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Ameliorative Effect of *Curcuma longa L.* Rhizomes against Biochemical Toxicity Induced by Dichlorvos in Female Albino Rats

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ABSTRACT

Background/aim: Organophosphorus (OP) compounds contain a heterogeneous types of chemicals particularly designed for the command of pests, weeds or plant diseases. The present study mainly focused on the possible potential chemoprotective role of 20% methanolic extract of *Curcuma longa* L. rhizomes against biochemical toxicity following dichlorvos exposure for 35 days in albino rats (females).

Materials and methods: Female albino rats were divided into four groups of fifth rats each: Group I served as control. Group II was administered orally with dichlorvos (DDVP) 10 mg/kg body weight. Group III received 20% methanolic extract of *C. longa* L. rhizomes 500 mg/kg body weight. Group IV received both DDVP 10 mg/kg body weight plus 20% methanolic extract of *C. longa* L. rizhomes 500 mg/kg body weight. All animals were scarified after 35 consecutive days of the beginning of the experiment. Samples of blood were taking for biochemical analysis which include total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL- C), triglycerides (TG), total proteins (TP), and urea concentrations.

Results: The data of present study demonstrated that plasma total cholesterol, triglycerides, and HDL-C concentrations were non-significantly increased whereas the LDL-C level significantly increased ($p<0.05$) by DDVP treatment. Also, non–significant differences was seen in VLDL-cholesterol concentration between groups. Total proteins concentration was significantly reduced ($p< 0.05$) compared with the control animals. Furthermore, renal markers such as urea concentration were significantly ($p< 0.05$) increase in DDVP treated rats.

Co-administration of 20%methanolic extract of *C. longa* L. rizhomes was able to restore all the parameters were studied to near-normal values. Oral feeding of 20% methanolic extract of *C. longa* L. to DDVP- treated female rats at the dose of 500mg/kg body weight caused significant ($p<0.05$) decreasing of elevated parameters compared with DDVP group. Female rat treated with 20% methanolic extract of *C. longa* L. alone did not exhibited any significant differences.

Conclusion: Treating rats with 20% methanolic extract of *C. longa* L. rizhomes caused improvement of DDVP negative effects on serum lipid profile, total protein and urea concentrations in comparison with control group.

KEYWORDS: Dichlorvos, *Curcuma longa* L., Lipid profile, Total proteins, Urea, Albino rats.

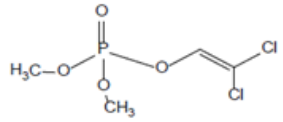
1. INTRODUCTION

For centuries, pesticides have been employed in agriculture to improve food production by eliminating unwanted insects and controlling vectors of disease (Prakasam, 2001). However, the great interest upon their harmful effects on human, animal and environmental health contribute to shortage their use by application various rules (Dikshit, 2003).

Among general pesticides, organophosphorus (OP) compounds are greatly used in agriculture, medicine, and industry (Storm, 2000). The particular site of action of organophosphate pesticides is the central and peripheral nervous systems because they repress acetylcholinesterase (AChE), the enzyme that hydrolyses the neurotransmitter acetylcholine (ACh). OP toxicity could be include other systems such as pancreas (Yurumez, 2007), liver (Kalender, 2005), heart (Ogutcu, 2006), kidney (Kalender, 2007), and reproductive system (Uzunhisarcikli, 2007). After absorption, OP compounds accumulate fastly in fat, liver, kidneys and salivary glands (Kumar, 2010).

Dichlorvos (2,2-dichlorovinyl dimethyl phosphate, DDVP) is a highly volatile insecticide of the organophosphate class. It has toxicity class I - highly toxic. It is utilized in resistance to a huge range of mite, household pests, and insect pests of plants, animals of farm and as an antihelminthic. It is also utilize to controlling parasites in fish farming (Celik, 2008; Ogutcu, 2008; Das, 2013). It is used randomly in different insecticide formulations because it's inexpensive production, accessibility, efficacy and affordability (Edem, 2012). Exposure to dichlorvos by the general public may happen via air, water, or food because it is easily absorbed through all ways of exposure (Raheja and Gill, 2002).

Synonyms: DDVP
Molecular Formula: $C_4H_7Cl_2O_4P$
Structural Formula:



Molecular Weight: 221

Figure.1.Dichlorvos (2, 2-dichlorovinyl dimethyl phosphate) (Das, 2013)

Effects of dichlorvos mainly neurons (decreased mRNA expression of NF-68 and GABAA receptors), (Hogberg, 2009). Various degrees of damages could be noticed in liver, kidneys and lungs (Yurumez, 2007). Substantial adverse health impacts on many organ systems, including the respiratory system (Atis, 2002) and reproductive system (Okamura , 2005; Oral , 2006) has been linked to the exposure to dichlorvos. Damaging of tissue as a result of organophosphate poisoning are frequently shown, but stopping this potentially severe complication has not been the subject of a great deal of research.

