20% of avermectinB1b. Individual compounds have very similar biological and toxicological properties and for all practical purposes, can be considered equivalent. Aamectin was widely employed to control insects and mites of a wide range of agricultural products such as fruit, vegetable and or namental crops (Lankas and Gordon, 1989). Abamectin acts by stimulating the release of γ-aminobutyric acid an inhibitory neurotransmitter, thus causing paralysis as well as insecticide and acaricide with contact and stomach action (Pesticide Manual, 2000 and Liu et al, 2003).

Environmental exposure to these agents may cause serious health risks. To establish any toxicological data, acute toxicity tests

are considered to be the base line or preliming studies for chronic toxicity tests. In this respect abamectin is commonly used in Egypt, however, no or very littlie data are available in the literature about its influences of technical and formulation of abamectin. Generally, pesticides are usually applied in the formulation form where the active ingredient is mixed with organic solvent, emulsifying and wetting agents to enhance their water miscibility and penetration. Pesticide formulation is therefore, the process of transforming a pesticide chemical into a product which can be applied by practical methods to permit its effective, safe and economical use. However, it has been reported that formulation may cause synergism or antagonism to the toxicity of active ingredient (El-Sebae, 1985 and Abdel-Rahim *et al*, 1994 and Abdel-Rahim 2008). *In vivo* and *in vitro* metabolism studies of avermectins using vertebrate and invertebrate organisms have elucidated the pharmacokinetics of avermectins and its metabolites (Yoon *et al*, 2002). Abamectin is highly toxic to insects and may be highly toxic to mammals (Lankas and Gordon, 1989). Symptoms poisoning in laboratory animals include pupil dilation, vomiting, convulsions and or tremors and coma (US EPA, 1990). The male mice develop dermatitis and changes in blood formation in the spleen, while females exhibited tremors and weight loss (US EPA, 1990).Elbetieha and Da'as (2003) reported that, the body weight gain was significantly lower in males rats that ingested abamectin. In connection, as a safe chemical in mammals, abamectin has been used as an anthelmintic agent in both animals and humans (Kaplan *et al*, 1994). However, some people committed suicide by ingesting abamectin and caused death in Taiwan (Chung *et al*, 1994). So far, the cause of the patient's death is still unknown. Abamectin intoxication may affect the function of hepatocytes although the permanent liver damage is usually not revealed immediately.

Pervious studies have shown that abamectin causes serum AST stimulation (Hsu *et al*, 2001). Cytochrome P450 is the major enzyme responsible for avermectin metabolism in human liver microsomes (Zeng *et al*, 1998). Stimulation of AST, a cytosolic enzyme of the hepatocytes, reflects the increase of plasma membrane permeability resulting from the damage of hepatocytes (Plaa and Hewitt 1982 and H su *et al*, 2001) and is used to detect liver damage (Klaassen and Eaton, 1991).

The aim of the present study is to compare the effect of technical and formulations of abamectin (vertimec 1.8% and vapcomic 1.8%EC) food intake , feed efficiency, blood picture (blood hemoglobin, RBCs and WBCs), plasma soluble proteins profile (total protein, albumin and globulin), thyroid hormones (T4 and T3), activities of some plasma enzymes (cholinesterase, acid and alkaline phosphatases) and liver function (plasma bilirubin content and activities of AST and ALT), to evaluate the synergetic effect of adjuvant of abamectin formulation on intoxication harmful.

MATERIALS AND METHODS

Abamectin [5-o-demethylavermectin A1a (i) mixture with 5-o-demethyl-25 de (1-methylpropyl-25-(1-methylethyl) avermectin A1b (ii)] technical (98% purity) and two abamectin formulations (vertimec 1.8% EC Syngenta-Agro Switzerland and vapcomic1.8% EC Tide International. China). The both abamectin formulation obtained from the Central Agriculture Pesticide Laboratory, ARC, but the pure one from Syngenta Agro Egypt.

Health adult male albino rats (42 animals), *Rattus norvegicus*, Sprague Dawley strain weighing 100-150 g. were obtained from the animal house of Nutrition Institute, Cairo and housed in the laboratory animal center of Central Agricultural Pesticides (ARE), Ministry of Agricultural, Dokki, Giza, Egypt. The animals were kept under normal health laboratory conditions for two weeks in their cages prior to the experiment of acclimatization. Rats were housed individually in a room with a well aerated under hygienic conditions. They were allowed free access to tap water and fed on a diet consisting of a mixture of casein 20%, cotton seed oil 10%, and cellulose 5% salts mixture 4% (Schneeman *et al*, 1989), vitamins mixture 1% (Philip *et al*, 1993) and starch 60% (Lane-Pert and Pearson, 1971). Rats were divided into 7 groups (6 rats each). The first group served as normal health control. The second group was ingested orally with sublethal dose of pure abamectin which was 1/20 of oral LD50 of technical abamectin. The third group was ingested orally with the sublethal dose of abamectin formulation (vertimic 1.8% EC of technical abamectin). The fourth group was ingested with the sublethal dose of abamectin formulation (vapcomic 1.8% EC 1/20 of the oral LD50 of technical abamectin). The fifth group was ingested orally with the sublethal

dose of pure abamectin (1/40 of oral LD50 of technical abamectin). Sixth group ingested was orally with sublethal dose of abamectin formulation (vertimec 1.8% EC which was 1/40 of oral LD50 of technical abamectin). Seventh group was ingested with the sublethal dose of abamectin formulation (vapcomic 1.8 %EC 1/40 of the oral LD50 of technical abamectin).

