Research Article

Protective role of Vitamin E: on diazinon-induced hepatotoxicity by biochemical and histological alterations in Wistar rats

D. Damodar[1], Urban John D'Souza[2], Shankar Bhat[3]

[1]Department of Physiology, KVG Medical College & Hospital, Sullia, Karnataka India,
[2]Faculty of Medicine & Health Sciences, Universiti Malaysia Sabah, Malaysia
[3]Department of Physiology, Yenepoya University, Karnataka, India

Correspondence to: Urban John D'Souza, E-mail: dsouzaurbanjohn@gmail.com

Received June 23, 2015. Accepted August 8, 2015

Abstract

Background: Pesticides are developed for welfare of human beings, though they impose and challenge our existence by their long-term toxicity. Organophosphates such as diazinon contain phosphorus and derivatives of phosphoric acids. **Aims and Objectives:** To evaluate the toxic effects of diazinon in separate lower doses on hepatotoxicity and possible ameliorative properties of vitamin E on diazinon-induced alterations on biochemical and histological parameters on liver functions. **Materials and Methods:** Toxic effects of diazinon, dose levels 0 mg, 6 mg, 7.5 mg, and 10 mg/kg body weight daily orally for 30 days and ameliorative effect of vitamin E (2 mg) on diazinon-induced biochemical and histological alterations were investigated in Wistar albino male rats. The serum was used to evaluate the level of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), alkaline phosphatase (ALP), cholesterol, triglyceride, total protein, albumin, and malondialdehyde (MDA). Liver paraffin sections were cut into 5 μm thickness and stained with hematoxylin and eosin for light microscopic examination. **Results:** Diazinon resulted in an increase in MDA level significantly, decrease in albumin, total protein, cholesterol levels, and rise in AST and ALT levels. LDH and ALP levels were elevated significantly ($p < 0.001$). Hepatocytes showed pyknotic changes in nucleus, ballooning degeneration (fatty changes), periportal inflammation and Kupffer cells hyperplasia in diazinon-treated groups. Pretreatment of the rats with vitamin E showed an insignificant protection in diazinon-induced liver damage. **Conclusion:** In conclusion, this study suggests that diazinon induces hepatotoxicity in low doses and vitamin E partly ameliorates biochemical and histological alterations induced by diazinon.

KEY WORDS: Diazinon; hepatotoxicity; vitamin E; rats; liver histology

Introduction

In present time, chemicals and compounds accumulated or daily exposed to humans are harmful in many ways. Pesticides are used for welfare of human beings, but they present us a challenge in form of toxicity sooner or later. They can be directly exposed to us or indirectly through food chain. Indiscriminate use of pesticides is on increase. Length and breadth of world, is one of the largest user of agricultural pesticides such as organophosphates, carbamates etc. Please rephrase for sense.Pesticides are toxic compounds to all living organisms; however, their effects vary with species to species. But excessive use of these pesticides creates many problems to all of us. These days, synthetic chemical pesticides are in practice because of their active and best results. But their excessive use causes serious damage to ecosystem—terrestrial as well as aquatic and consequently the flora and fauna of surrounding. Hence, the exposure to these pesticides may involve large sectors of population, which include agriculture workers and their families, besides the general population who may be exposed through home application of pesticides or

Access this article online	
Website: http://www.njppp.com	Quick Response Code:
DOI: 10.5455/njppp.2015.5.2306201569	

residues on food.[1,2] Accidental exposure to pesticides at the work place and their presence in the environment has aroused concern over their possible adverse effects on human health.

Organophosphates such as diazinon contain phosphorus and derivatives of phosphoric acids.[3] They inhibit the enzymatic activity of acetylcholine esterase (AChE), the key enzyme that hydrolyzes the neurotransmitter acetylcholine. Inhibition of acetylcholine esterase results in the accumulation of acetylcholine that overstimulates cholinergic receptors, which in turn stimulates biological disturbances in the organism, including increased sweating, salivation, bronchoconstriction, bronchial secretion, increased gastrointestinal motility, tremors, diarrhea, and muscular twitching.[4–7]

A number of chemicals have been reported to cause severe biochemical and histological alterations, which sometimes become difficult to manage by medical therapies. It is important for us to find substances that can be used for better management of the biochemical and histological disturbances. Anti-oxidants constitute the primary defense system that limits the toxicity associated with free radicals. Several experimental reports have shown that vitamins could ameliorate pesticide toxicity.[8,9] Vitamin E has long been recognized as being the major lipid soluble, chain-breaking antioxidant that has the ability to quench free radicals from initiating peroxidative tissue injury.[10] Thus, this study was conducted to investigate the effect of vitamin E administration on some biochemical parameters and histology of liver in male Wistar rats exposed to diazinon.

Materials and Methods

Diazinon (o, o-diethylo-2-isopropyl-6 methylpyrimidine-4-yl phosphorothioate) of 99% purity was generously provided by Devidayal Agro Chemicals Mumbai, India. Vitamin E (α-tocopherol) was purchased from Sigma Chemical Co.