Rhizomes of *Curcuma longa* (family: Zingibaeraceae), generally well-known as turmeric and utilized in traditional form as a origin of coloring material for nutrients, cosmetics, and as a medicinal formulations. Medical benefits of the *C. longa* L. rhizomes result from volatile oil as a carminative, antifungal, and yellow curcuminoids for anti-oxidative and anti-inflammatory characteristics (Pothitirat and Gritsanapan, 2006; Sarah , 2009; Akram, 2010). Anticancer activities has resumed scientific interest in its potential to hinder and treat the disease (Akram, 2010). The bright yellow color of turmeric results chiefly from fat-soluble, polyphenolic pigments known as curcuminoids. Curcumin, the main curcuminoid found in turmeric, is usually considered its most active ingredient. Another curcuminoids discovered in turmeric contain demethoxycurcumin and bisdemethoxycurcumin. Anti-inflammatory, hepatoprotective, anti-microbial, wound healing, anti-cancer, anti-tumor and anti-viral are the principal actions have been found for *C. longa* L. rhizome (Sikora, 2011).

Lipids have a significant role in almost all aspects of biological activities processes in the body. Disturbances of its level in tissues and serum are usually associated with many abnormalities. All lipids related abnormalities are responsible for cardiovascular mortality, fatal myocardial infarction, and brain stroke (Upadhyay, 2015), gallstone formation (Stinton & Shaffer, 2012), atherosclerosis, and coronary artery disease. Plasma concentrations of creatinine and urea could be used as indicators of nephrotoxicity. Low clearance values for creatinine and urea indicate impaired ability of the kidneys to filter these waste products from the blood and excrete them in the urine. As clearance levels decrease, blood levels of creatinine and urea increase (Yousef, 2008). Urea is one of the first nitrogenous wastes to accumulate in the blood, and the BUN level becomes increasingly elevated as CKD progresses (Meyer & Hostetter, 2007).

The purpose of current study was (1): To investigate whether dichlorvos (DDPV) induced biochemical changes which include plasma lipid concentrations of TC, HDL-C, LDL-C, VLDL-C, and TG. Also, determination of TP and urea concentration. (2): To investigate the possible protective effects of 20% methanolic extract of *curcuma longa* L. rhizomes in mammalian experimental animals (female rats) after a 5-week exposure of dichlorvos.

2. MATERIALS AND METHODS

Preparation of plant extract: The plant used in this study *C. longa* L. rhizomes was purchased from a local herbal markets and extract was prepared according to Sato (1990). The plant powder was extracted with mixture of methanol and distilled water in a ratio of 20 % methanol: 80% distilled water (V/V) in average of 1 gram of rhizomes powder: 3 ml of mixture by employing blender for 30 min at room temperature. The suspension were filtered by gauze and the filtrate concentrated in oven at 40˚- 45˚ C. The crude extracts were collected and stored at 4˚ C for future use.

Experimental design: Twenty female albino Wister rats, 8-12 weeks old and weighing 190–240 gram, were obtained from the Animal House of the University of Babylon, Iraq and maintained according to controlled conditions. Animals were housed in cages throughout the experiment, fed on pellet diet and water *ad libitum*, and allowed to acclimatize to the laboratory environment for 7 days before the beginning of the experiment. After acclimation for 1 week, the rats were divided into four groups (n=5) and treated daily for 35 consecutive days:

Control group: Normal saline was administered orally to this group. **2-Dichlorvos group:** Dichlorvos (10 mg / kg) was administered orally to this group (Aziz, 2012). DDVP was supplied by Bhart Com, India.

***C. longa* L. extract rhizomes group**: Rats were administered orally using oral feeding tubes with 20% methanolic extract of *C. longa* L. rhizomes at a dose of 500 mg / kg (Govind, 2011).

Interference group (DDVP+ *C. longa* L. rhizomes extract): Rats were administered orally with dichlorvos at a dose 10 mg / kg b.w then 20% methanolic extract of *curcuma L*. rhizomes at a dose of 500 mg / kg as same time.

Biochemical analysis: At the completion of the experimental period, the animals were anesthetized by light ether anesthesia, collection of blood was by heart puncture, put in a dry test tube and left at room temperature for 30

minutes to clot, then centrifuged at 3000 rpm for15 min to separate the serum and kept freezing at −20ºC until the biochemical analysis began (Ibrahim and El-Gamal, 2003). Biochemical analysis were estimated in serum by utilizing a commercially available spectrophotometric-enzymatic kits for total cholesterol, triglycerides, HDL-C & total proteins (Biolabo, France), LDL-C (Spectrum, Egypt) and urea (Biomeriex, France) and analyzed by UV-1100 spectrophotometer .

Statistical analysis: The means ± standard errors (SE) were used to described the outcome of this study. Data were analyzed applying statistical package for social sciences (SPSS) version 17.0. Significance was calculated employing one-way analyses of variance (ANOVA).The P-value less than 0.05 (P<0.05) was considered statistically significant**.**

3. RESULTS & DISCUSSION

Changes in lipid profile: The effects of DDVP, 20% methanol extract of *curcuma longa* L., and their combination on serum lipids profile in treated rats are shown in Table 1. There was non-significant increase in plasma total cholesterol (TC), Triglycerides (TG) and HDL-C concentrations while there was significant increase (P<0.05) in LDL-C concentration in DDVP group compared with control. Also, non–significant differences was seen in VLDL-C concentration between groups.