Abamectin formulations or technical doses were mixed with 0.5 ml corn oil. One dose was induced every two days during the experimental period (14 weeks) either for technical or formulations of abamectin. Food and water were supplied *ad Libitum* for the all groups during the experimental period.

Each rat was weighted every weeks and its daily food intake was determined. Feed efficiency was calculated as the following equation (body weigh gain / food intake). At the end of the experimental period (12 weeks), animals were killed by decapitation. Blood was collected, some of which was centrifuged at 3000 rpm to obtain the plasma which was kept frozen at - 20˚C until used for analysis. The other blood was used to determined the blood picture in which total hemoglobin was dertermined as described by Decra and Lewis (1975). Red blood cells (RBC`s) and white blood cells (WBCs) were counted after decapitation immediately as pointed out by Frankel and Reitman (1963). Plasma total bilirubin was determined as demonstrated by Jendrassik and Graf (1953). Determination of total soluble protein and albumin in plasma were carried out by the method of Bradford (1976) and Doumas *et al* method (1971) respectively, plasma globulin was calculated by the difference between total protein and albumin. Plasma AST and ALT activity was determined as shown by Ritman and Frankel (1957). Plasma total thyroxin (T4) was Determined by radioimmunoassay procedure described by Premachandra and Ibrahim (1976), and plasma triiodothyronine was measured by double antibody technique described by Chapra *et al* (1972). Cholinesterase, acid phosphatase, alkaline phosphatase and lactate dehydrogenases activities were determined according to the methods of EL- Lman *et al* (1960), Babson and Rea Kind and Kind (1959) and Dito (1979). Plasma glucoses values were determined according to the method of Trinder (1969).

All data pooled through this study were proceeded by General Linear Model procedures (GLM) of the statistical analysis system described in SAS User's Guide (SAS Institute, 2000). The significance

of the differences among treatment groups were tested using Waller-Duncan k-ratio (Waller and Duncan, 1969). All statements of significance were based on probability of $p<0.05$.

RESULTS AND DISCUSSION

The influences of abamectin on body weight gain, food intake and feed efficiency affected by technical and abamectin formulations are shown in table (1). Body weight of the studied animals was increased with the increase of age in the all rat groups fed on diets with or without the pesticide ingestion. Abamectin and its formulations administration caused decreases in the average gain of body weight and the severe influences were found in the animals treated orally with abamectin formulations. In this respect, the values of body weight gain lower relative to control were arranged in following order: Technical 1/40 LD50 <formulation (Syngenta) 1/40 LD50 < formulation (China) 1/40 LD50< technical 1/20 LD50 <formulation (Syngenta) 1/20 LD50 < formulation (China) 1/20 LD50.

The values of food intake of rats treated with the pesticide forms (table1) were about unchanged singnificantly. The food intake values were not paralleled to rats growth as well as feed efficiency. Results reported that oral ingestion of technical form of abamectin revealed lower feed efficiency than abamectin formulation, but formulation of China (vapcomic) was more effective than Syngenta formulation (vertemic). The low feed efficiency ratio may be due to the toxic effects of the pesticides and their adjuvant which in turn alter the rate of whole body metabolism. The present data are in agreement with those of Scheuhammer and Wilson (1990) and Abdel-Rahim(2007), they reported that gain in body weight and feed efficiency were reduced by pesticides induction, and formulation pesticide had more effect than those of technical ones. In connection, feed efficiency was changed paralleled with changed values of gain in body weight. The more efficiency China formulation abamectin (vapcomic) than Syngenta one (vertemic) may be due to that the adjuvant of China formulation were more toxic than those of Syngenta one. Also, the toxicity effects on body weight gain were paralleled with the dose value of the pesticide. These are in agreement with results of Kobeasy *et al* (2009) who found that the toxic influences of carbofuran were

elevated with dose increased and carbofuran formulations were more effective than technical ones administration.

Table (1): The abamectin toxicity on the body weight gain and feed efficiency of the male of albino rat.

Treatment		Initial body weight (g)	Final body weight (g)	body weight gain (g)	The gain % at normal rats	Feed intake	Feed efficiency (F.E)		Feed efficiency % at normal rats
							value	100 (F.C)	
The normal health control		156.0 ± 5.0	324.0 ±11.0	168.0 ±11.0 a	100.00	979.0 ±51.0 a	0.17 ±0.02 a	17a	100
Oral technical 1/20 LD50		136.0 ±4.0	236.0 ± 9.0	100.0 ±9.0 b	59.52	1041.0 ±67.0 a	0.10 ±0.01 b	10 b	59
Abamectin formulation 1/20 LD50	vertimic	135.0 ± 5.0	235.0 ±10.0	100.0 ±10.0 b	59.52	1198.0 ±101.0 b	0.08 ±0.01 b	8 b	47
	vapcomic	136.0 ± 7.0	231.0 ±12.0	95.0 ±8.0 b	56.55	1188.0 ±77.0 b	0.08 ±0.01 b	8 b	47
Oral technical 1/40 LD50		112..0 ± 4.0	235.0 ±11.0	123.0 ±11.0 c	73.21	982.0 ±79.0 a	0.13 ±0.01 c	13 c	76
Abamectin formulation 1/40 LD50	vertimic	142.0 ± 7.0	271.0 ±10.0	129.0 ±10.0 c	76.79	1137.0 ±112.0 b	0.11 ±0.01 b-c	11b-c	65
	vapcomic	138.0 ± 5.0	260.0 ±13.0	122.0 ±11.0 c	72.62	1220.0 ±59.0 b	0.10 ±0.01b-c	10b-c	59

- (%) relative to control. Each value represented the mean of 6 rats (mean ± SD).
- Means in the same column followed by the same latter are not significantly different at $p < 0.05$.