In rats treated with both DDVP plus 20% methanol extract of *C. longa* rhizomes, curcuma reduced effects which were caused by DDVP. There was significant decrease (P<0.05) of TC, TG and HDL-C concentrations compared with DDVP and the same parameters showed non-significant decrease compared with control. There was non–significant decrease of LDL-C concentration in group treated with both DDVP plus *C. longa* compared with DDVP and control.

Regarding to group treated with 20% methanol extract of *C. longa* L. rhizomes alone, non –significant differences in all treated parameters compared with control was observed.

Table.1.Effect of DDVP and *C. longa* rhizomes extract on serum lipid profile in treated groups (Mean ± S.E)

Groups	Total cholesterol mg/dL	Triglycerides mg/dL	HDL-C mg/dl	LDL-C mg/dl	VLDL-C mg/dl
Control	64.25±9.08 a	41.6±8.63a	83.30±1.59a	29.67±4.28a	5.35±1.39a
DDVP	83.71±14.37ab	47.99±11.49ab	95.65±14.61ab	71.45±16.62b	4.02±0.41a
C.Longa L. extract	70.14±5.45abc	36.94±7.71abc	57.89±11.36 ac	27.96±6.06a	8.22±2.76
DDVP+C.Longa	43.14±6.14ac	19.38±5.49ac	71.73±5.97ac	43.14±6.14 ab	5.64±0.57 a

Similar letters refer to non-significant difference at the 0.05 level Different letters refer to significant difference at the 0.05 level: In terms of the changes in total proteins, a significant decrease (P<0.05) was found in rats treated with DDVP, whereas non-significant increase were found in group treated with *C. longa* L. alone compared with control. Also, there was non-significant increase in both groups treated with *C. longa* alone and DDVP plus *C. longa* compared with DDVP (Table 2).

Table.2.Effect of DDVP and *Curcuma longa* extract on total protein (g/dL)

Group	Mean ± S.E
Control	10.89 ± 0.02 a
DDVP	8.03 ±077 b
C.Longa L. extract	12.03±0.81 a
DDVP + C.Longa	9.24± abc

Similar letters refer to non-significant difference at the 0.05 level Different letters refer to significant difference at the 0.05 level.

Renal profile biomarkers such as blood urea (Table 3) showed a significant increase (P<0.05) in the group of rats treated with DDVP while there was non-significant decrease in group treated with 20% methanolic extract of *Curcuma longa* alone compared with the control rats at the completion of the experiment. In addition, the presence of extract of *curcuma longa L.* plus DDVP led to a reduction in the elevation of urea and caused significant decrease (P<0.05) at the completion of 35 days of treatment compared with both control and DDVP rats.

Table.3.Effect of DDVP and *Curcuma longa* extract on urea concentration (mg/dL)

Group	Mean ± S.E
Control	58.01 ± 12.34 a
DDVP	110.6 ±19.03 b
C.Longa L. extract	24.41±9.54 ac
DDVP + *C.Longa*	20.88± 6.49 c

Similar letters refer to non-significant difference at the 0.05 Different letters refer to significant difference at the 0.05 level.

Every organ in the body is able to be affected by the harmful influences of chemicals (Helal, 2011). Cellular changes caused by the effect of pesticides bring about metabolic alteration in the organism (Dere, 2010). Lipids act a prominent role in virtually all aspects of biological processes in the body. Disturbances of their level in tissues and serum are usually associated with many abnormalities, including gallstone formation (Stinton & Shaffer, 2012), atherosclerosis, and coronary artery disease (Katz, 2015). The chronic small dose exposure to pesticides either directly or indirectly can be a major supporter for presence of pesticide residual levels in human blood (Muddasir , 2012).

In the present investigation, dichlorvos lead to non-significant increase in plasma TC, TG and HDL-C concentrations while there was significant increase ($P<0.05$) in LDL-C concentration compared with control. OP insecticides mostly cause an increase in total cholesterol and total lipid levels (Kalender, 2005; Ogutcu, 2008). Increased serum cholesterol may be associate with the impacts of the pesticide on the permeability of liver cell membranes (Yousef, 2006) or may be attributed to the blockage of the liver bile ducts, bringing about a diminishing or cessation of cholesterol secretion into the duodenum (Zaahkouk, 2000). Also, elevation in the serum cholesterol level may be a sign of liver damage (Ogutcu, 2008).

Additionally, in this study, DDVP brought about elevation although it was not significant in the serum levels of TG possibly associate with to the lowering of the lipase enzyme activity of both the hepatic triglyceride and plasma lipoproteins (Buyukokuroglu, 2007).