Blood picture and thyroid gland function were presented in table (2) which showed that total hemoglobin (Hb) content was decreased by ingestion of abamectin. The decreases value of vapcomic the pesticide formulation of China (1/20 LD50) was more than those of the other treatments but the lowest one was observed by technical one (1/40 LD50). Similar trend was observed for RBCs count, but the count of WBCs was significantly unchanged relative to control. The reduction of Hb values and RBCs count may be attributed to the toxicity of the studied pesticide, also associated with chronic abamectin and its formulations exposure and malignant tumors of animal organs (Hoffman *et al*, 1991). The higher effect of oral abamectin formulations may be due to the synergistic influences of their adjuvant to active ingredient. These results are confirmed by the finding of Abdel-Rrahim *et al* (2008) who found that dimethoate

ingestion reduced total Hb and RBCs count and pesticide formulations were more effective than that of technical one. In case thyroid gland function, the alteration of plasma thyroid hormones (T4 and T3) may have resulted from changes in the pituitary-thyroid axis as a consequent of the stressing effect of both forms of abamectin. The hypothalamic nudei secrets thyrotrophin relating hormone (TRH) (Motto *et al*, 1975), which stimulates the anterior lobe to secrete thyrotropic hormone (TSH) which in turn stimulate thyroid function (Dickosn, 1977). The increase in T4 and T3 stimulate glycolytic process for energy production to maintain the animal living process (Murrey *et al*, 2006). The present results are in harmony with the finding of Abdel-Rahim 2007 and 2008 who found that pesticides significantly unchanged plasma T4 and T4 hormones. These were paralleled with that thyroid system plays an active effects in the general metabolic changes (Chatterijea and Shinde, 2002).

Table (2): The abamectin toxicity on the blood picture and thyroid hormones of male albino rats.

Treatment		Total hemoglobin		RBC`s count		WBC`s count		T4		T3	
		g/dl	%	Count x 10^3 x 10^3	%	Count x 10^3	%	Mg/dl	%	Mg/dl	%
The normal health control		14.96 ±0.81a	100	6.09 ±0.040 a	100	6.02 ±0.41a	100	4.11 ±0.30 a	100	90.00 ±7.12 a	100
Oral technical 1/20 LD50		12.04 ±0.63 b	71	4.34 ±0.32 b	71	6.11 ±31a	101	3.94 ±0.22 a	96	87.00 ±6.45 a	97
Abamectin formulation 1/20 LD50	vertimic	11.96 ±0.60 b	68	4.13 ±0.23 b	68	5.88 ±0.20 a	98	3.85 ±0.24 a	94	83.00 ±5.55 a	92
	vapcomic	11.00 ±0.57 b	63	3.81 ±0.19 b	63	5.55 ±0.31a	92	3.58 ±0.19 a	87	80.00 ±4.81 a	89
Oral technical 1/40 LD50		14.73 ±0.81a	99	6.05 ±0.34 a	99	6.10 ±0.42 a	101	4.00 ±0.19 a	97	90.00 ±6.98 a	100
Abamectin formulation 1/40 LD50	vertimic	14.21 ±0.72 a	96	5.87 ±0.32 a	96	5.94 ±0.33 a	99	3.80 ±0.27 a	92	84.00 ±5.47 a	93
	vapcomic	13.51 ±0.81a	82	5.01 ±0.29 c	82	5.87 ±0.29 a	99	3.90 ±0.19 a	95	83.45 ±6.01 a	93

-(%) relative to control. Each value represented the mean of 6 rats (mean ± SD).
- Means in the same column followed by the same latter are not significantly different at $p < 0.05$.

The changes of total soluble protein and albumin levels were found in plasma either by pure abamectin or abamectin formulations ingestion. Data shown decreases in total soluble protein and albumin,