This recent study in agreement with earlier studies which illustrated an increase of the serum TG concentrations in the experimental animals that were treated with various insecticides, involving the organophosphate dichlorvos and carbamate furadan (Buyukokuroglu, 2007). Also, single half lethal dose of diazinon (DZN) (300mg/Kg body weight) caused significant increase in the serum levels of TG (Abd Elmonem, 2014). On the other side, the daily oral administration of DZN at the dose levels of 1/2 and 1/32 LD50 produced a significant increase of plasma LDL-C. However, a significant decrease of plasma LDL-C that lasted for similar periods of time was remarked in the rats that were gave the 1/8LD50 dose level (Ibrahim and El-Gamal, 2003; Imran, 2010) reported that cholesterol, HDL-C and LDL-C level was raised significantly and triglycerides were reduced in all groups when gave a treat with malathion. In other study, DZN caused a slight but insignificant change in the plasma levels of TG (Ibrahim and El-Gamal, 2003).

Some differences observed compared to previous studies in the lipid profile may be different according to the exposure time and dose of dichlorvos used in this study which was lower than oral LD50 of dichlorvos which is 80 mg/kg for male rats (Okamura, 2005).

All results of this study may indicate liver damage. Dichlorvos causes hepatotoxicity in rats and leading to oxidative stress (Gupta, 2005). Also, the electron microscopic studies reveal that damage happened to the liver cells such as loss of mitochondrial matrix and cristae, dilatation of endoplasmic reticulum in hepatocyte 4 weeks after treatment of rats with dichlorvos (Ogutcu, 2008). These results may due to the effect of DDVP on oxidant/antioxidants system which revealed by many reports. Treatment with DDVP induced an increase in the level of MDA and minimized activities of antioxidant enzymes ($P< 0.05$), causing induction of erythrocyte lipid peroxidation and changes in antioxidant enzyme activities, proposing that reactive oxygen species (ROS) may be included in the toxic effects of DDVP (Eroglu, 2013). Long period dichlorvos inhalation can change plasma prooxidant-antioxidant balance, therefore the need for cautious long term employing (Helal, 2011). Dichlorvos not only has toxic influences on mammals, besides has toxic influences on fish, birds, honey bees, and non-target invertebrates (Ural and Koprucu, 2006). When dichlorvos was provided at 1/50 LD50 oral dose, pathological changes were detected in hepatic cells (Ogutcu, 2008).

Observation of earlier studies have demonstrated that excessive free radical production causing oxidative stress might be an important mechanism of organophosphate toxicity (Prakasam, 2001). Dichlorvos, a volatile organophosphate compound with strong pesticide activity has been reported to modify the biological pro-oxidant – antioxidant balance in several toxicity studies (Edem, 2012). Another study also exhibited that dichlorvos caused in oxidative stress in rats through abnormal production of ROS (Sharma and Singh, 2012). Furthermore, Lucic (2002) showed that DDVP significantly decreases butyrylcholinesterase (BuChE) activity in female and male rat plasma (40–60%; $P<0.05$), and the alterations in concentrations of lipids and lipoproteins were observed throughout the experiment. This contribute to the hypothesis that BuChE may perform a role in lipid and lipoprotein metabolism.

An increasing interest in curcumin as a cardiovascular disease (CVD) protective agent by means of reduced blood TC and LDL-C level (Kim and Kim, 2010). As well, this results showed that hyperlipidemic effect of DDVP although not significant improved with the usage of *C. longa* rhizomes. The precise mechanism by which it diminishes levels of other lipids is not known but studies have reported that spices perform a vital role in lipid metabolism, because of their active principles. The spices are well-known to affect bile acid excretion and as a result of that influence lipid levels. The reduced levels of phospholipases (PLs) and TGs may also be in consequence of reduced free fatty acids (FFA) synthesis by curcumin, which can suppress the enzymes involved in FFA synthesis

(Rukkumani, 2002). Arafa (2005) referred that cholesterol concentration alterations by curcumin possibly in consequence to its impact on cholesterol absorption, breaking down or removal. In addition, curcumin exhibits a messaging molecule which make communication with genes in hepatic cells, leading to the enlargement the manufacture of mRNA in order for leading the formation of receptors of LDL-C. Hepatic cells are capable of remove more LDL- C originating in the body due to additional amount of LDL receptors (Jain, 2006), therefore LDL-C concentration was reduced.

The results with agreement with previous studies which reveals that curcumin-treated groups were brought down significantly elevated lipid profile parameters (Rukkumani, 2005). The potential mechanism in the hypocholesterolemic impact of curcumin examined by determination cholesterol 7a-hydroxylase (CYP7A1), a rate limiting enzyme in the biosynthesis of bile acid from cholesterol, at the mRNA level. The curcumin-supplemented diet as well significantly diminished the atherogenic index (AI) by 48% as relative to control group. Hepatic TG concentration was significantly minimized by 41% in rats nourished with curcumin-supplemented diet compared to control group ($P < 0.05$). Conversely, the curcumin nourishment significantly raised fecal TG and TC. The curcumin nourishment up-regulated hepatic CYP7A1mRNA level by 2.16-fold, in comparison with control group recommended that the raises in the CYP7A1 gene expression may partly account for the hypocholesterolemic impact of curcumin (Kim and Kim, 2010).