but globulin contents were significantly unchanged. This means that the alterations in values of total protein were principally correlated with the changes in albumin levels in plasma. Formulation form of vapcomic caused superior decreased in protein content relative to treatment with technical form. In connection, the oral treatment by abamectin formulation of Syngenta (vertimic) was less effective than that of China one, but the both formulations produced toxicity more than that of pure abamectin. These may be due to the different kinds of their adjuvant. The decrease in total soluble protein and albumin values in plasma of the treated animals may be due to the inhibition of protein biosynthesis through specific enzymes in cell processes and low significant excretion of hormones in the present studies of thyroid hormones which regulate protein biosynthesis (Wilson *et al*, 1982 and Soliman *et al*, 1983). Liver function was changed under the different former of abamectin induction. These observed by the highly significant increase of plasma bilirubin content and stimulations in the activities of AST and ALT. Bilirubin is considered one of the most important liver function tests. Hemoglobin is the principle source of bilirubin which produced by the breakdown of hemoglobin. The present results of hemoglobin levels and RBCs count confirmed these results of bilirubin (table3). Also, the activities of transaminases (AST and ALT) of plasma were stimulated under the effects of either technical or formulation abamectin. In addition the abamectin formulations had profound effects on AST and ALT activities compared to technical form, but formulation of Syngenta was less toxic relative to China one. Similar trend was observed by Hsu *et al*, (2001) and Abdel-Rahim (2008). They found that the bilirubin level and transaminases activity were elevated by pesticides ingestion. These stimulations in ALT activity indicated slight liver cell necrosis and magnitude of increase correlated with the extent necrosis (Murray *et al*, 2006). Also, the increases in plasma bilirubin and stimulation in AST and ALT activities are unlikely to be due to damage in liver andRBCs (Chatterjea and Shinde, 2002). As certain hepatic damage is considered pathologically irreversible (Helling *et al*, 1995), the stimulation of AST may render liver to be more susceptible to other pathogen/toxicants (Hsu *et al*, 2001). Although AST markedly stimulated and remained above normal level after abamectin ingestion in 24h, abamectin alone was barely the only cause for human death in the clinical finding (Chung *et al*, 1999). In earlier study more than

50% of rats died after commercial grade (2% EC) but not technique grade (98% purity of abamectin with 20 mg/kg oral) induction within 24h. It was proposed that the additives in the commercial product might be associated with the death of abamectin intoxicated cases (Hsu *et al*, 2001).

Table (3): The abamectin toxicity on plasma total soluble protein profile and liver function of male albino rat.

Treatment		Total soluble protein		Albiumin		Globulin		Total bilurobin		AST activity		ALT activity	
		g/dl	%	g/dl	%	g/dl	%	mg/dl	%	U/L	%	U/L	%
The normal health control		6.95 ±0.41 a	100	4.52 ±0.27 a	100	2.43 a	100	0.35 ±0.02 a	100	57.00 ±3.17 a	100	30.0 ±2.17 a	100
Oral technical 1/20 LD50		4.91 ±0.29 b	71	2.56 ±0.17 b	57	2.35 a	97	3.86 ±0.12 b	1103	98.00 ±5.96 b	172	60.0 ±4.27 b	200
Abamectin formulation 1/20 LD50	Vertmic	4061 ±0.24 b	66	2.46 ±0.11 b	54	2.15 a	88	3.97 +0.13 b	1134	100 ±6.66 b	175	65.0 ±4.44 b	217
	vapcomic	4.00 +0.31 b	58	2.11 ±0.13 b	47	1.89 a	78	4.02 ±0.31 b	1149	107 ±7.21 b	188	70 ±5.71 b	233
Oral technical 1/40 LD50		5.89 ±0.30 a-b	85	3.10 ±0.18 b	69	2.79 a	115	1.30 ±0.09 c	371	77.00 ±3.98 c	135	50.0 ±3.09 c	167
Abamectin formulation 1/40 LD50	Vertmic	5.48 ±0.29 b	79	2.90 ±0.19 b	64	2.58 a	106	1.34 +0.10 c	383	8.3 ±4.45 c	146	55.0 ±3.11 c	183
	vapcomic	5.00 ±0.32 b	72	2.52 ±10 b	56	2.48 a	102	1.99 ±0.11 c	569	90.0 ±6.71 c	158	60.0 ±4.10 c	200

-(%) relative to control. Each value represented the mean of 6 rats (mean ± SD).
- Means in the same column followed by the same latter are not significantly different at $p < 0.05$.

Technical and formulations of abamectin treatments inhibited the activity of cholinesterase of rat plasma relative to control, but effects of abamectin formulation form was more than that of technical one (table4). The inhibition in plasma cholinesterase activity is usually used as an indicator exposure to pesticides (Goel *et al*, 2000 and 2007). Chandrasekara and Pathiralne (2007) showed that pesticides reacted with cholinesterase in a manner analogous to that of the normal substrate. The resultant excess of acetylcholine at neuromuscular function can act as a blocking agent, depolarizing the motor and plate. The more effect of formulation than technical pesticide may be due to that adjuvant may cause synergism to the toxicity of pure abamectin. The data demonstrated that acid and

alkaline phosphatases activities of rat plasma under the effect of abamectin forms treatment were stimulated (table4). Furthermore, acid phosphatases were more affected than alkaline one. These data were confirmed by those of thyroid gland of the present study and Abdel-Rahim (2008). The stimulation of phosphatases activity may be render to the abundant inorganic phosphate which is needed for energy compounds synthesis (Elliott and Elliott, 2001). In this respect Enan and Berberian (1986) found that the stimulated acid and alkaline phosphatases activity mat be associated with all disintegration resulting form pesticides treatment. Alkaline and acid phosphatases are much more abundant in organs tissue especially liver and spleen. The stimulation of the enzymes activity may rise due to many cases. However, the diagnostic specificity attributed to alkaline phosphatases and slightly to acid one often fails to work out in practice because of the many condition in which liver may be involved secondarily. Moreover, the rise in alkaline phosphatases may not become evident until acid phosphatases has begun to fall (Challerjea and Shinde, 2002). It is known that abamectin interact with γ-amino butyric acid receptor (brain) in both vertebrates and invertebrates (Coccini *et al*, 1993). It interacts with glutamate-gated chloride channels in invertebrates via rather complicated ways and results in an increase in chloride ion influx with subsequent paralysis in the target organism (Cully *et al*, 1994 and Hsu, 2001). Evidences suggest that the formation of oxygen free radical can be a major factor in the toxicity of pesticide (Banerjee *et al*, 2001 and Abdollahi et al, 2004).