From the results achieved, we conclude that *C. longa* efficiently protect the system against DDVP-induced dyslipidemia and are possible to be suitable for the treatment of hyperlipidemia. This results emphasis protective effect of *C. longa* indicated by many previous studies. In rats which were gave a treatment of curcuma after causing of fatty liver by oxytetracycline, curcuma improved the oxidative dangerous impact of oxytetracycline preventing the fibrosis proceed and following damage of liver caused by oxytetracycline giving and diminish peroxidation of lipid by sustaining the functioning of antioxidant enzymes (catalase, superoxide dismutase and glutathione peroxidase) (Helal, 2011). Administered of 50% EtOH extract of *C. longa* to male rats at a dose of 1gm/kg body weight brought about significant decreasing of serum cholesterol, triglycerides and phospholipids (Purohit, 1999).

Also, the capability of *C. longa* for defend the liver from inflammation can be a result of its anti-inflammatory impact by suppression the expression of cyclo-oxygenase-2 (Shakibaei, 2007). *C. longa* defense possibly by acting as scavenger of nitrogen oxide and reactive oxygen species and improvement antioxidant protection by raising the level of reduced glutathione, or by raising the antioxidant factors in the body (Kaur, 2006).

Serum total proteins was decreased in DDVP group. This decreasing might be having a relationship to dysfunction of liver and diminished synthesis of protein. Ajiboye, (2014) implies that total proteins and albumin are plasma proteins that measure synthetic function of the liver and help in maintaining blood osmotic pressure. Hypoproteinaemia is the deficiency of protein in the plasma, partly due to dietary insufficiency or because depletion of albumin in the DDVP-induced rats when compared with the control and the toxic effect of the pesticides resulted in a noticeable decrease in the serum total proteins and albumin. Also, previous studies have reported that toxicant have a negative effect on the serum total proteins and albumin leading to a decrease in the concentration levels (Nuhu and Aliyu, 2008). In addition, rats exposed to OP pesticides caused changes in the level of serum total proteins and reflect disorders in the synthesis and metabolism of proteins.

Uric acid and urea are end products of protein metabolism that require to be excreted by the kidney, hence, a significant increase of these parameters, as noticed in this study in DDVP group, gives a sign of functional damage to the kidney. These comments are mostly in agreement with other studies on pesticides as DZN which can caused an raising in urea level which can be because its effect on liver function, as urea is the end product of protein catabolism (Abd Elmonem, 2014). Elevated serum urea as well associated with an increased protein catabolism in mammalian body or more formation and efficient conversion of ammonia to urea due to increased synthesis of enzyme included in urea production (Weiner, 2015).

Giving of DDVP to the rats caused dysfunction of kidney which seem through significant increasing in the level of serum urea, despite in treating rats with DDVP plus *C.longa* group, renal function marker inhibited which might be because beneficial effect of *C.longa* on liver and kidney functions. As well, it might be as a result of the beneficial effect of curcumin against renal damage by increasing level of GSH in kidney and activity of gluthation peroxidase causing repressing of oxidative stress (Venkatesan, 2000).

This results in agreement with previous study have shown that dose of *C.longa* (500mg/km body weight) used in this study was effective against the toxicity of DDVP which significantly increased chromosomal aberration and mitotic index and induce histopathological changes in both kidney and liver (Aziz, 2012). Also, Helal , 2011 revealed that *C.longa* exhibited a significant reduction in levels of serum urea and creatinine in comparison with control group.

CONCLUSION

The data obtained in the present study, suggest that the organophosphate, DDVP, may interfere with lipid, urea and protein metabolism in rats as a model of mammalian animals. Treatment with 20% methanolic extract of

C. longa L. rhizomes together with DDVP ameliorated DDVP negative effects in the activities of the measured parameters in this study whereas extract of *C. longa* L. alone did not induce any significant alteration in the lipid profile and significant increase in total protein concentration in the serum.

REFERENCES

Abd Elmonem HA, Assessment the Effect of Pomegranate Molasses against Diazinon Toxicity in Male Rats, IOSR Journal of Environmental Science, Toxicology and Food Technology, 8(2), 2014, 135-141.

Ajiboye BO, Salawu SO, Okezie B, Oyinloye BE, Ojo AO, Onikanni SA, Oso AO, Asoso OS and Obafemi TO, Mitigating potential and antioxidant properties of aqueous seed extract of Leea guineensis against dichlorovos-induced toxicity in Wistar rats, Journal of Toxicology and Environmental Health Sciences, 6(7), 2014, 132-146.

Akram M, Shahab-Uddin, Ahmed A, Usmanghani K, Hannan A, Mohiuddin E and Asif M, Curcuma Longa and curcumin, A review article Rom. J. Biol, Plant Biol, 55(2), 2010, 65–70.

Aljebori AM and Alshirifi AN, Effect of Different Parameters on the Adsorption of Textile Dye Maxilon Blue GRL from Aqueous Solution by Using White Marble, Asian journal of chemistry, 24(12), 2012, 5813-5816.