Table (4) observed also that either technical or formulation of abamectin by oral treatments in short-term experimental period (12 weeks) increased significantly blood glucose content to a range of 144 to 171%. Moreover the abamectin formulations were more potent than technical one, also the influences of the oral high dose (1/20 LD50) were higher than that of the low dose (1/40 LD50). The present results revealed that the adjuvant materials played a remarkable role in the readjustment of the blood glucose values produced by abamectin treatments. The increases in blood glucose levels may be due to the increases in the rate of glucose transport from the tissue to the blood, increased glycogenolysis and gluconeogenesis (Afia and Abdel-Rahim *et al*, 2009) or decreased rate of removal of glucose form the blood by tissue. Present results showed a disorder in thyroid function

as shown by blood T4 and T3 levels in intoxicated rats by the pesticide (Table2) relative to control. It is well established that abamectin induces hepatoxicity by activation therefore; it selectively causes toxicity in liver cells marinating semi-normal metabolic function (Hsu *et al*, 2001). Pesticide is bio-transformed by the cytochrome P-450 system in the endoplasmic reticulum to produce (R`) free radical which combined with cellular lipids and proteins in the presence of oxygen to form peroxyl radical (ROO`). This peroxy radical might attack lipids on the membrane of endoplasmic reticulum faster than the normal radical (R`). Thus ROO` leads to elicit lipid peroxidation and the destruction Ca2+ homeostais and finally in cell death (Narayana *et al*, 2005 and Atia and Abdel-Rahim, 2009). These in changes of structure of endoplasmic and other membrane loss the enzymes, metabolic enzymes activation and reduction of protein biosynthesis were leading to liver damage. These mains that the pesticide exposure caused oxidative stress in rat tissue (Verma *et al*, 2007 and Abd el-Rahim 2008). Consequently, the WHO (1991) emphasized that the final toxic classification of any pesticide is intended to be by its adjuvant.

Table (4): The abamectin toxicity on blood glucose and activities of cholinesterase, acid and alkaline phosphatases and lactate dehydrogenases in plasma of male albino rat.

Treatment		cholinesterase		alkaline phosphatases		Acid phosphatases		lactate dehydrogenases		glucose	
		Mg/dl	%	IU/L	%	IU/L	%	U/L	%	mg/dl	%
The normal health control		105 ±8.11 a	100	118.0 ±7.77 a	100	17.66 ±0.92 a	100	202.0 ±12.0 a	100	90.0 ±7.02 a	100
Oral technical 1/20 LD50		82.0 ±5.21 b	78	216.0 ±12.61 b	183	47.61 ±3.01 b	270	357.0 ±19.0 b	177	148.0 ±10.0 b	164
Abamectin formulation 1/20 LD50	vertimic	78.0 ±4.0 b	74	240.0 ±10.16 b	203	51.21 ±2.72 b	290	363.0 ±20.0 b	180	154.0 ±10.27 b	171
	vapcomic	72.0 ±3.11 b	69	251.0 ±12.18 b	213	55.11 ±3.12 b	312	381.0 ±29.0 b	189	160.0 ±11.11 b	175
Oral technical 1/40 LD50		89.0 ±4.97 b	85	177.0 +8.82 c	150	30.21 ±1.32 c	171	285.0 ±17.0 c	141	130.0 ±8.01 c	144
Abamectin formulation 1/40 LD50	vertimic	81.0 ±4.21 b	77	194.0 ±10.0 c	164	34.45 ±2.0 c	195	293.0 ±18.0 c	145	134.0 ±7.26 c	149
	vapcomic	77.0 ±4.0 b	73	200.0 ±13.11c	169	50.02 ±2.71 b	283	367.0 ±27.0 b	182	151.0 ±12.0 b	168

-(%) relative to control. Each value represented the mean of 6 rats (mean ± SD).
- Means in the same column followed by the same latter are not significantly different at $p < 0.05$.

Conclusion

Borne disease from the obtained results was can conclude that abamectin technical is less toxic than abamectine formulation which was vapcomic 1.8%EC (Tide international-China) and vertimic 1.8%EC (Syngenta-Agro Switzerland). The effect of vapcomic 1.8% EC on male adult albino rats (biochemical effects) is pronounced than that of vertimic 1.8% EC. The present studies advice to prevent exposure of any people to these compounds to avoid their injurious hazard risk.

REFERENCES

Abdellahi, M; Ranjbar, A; Shadnia, S; Nikfar, S and Rezaice, A (2004): Pesticides and oxidative stress: a review, Med. Sci. Monit. 6:141-147.

Abdel-Rahim, E. A; Diab, Rashed M.M and Ebtsam, A.M (1994). Biochemical studies on the effect of pure and formulated malathion on hemoglobin fractions. Cytochrome-C system and growth rate of albino rats by dermal and oral administration. Crop. Health Conference 21-24 March, Fayoum, Egypt.

Abdel-Rahim, G.A (2007): Biochemical studies on the effects of carrot diet as antitoxiadant agent prevent from chlorpyrifos toxicity in albino rats. Egypt. J. Appl. Sci. 22(11B) 414-426.

Abdel-Rahim, G.A (2008): Reduction of the hazard influences of dimethoate by guava antioxidant on body growth rate and blood constituents of albino rats. J. Biol. Chem. Environ. Sci., 3(4): 343-362.

Atia, A.I and Abdel-Rahim, G.A (2009): Detoxification treatments of free gossypol in cotton seed meal by microbial treatment of mixed cultures and biochemical evaluation on rabbits. J. Red. Res. App. Sci. 2(2) 397-415.

Babson, A.L and Read. A.P (1959): determination of total acid phosphatase in serum.Am. J. Clin. Path. 32;89-91.

Banerjee, B.D; Seth, V. and Ahmed, R.S (2001): Pesticides induced oxidative stress: Perspectives and trends. Rev. Environ-Health. 16:1-40.

Bradford, M. M (1976): A rapid sensitive method for the quantiation of microgram quantities of protein utilizing the principle of protein dye binding. Analytical Biochemistry, 72, 248.

Chandrasekara, L.W.H and Pathiralne, A (2007): Body size-related difference in the inhibition of brain acetylcholinesterase activity in juvenile Nile tilapia by chlorpyrifos and carbasulfan. Ecotoxicology and Environmental Safety. 67:109-119.

Chapra, I.J; Ho, R.C. and Lam, R (1972): An improved radioimmunoassay of thriiodothyronine in serum and its application to clinical and physiological studies. J. Lab. Clin. Med. 80:729.

Chatterjea, M.N and Shinde, R.(2002): Textbook of medical Biochemistry (5th ed) Jay Pee Brother, medical publishers (P) LTP. New Delhi.

Chung, K; Yang, C.C., Wu; Ml; Deng, J.F and Tsai, W.J (1999). Agricultural avermectins and uncommon but potentially fatal cause of pesticide poisoning. Ann. Emerg. Med. 34:51-57.

Coccini, T.; Candurs, S.M; Manzo, L; Costa, L.G. and Toini, M.(1993): Interaction of the neurotoxic pesticide ivermectin and lindane with the enteric GABAa receptor-ionophore complex in the guinea pig. Eur. J. Pharmacol. 248:1-6.

Cully, D.F; Vassilatis, D.K; Liu, K.K; Paress, P.S; Vander Ploeg. L.H; Schaeffer, J.M. and Arena, J.P (1994): Cloning of an avermectin-sensitive glutamate-gated chloride channel from caenorhabditis elegans. Nature. 371:707-711.

Decra, J.V. and Lewis, S.M (1975): Measurement of hemoglobin (Cyanmethemoglobin method) In: "Practical Hematology" (5th ed). Cgutchill Livingstone Edinburgh, London and New York, PP.32.

Dickson, W.M (1977): Endocrine gland. In: M.J. Swanson (ed). Dukes, physiology of Dorrnestic Animal, P. 740-746. Central Univ., Press Ithaca, New York.

Dito, W.R (1979): Lactate dehydrogenases: A brief review. In: Griffiths, J.C. ed. Clinical enzymology. New York, Masson Publishing. USA.

Doumas, B. T; Waston, W.A and Biggs, A.G (1971): Biuret method for quantitative estimation of total protein in serum or plasma. Clin. Chem. Acta. 31:87.

Elbetieha, A and Da`as, S.I (2003): Assessment of antifiertility activities of abamectin pesticide in male rats. Ecotoxicology and Environmental Safety, 55: 307- 313.

Elliott, W.H and Elliott, D.G (2001): Biochemistry and Molecular Biology (2nd ed) Oxford Univ. Press. Published in USA.

El-Lman, G.L; Andros, K.D and Featherslone, R.M (1960): A new and rapid colorimetric determination of acetyl cholinesterase activity. Arch. Biochem. Biophys. 82:88-92.

El-Sebae, A. H (1985): Management of pesticide residues in Egyptian environment. Appropriate waste management for developing countries, Kriton curi, (Ed.) Plenum Publishing Crop, P. 563-581.

Enan, E.E. and Berberian, A (1986): Interaction of pesticide exposure level with some biochemical enzymes among field workers. J. Egypt. Soc. Toxicol. 3:76-87.

Frankel, S and Reitman, S (1963): Clinical laboratory methods. The C. V. Mosbye Company pp.1102.

Goel, A; Chauhan, D.P and Dhawan, D.K (2000): Protective effect of zinc in chlorpyrifos induced hepatotoxicity, biochemical and trace elemental study. Biol. Trace Elem. Rec. 74:171-183.

Goel, A; Dani, V and Dhawan, D.K. (2007): Zink mediates normalization of hepatic drug metabolizing enzymes in chlorpyrifos-induced toxicity. Toxicology Letters. 169:26-33.

Goel, A and Dhawan; D.K (2001): Zink supplementation prevents liver injury in chlorpyrifosp-treated rats. Biol. Trace. Elem. Res. 82:185-200.

Helling, T.S; Wogahn, B.M.; Olson, S.A; Evans, L.S; Reddy, B.R and Van Way. C(1995). The effect of prostaglandin E1 on liver adenine nucleotides and cytoplasmic enzymes in porcine model of normothermic hepatic ischemia. Hepatology. 22:1554-1559.