Alqaragully MB, AL-Gubury HY, Aljeboree AM, Karam FF and Alkaim AF, Research Journal of Pharmaceutical, Biological and Chemical Sciences, 6(5), 2015, 1287-1296.

Al-Saadi A.H, Zaidan K.I, Dental sex determination by multiplex PCR in iraqi samples, Research Journal of Pharmaceutical, Biological and Chemical Sciences, 6(6), 2015, 1572-1577.

Al-Terehi M, al-kilabi IH, AL–Mamoori AMJ, Al-Jboori MJ, Al-Saadi AH and Zaidan HK, International Journal of ChemTech Research, 9(3), 2016, 407-411.

Al-Terehi M, Al-Saadi AH, Al-Sherefi AN and Zaidan HK, Optimization Polyplexe Stability in Different Glucose Concentrations, International Journal of ChemTech Research, 9(3), 2016, 396-401.

Al-Terehi M, Al Saadi AH, Zaidan HK and Al-Harbi SJ, Protective Effects of Glycyrrihza glabra Plant Extract against Cyclophosphomide in Kidney and Liver Tissues in White Albino Rats, International Journal of ChemTech Research, 9(3), 2016, 402-406.

Al-Terehi M, Al-Saadi AH, Some herbal medicinal plants activity against Candida spp which resistance to antifungal drugs, International Journal of PharmTech Research, 8(10), 2015, 146-150.

Al-Terehi M, Al-Saadi AH, Some plants extracts synergism effects in pathogenic bacteria." International Journal of PharmTech Research 8(10), 2015, 158-165.

Al-Terehi M, Zaidan HK, Effective of different factors on trace elements concentrations in Iraqi lactating mother'smilk, International Journal of PharmTech Research, 8(10), 2015, 151-157.

Arafa M, Curcumin attenuates diet-induced hypercholesterolemia in rats. Jornal of pharmacy and pharmacology, 11(7), 2005, 228-234.

Atis S.C, Omeleko˘glu U.C, kun B, Ozge A, Ersoz G and Talas D, Electrophysio-logical and histopathological evaluation of respiratory tract, diaphram, and phrenic nerve after dichlorvos inhalation in rats, Inhal. Toxicol, 14, 2002, 199–215.

Aziz DZ, Study of some genotoxic and histopathological effects for dichlorvos and inhibition of these effects in white female rats by using the extract of turmeric rhizomes curcuma longa L. Master Thesis, University of Babylon 2012.

Buyukokuroglu ME, Cemek M, Yurumez Y, Yavuz Y and Aslan A, Antioxidative role of melatonin in organophosphate toxicity in rats, Toxicol Letters, 172, 2007, 208.

Celik I, Yilmaz S and Turkoglu V, Hematotoxic and hepatotoxic effects of dichlorvos at sublethal dosages in rats. Hum. Exp. Toxicol. 18, 2008, 33–37.

Das S, A Review of Dichlorvos Toxicity in Fish, Current World Environment, 8(1), 2013, 143-149.

Dere E, Ferda A and Ugur S, The Effect of DichlorvosI on Acetylcholinesterase Activity in Some Tissues in Rats. Acta Veterinaria, 60(2-3), 2010, 123-131.

Dikshit AK, Pachauri DC and Jindal T, Maximum residue limit and risk assessment of beta-cyfluthrin and imidacloprid on tomato (*Lycopersicon esculentummill*), Bull Environ Contam Toxicol, 70, 2003, 1143–1150.

Edem VF, Kosoko A, Akinyoola SB, Owoeye O, Rahamon SK and Arinola OG, Plasma antioxidant enzymes, lipid peroxidation and hydrogen peroxide in wistar rats exposed to Dichlorvos insecticide, Archives of Applied Science Research 4 (4), 2012, 1778-1781.

Eroglu1 S, Pandir1 D, Uzun G, Fatma and Bas H, Protective role of vitamins C and E in diclorvos-induced oxidative stress in human erythrocytes in vitro. Biol Res 46, 2013, 33-38.

Govind P, Active principles & median lethal dose of curcuma longa Linn, IRJP 2(5), 2011, 239-241.

Gupta SC, Siddique HR, Saxena DK and Kar D, Hazardous effect of organo-phosphate compound, dichlorvos in transgenic Drosophila melanogaster (hsp70-lacZ), induction of hsp70, antioxidant enzymes and inhibition of acetylcholinesterase, Biochem Biophys Acta, 1725, 2005, 81-92.

Helal EGE, Abd El-Wahab SM and Zedan GA, Effect of curcuma longa L. on fatty liver induced by oxytetracycline in albino rats, The Egyptian Journal of Hospital Medicine, 43, 2011, 109 – 120.

Hogberg HT, Kinsner-Ovaskainen A, Hartung T, Coecke S and Bal-Price AK, Gene expression as a sensitive endpoint to evaluate cell differentiation and maturation of the developing central nervous system in primary cultures of rat cerebellar granule cells (CGCs) exposed to pesticides. Toxicology and Applied Pharmacology 235, 2009, 268–286.