Hoffman, D.J; Spann, W.J; Lecaptain, L.J; Bunch, C.M and Rathener, B.A (1991): Developmental toxicity of diphenyl ether herbicides in nestling American Kastrds. J. Toxi. Environ. Health, 26 (2) 201-212.

Hsu, D.Z; Hsu, C.H; Huang, B.M and Liu, M.Y (2001): Abamectin effects on aspartate amino transferase and nitric oxide in rats. Toxicology. 165: 189-103.

Jendrassik, L and Graf, P. (1953): Bilirubin, determination of bilirubin in blood serum. (1st ed), Brayes Clin. Lab. Methods. Published b John D.Bauer Philip. G. Ackermann and Gelson, Toro Sand Louis. pp357.

Kaplan, R.M; Courtney, C.H; Kunkle, W.E; Zeng, Q.Y, Jernigan, A.D. and Eagleson, J.S. (1994): Efficacy of injectable abamectin against gastrointestinal tract nematodes and lungworms of cattle. Am. J. Vet. Res. 55: 353-357.

Kind, R. R. N. and Kind, E.G (1954): Estimation of plasma phosphatase by determination of hydrolysed phenol with aminoantipyrine. J. Clin. Path. 7:322-326.

Klaassen, C.D and Eaton, D.L (1991): Principles of toxicology. In: "Amdur, M.O., Doull, J and Klaassen, C.D (Eds.), Toxicology. (4th ed) Mc-Graw-Hill, New York P.12-49.

Kobeasy, M.I; Salem, S.M; Farid, M.M; Ahmed,S.H and Abd-Allah, A.A(2009): Toxicity studies on the effect of carbofuran adjuvant on rats fertility. J. Biol. Chem. Environ. Sci. 4(2)501-515.

Lane-Pert, W. and Pearson, A.E. (1971): Dietary requirements. In: " laboratory animal principles and practice", P.142.Academic press, London and New York.

Lankas, G.R. and Gordon, L.r. (1989): Toxicology. In: "Campbell W.C (Ed) Ivermectin and Abamectin. Springer-verlag. New York.

Liu, M. Y; Chiang, P. J; Hsu, D. Z and Deng, J. F (2003): Abamectin attenuates gastric mucosal damage induced by ethanol through activation of vagus nerve in rats. Alcohol. 30: 61-65.

Motto, M; Crosignani, P.G and Matwni, L (1975): Hypothalamic hormones: Chemistry, physiology, pharamacology and clinical uses. Academic press, London, New York, San Francisco .p: 261-268.

Murrey, R.K; Granner, D. Kand Rodwell, V.W (2006): Harper's illustrated biochemistry (27th ed) Mc-Grow Hill Comp. Inc. Boston, New York Singapore.

Narayana, K; Prashanthi, N; Nayanatara , A; Kumar, H; Abhilash, K and Bairy, K.L (2005): Effect of methylparathion on rat sperm morphology and sperm count, but not fertility, are associated with decreased ascorbic acid level in the testis. Mutation Research, 588:28-43.

Pesticide Manual (2000): A world compendium to pesticide manual (20th ed) Eido: CDS. Tomlin, British Crop Protection Council pp. 309-310.

Phlip , G.R; Forrest, H.N and George, C.F(1993). AIN-93 purified diets for laboratory rodents: final report of the American Institute of Nutrition Ad. Hoc. Writing committee on the reformulation of the AIN-76A rodent diet. J. Nutra. 123: 1935-1951.

Plaa, G.L. and Hewitt, W.R (1982): Detection and evaluation of chemically induced liver injury. In: " Hayes, W. (Ed), principles and methods of Toxicology. Raven Press, New York P. 407-445.

Premachandra, B.N and Ibrahim, I.I. (1976): A simple and rapid thyroxine radioimmunoassay (T4 – RIA) in unextracted human serum, composition of T4 – RIA and displace placement assay T4 (1) in normal and pathological sera. Clin. Chem. Acta 43:70-75.

Ritman, S and Frankel, S (1957): A colorimetric method for the determination of serum glutamic oxaloacetate acid and glutamic pyruvate transaminases. Am. Clin. Path. 28, 156.

SAS Institute (2000): SAS/STAT. User's Guide. SAS. Institute. Inc. Cary. N.C.

Scheuhammer, A.M. and Wilson, K. (1990): Effect of lead and pesticides on Delta-aminolrulinic acid dehydratase of rinclores (*Streptopelia risoria*). Environ. Toxical and Chem:9,11-22.

Schneeman, B.O; Rice, R and Richter, B.D (1989). Reduction of plasma and hepatic triacylglycerides with whole milk containing diets in rats. J. Nutr. 119:965-970.

Soliman, S.A; Chanlet, E; Curley, A; El-Gendy, K.S; Ahmed, N.S. and Farmer, J.S (1983): Effect of neurotoxic organophosphates on the levels of some enzymes and other biochemical components in sheep blood. Proc. Int. Conf. Env. Haz. Agrochem. 1:494-502.

Trinder, P. (1969): Enzymatic determination of glucose in blood serum. Ann. Clin. Biochem. 6:24-26.

US. EPA (1990): Pesticide Fact Sheet No 89.2 : Avermectin B1. Office of Pesticides and Toxic Substances. Washington. D.C. pp.10-143.