Ibrahim NA and El-Gamal BA, Effect of Diazinon, an Organophosphate Insecticide, on Plasma Lipid Constituents in Experimental Animals, Journal of Biochemistry and Molecular Biology, 36(5), 2003, 499-504.

Imran A, Ashrafa M, Omera MO, Rasheed MA and Irfana HM, Effect of Malathion on Serum Cholinesterase Activity and Lipid Profile in Rabbits, IJAVMS, 4(2), 2010, 36-37.

Jain S, Rains J and Jones K, Effect of Curcumin on protein glycosylation, lipid peroxidation, and oxygen radical generation in human red blood cells exposed to high glucose levels, Free radical Biol, And Med, 41, 2006, 92-96.

Kalender S, Kalender Y, Durak D, Ogutcu A, Uzunhisarcikli M, Cevrimli B.S and Yildirim M, Methyl parathion induced nephrotoxicity in male rats and protective role of vitamins C and E. Pestic, Biochem, Phys, 88 (2), 2007, 213–218.

Kalender S, Ogutcu A, Uzunhisarcikli M.A, Ikgoz F, Durak D, Ulusoy Y and Kalender Y, Diazinon-induced hepatotoxicity and protective effect of vitamin E on some biochemical indices and ultrastructural changes. Toxicology, 211(3), 2005, 197–206.

Kaur G, Tirkey S, Bharrhan V, Chanans and Chopra K, Inhibition of oxidative stress and cytokine activity by curcumin in amelioration endotoxin induced experimental hepatotoxicity in rodent. Clinical and Experimental Immunol, 145, 2006, 313-321.

Kim M and Kim Y, Hypocholesterolemic effects of curcumin via up-regulation of cholesterol 7a-hydroxylase in rats fed a high fat diet, Nutr Res Pract, 4(3), 2010, 191-195.

Kumar SV, Fareedullah M, Sudhakar Y, Venkateswarlu B and Kumar E.A, Current review on organophosphorus poisoning. Applied Science Research, 2(4), 2010, 199-215.

Lucic A, Bradamante V, Radic B, Peraica M, Domijan A, Fuchs R and Stavljenic Rukavina A, The Effect of Dichlorvos Treatment on Butyrylcholinesterase Activity and Lipid Metabolism in Rats, Arh Hig Rada Toksikol, 53, 2002, 275–282.

Meyer TW and Hostetter TH, Uremia, New England Journal of Medicine 357(13), 2007, 1316– 1325.

Muddasir B, Dhar J, Aslam Shafiqa A, Sabia Q, Tariq J and Bhavna G, Pesticide Residues In Blood Serum Samples from Inhabitants of "Dal Lake" hamlets in Jammu & Kashmir, India (2008-2010). IOSR Journal of Environmental Science, Toxicology and Food Technology 1(2), 2012, 26-31.

Murray RK, Granner DK, Mayes PA and Rodwell VW, Harpers Biochemistry 22nd Edition, Lange Medical publication, 1990.

Nuhu AA, Aliyu R, Effects of Cassia occidentalis aqueous leaf extract on biochemical markers of tissue damage in rats. Trop. J. Pharm. Res, 7(4), 2008, 1137-1142.

Ogutcu A, Suludere Z, Kalender Y, Dichlorvos-induced hepatotoxicity in rats and the protective effects of vitamins C and E. Environmental Toxicology and Pharmacology 26, 2008, 355–361.

Ogutcu A, Uzunhisarcikli M, Kalender S, Durak D, Bayrakdar F, Kalender Y, The effects of organophosphate insecticide diazinon on malondialdehyde levels and myocardial cells in rat heart tissue and protective role of vitamin E. Pestic. Biochem. Phys. 86 (2), 2006, 93–98.

Okamura A, Kamijima M, Shibata E, Ohtani K, Takagi K, Ueyama J, Watanabe Y, Omura M, Wang H, Ichihara G, Kondo T and Nakajima T, A comprehensive evaluation of the testicular toxicity of dichlorvos in Wistar rats. Toxicology, 213, 2005, 129–137.

Oral B, Guney M, Demirin H, Ozguner M, Giray S.G, Take G, Mungan T, Altuntas I, Endometrial damage and apoptosis in rats induced by dichlorvos organophosphate poisoning in rabbits. Int. J. Biochem, 16, 2006, 687- 690.

Pothitirat W, Gritsanapan W, Variation of bioactive components in Curcuma longa in Thailand. Current Science, 91 (10), 2006, 1397 – 1400.

Prakasam A, Sethupathy S and Lalitha S, Plasma and RBCs antioxidant status in occupational male pesticide sprayers. Clin. Chim. Acta 103(2), 2001, 107–112.

Purohit A, Antifertility Efficacy of Curcuma Longa (50% E to H Extract) With Special Refference to Serum Biochemistry and Fertility Test. Ancient Science of Life 18 (3&4), 1999, 192 – 194.

Raheja G and Gill K.D, Calcium homeostasis and dichlorvos induced neurotoxicity in rat brain, Mol, Cell, Biochem, 232, 2002, 13–18.

Rukavina A, The effect of dichlorvos treatment on butrylcholinesterase activity and lipid metabolism in rats, Arh. Hig. Rada Toksikol, 53, 2002, 275–282.

Rukkumani R, Aruna K, Varma P.S, Rajasekaran K.N and Menon V.P, Comparative Effects of Curcumin and Its Analog on Alcohol- and Polyunsaturated Fatty Acid-Induced Alterations in Circulatory Lipid Profiles, J Med Food 8 (2), 2005, 256–260.

Rukkumani R, Sribalasubashini M, Viswanathan P, Menon V.P, Comparative effects of curcumin and photo-irradiated curcumin on alcohol and polyunsaturated fatty acid induced hyperlipidemia, Pharmacol Res, 46, 2002, 257–264.

Ryhanen R, Herranen J, Karhonen K, Penttila I, Popvilanpi M and Puhakainen E, Relationship between serum lipids, lipoproteins and pseudocholinesterase during organophosphate poisoning in rabbits, Int. J, Biochem, 16, 1984, 687-690.

Sarah N, Oluwatosin A and Edith A, Oral administration of extract from Curcuma longa lowers blood glucose and attenuates Alloxan-Induced hyperlipidemia in diabetic rabbits. Pakistan Journal of Nutrition 8 (5), 2009, 625-628.

Sato T, Onse Y, Nagase H and Kito H, Mechanism of antimutagenicity of aquatic plant extracts against (benzo (a) yrene) in the Samonella assay .J Mut Res, 241, 1990, 283-290.

Shakibaei M, John G, Schulze-Tanzil I, Lehmann and Mobasheri, Suppression of NF-kappa B activation by curcumin leads to inhibition of expression of cyclo-oxygenase-2 and matrix metalloproteinase-9 in human articular chondrocytes: Implications for the treatment of osteoarthritis. Biochemical Pharmacol. 73, 2007, 1434-1445.

Sharma P and Singh R, Dichlorvos and lindane induced oxidative stress in rat brain: Protective effects of ginger. Pharmacognosy Res. 4(1), 2012, 27–32.

Sikora E, Scapagnini and Barbagallo, Curcumin, inflammation, ageing and age-related diseases. Immunity and Ageing 7, 2011, 1- 4.

Stinton LM and Shaffer EA, Epidemiology of gallbladder disease, cholelithiasis and cancer, Gut Liver 6, 2012, 172–187.

Storm E, Karl KR and Doull J, Occupational exposure limits for 30 organophosphate pesticides based on inhibition of red cell acetylcholinesterase. Toxicology, 150, 2000, 1–29.

Upadhyay RK, Emerging Risk Biomarkers in Cardiovascular Diseases and Disorders, Journal of Lipids, 2015, 1-50.

Ural MS and Korrucu SS, Acute toxicity of dichlorvos on Fingerling European Catfish, Silurus glanis, Bull Environ Contam Toxicol, 76, 2006, 871-876.

Uzunhisarcikli M, Kalender Y, Dirican K, Kalender S, Ogutcu A and Buyukkomurcu F, Acute, subacute and subchronic administration of methyl parathioninduced testicular damage in male rats and protective role of vitamins C and E. Pestic. Biochem. Phys, 87 (2), 2007, 115–122.

Venkatesan N, Pulmonary protective effects of curcumin against paraquat toxicity, Life Sci, 66 (2), 2000, 21 – 28.

Weiner I.D, Mitch W.E and Sands J.M, Urea and Ammonia Metabolism and the Control of Renal Nitrogen Excretion. *CJASN* 10 (11), 2015.

Yousef MI, El-Demerdash FM and Radwan F.M.E, Sodium arsenite induced biochemical perturbations in rats: Ameliorating effect of curcumin. Food and Chemical Toxicology, 46, 2008, 3506–3511.

Yousef MI, Awad TI and Mohamed E.H, Deltamethrin-induced oxidative damage and biochemical alterations in rat and its attenuation by vitamin E. Toxicology 227(3), 2006, 240–247.

Yurumez Y, Ikizceli I, Sozuer E.M, Soyuer I, Yavuz Y, Avsarogullari L and Durukan P, Effect of Interleukin-10 on Tissue Damage Caused by Organophosphate Poisonin, Basic & Clinical Pharmacology & Toxicology 100, 2007, 323–327.

Yurumez Y, Yavuz YS, Ahin OC, Iftci IH, Ozkan S and Buyukokuroglu M.E, Can diphenhydramine prevent organophosphate-induced acute pancreatitis? An experimental study in rats. Pestic, Biochem, Phys, 87, 2007, 271–275.

Zaahkouk SAM, Helal EGE, Abd-Rabo TEI and Rashed SZA, Carbamate toxicity and protective effect of vit. A and vit, E on some biochemical aspects of male zilli Gerv, J. Environ. Sci, Health, 32, 2000, 2585–2598.