Verma, R.S; Mehta, A and Srivastava, N. (2007): *In vivo* chlorpyifos induced oxidative stress: Attenuation by antioxidant vitamins. Pest. Biochem. Physi. 88:191-196.

Waller, R.A. and Duncan, D.B (1969): A bayes rule for symmetric multiple comparisons problem. J. Am. Statis. Assoc. 64: 1484-1503.

WHO (1991):World Health Oganization Guidelines to the WHO recommended classification of pesticides by hazard. IPCS. pp.39.

Wilson, D; Rowe, L.D; Lovering, S.L; Witzel, D.A and Witzel, D.V. (1982): Acute

toxicity of tri-orthocresylphosphate in sheep and swine. Am. J. Vet. Res. 4 (11): 1954-1960.

Yoon, K.S; Nelson, J.O and Clark, J.M (2002): Selective induction of abamectin metabolism by dexamethasone, 3-methylcholanthrene, and Phenobarbital in Colorado potato beetle, *Leptinotarsa decemlineata* (Say) pest. Biochem. Physi. 73:74-86.

Zeng, Z; Andrew, N.W; Arison, B.H; Luffer-Atlas, D and Wang, R.W (1998): Identification of cytochrome P450 IA4 as the major enzyme responsible for the metabolism of ivermectin by human liver microsomes. Xenobiotica. 28, 313-321.

التأثيرات السامة لمبيد الآباميكتين و مستحضراته على نمو الجسم و مكونات الدم فى ذكور فئران الالبينو.

نبيل محفوظ ابراهيم[1] - عصام عبد الرؤوف عويس[1] - محمد ابراهيم قبيصي[2] – ياسمين امام عبد المبدىء[1].

[1] قسم الحشرات الإقتصادية و المبيدات – كلية الزراعة جامعة القاهرة.

[2] قسم الكيمياء الحيوية – كلية الزراعة جامعة القاهرة.

ركزت هذة الدراسة على توضيح سمية مبيد الاباميكتين النقي و مستحضراته (الفيرتميك 1.8% و الفابكميك 1.8%) باستخدام جرعات 20/1 و 40/1 من الجرعة النصف المميتة لمدة 12 اسبوع على نمو الجسم و مكونات الدم لذكور الالبينو ، تمت معاملة الجرعات كل يومين عن طريق الفم. و قد تم تقدير كلاً من نمو الجسم و كرات الدم الحمراء و البيضاء و محتوى الدم من الهيموجلوبين و محتوى البلازما من البروتين الذائب (البروتين الكلى – الالبيومين – الجلوبيولين) و هرمونات الغدة الدرقية (الثيروكسين – ثلاثى ايودو ثريوتبن)، كما تم ايضاً تقدير وظائف الكبد (AST – ALT- البليروبين) بالاضافة لنشاط أنزيم الكولين استريز و الفوسفاتيز القاعدى و الحامضى و أنزيم ديهيدروجينيز حامض اللاكتيك، وايضا محتوى الدم من الجلوكوز. و قد تمت التجارب فى الظروف العادية تحت تأثير المعاملة بالمبيد و مستحضراته بالاضافة الى تجربة المقارنة.

و قد لوحظ انخفاض نمو الجسم معنوياً بعد المعاملة بالمبيد و مستحضراته على مستوى الجرعات المستخدمة مقارنة بتجربة المقارنة. كما انخفضت فاعلية التغذية معنوياً نتيجة المعاملة بالمبيد مما ادى لانخفاض نمو الجسم. كما لوحظ انخفاض محتوى الدم من الهيموجلوبين و كرات الدم الحمراء على العكس لم يتأثر محتوى الدم من الثيروكسين و ثلاثى ايودوثربومبين، و كذلك كرات الدم البيضاء تحت تأثير المعاملة بالمبيد و مستحضراتة و ان هذة المعاملات ادت لزيادة نشاط انزيمات وظائف الكبد و المحتوى من البيلبروبين ، بالاضافة الى ان البروتين الذائب الكلى و البيومبين فى البلازما قد انخفض انخفاضاً معنوياً و لكن محتوى الجلوبيولين فى البلازما لم يتغير تحت نفس الظروف و بالنسبة لمستوى السكر و نشاط انزيمات البلازما فان المعاملة بالمبيد و مستحضراته قد ادت لارتفاع سكر الدم و ادت لتثبيط أنزيم الكولين استريز على العكس ادت المعاملات السابقة لرفع نشاط انزيمات الديهيدروجينيز حامض اللاكتيك و كذالك الفوسفاتيز الحامضى و القاعدي و كانت نسبة الارتفاع فى مكونات الدم و كذلك تنشيط او تثبيط انزيمات البلازما اكثر وضوحاً نتيجة المعاملة بمستحضرات المبيد مقارنة بالمبيد النقي. كما ان المعاملة بالجرعة الاعلى (20/1 من الجرعة السامة النصفية) كانت اكبر تأثيراً من الجرعة الأقل (40/1 من الجرعة السامة النصفية).

و من هنا يمكن القول ان المعاملة بمبيد الاباميكتين النقي و مستحضراته 1.8% (الفيرتميك و الفابكوميك) قد ادت الى اضطراب فى عمليات التمثيل الغذائي للحيوان و كانت لمستحضرات المبيد تأثير اعلى من المبيد النقي مما يؤدى للتوصيه بعدم التعرض لتلك المركبات الضارة بالصحة.