Animals and Treatment

Adult male Wistar albino rats weighing approximately 200–230 gm obtained from the KVG Medical College, Sullia, India, animal house were used. The rats were maintained in polypropylene cages with paddy husk bedding under the laboratory conditions of 28 ± 2 °C temperature for two weeks for acclimatization. The rats had access to food and water ad libitum. Prior to administration of test substances, rats were assigned to each group by randomization of body weights. All experimental procedures and animal maintenance were done under the guidelines of Institutional Ethic Committee for the use of animals in the experiment.

After two weeks of acclimatization, rats were randomly divided as follows (n= 6):

Group I: 0 mg Diazinon/kg body weight
Group II: Vitamin E (2 mg)/animal/day
Group III: 6 mg Diazinon/kg body weight
Group IV: 7.5 mg Diazinon/kg body weight
Group V: 10 mg Diazinon/kg body weight
Group VI: 6 mg Diazinon + 2 mg vitamin E
Group VII: 7.5 mg Diazinon + 2 mg vitamin E
Group VIII: 10 mg Diazinon + 2 mg vitamin E

Each non-fasted rat received the appropriate dose in the morning between 10:00 and 11:00 h by oral gavage. The exact dosage for each rat was corrected for individual body weight every third day by appropriate volume adjustment. The control group received 1 ml saline once in a day and treatment Groups III, IV, V received diazinon single dose daily for 30 days. To Groups VI, VII, VIII rats, vitamin E in 2 mg/animal/day was administered through gavage for a continuous period of seven days followed by vitamin E (2 mg) + diazinon 6 mg, or 7.5 mg or 10 mg/kg body weight for 30 days. Rats were sacrificed after 24 h of last treatment day by cervical dislocation. Blood was collected and centrifuged to obtain serum. Liver was quickly removed and fixed in Bouin's fluid, processed in series of graded ethanol and embedded in paraffin for histology. Paraffin sections were cut into 5 μm thickness and stained with hematoxylin and eosin for light microscopic examination. The serum was used to evaluate the level of serum malondialdehyde (TBARS), aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), alkaline phosphatase (ALP), cholesterol, triglyceride, total protein and albumin.

Statistical Analysis

Statistical analyses were based on comparing the data among the control, diazinon, and diazinon plus vitamin E-treated groups. Data are expressed as Mean ± SD. The statistical significance was determined using one-way analysis of variance followed by Bonferroni test. The level of significance was $p < 0.05$.

Results

Effects of Diazinon and Vitamin E on Serum MDA level

The diazinon administration highly significantly ($p < 0.001$) increased oxidative stress in a dose-dependent manner as indicated by enhanced malondialdehyde (MDA) production [Figure 1] when compared to control. The MDA level is significantly higher in rats given 10 mg diazinon when compared to 6 or 7.5 mg group. In rats given diazinon plus vitamin E, the MDA level insignificantly reduced when compared to diazinon-treated groups; however, it was significantly higher in rats given 7.5 and 10 mg diazinon plus vitamin compared to control and the group give vitamin E alone [Figure 2].

Effects of Diazinon and Vitamin E on Serum Alkaline Phosphatase Level

Activities of alkaline phosphatase showed a significant ($p < 0.001$) increase in all the three tested doses of diazinon in rats when compared to control. It was also revealed that there was significant ($p < 0.001$) increase in alkaline phosphatase level in 7.5 mg/kg and

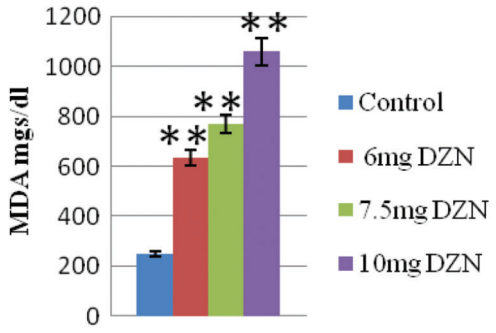

Figure 1: Effect of on Serum MDA (mg/dl) level. Control vs 6 mg or 7.5 mg or 10 mg/kg = $^{**}p < 0.001$. 6 mg/kg vs 10 mg/kg = $p < 0.001$; 7.5 mg/kg vs10 mg/kg = $p < 0.001$.

10 mg/kg diazinon-treated rats when compared to 6 mg diazinon-administered rats [Figure 3].

The alkaline phosphatase activity significantly ($p > 0.001$) increased in all vitamin E plus diazinon-treated groups when compared to vitamin E and control group [Figure 4].

Effects of Diazinon and Vitamin E on serum Lactate Dehydrogenase (LDH) level

Exposure of rats to diazinon was also shown by this study to cause a significant ($p < 0.001$) increase in serum LDH level compared with control group [Figure 5].

The LDH activity was significantly ($p > 0.001$) higher in all vitamin E plus diazinon-treated groups when compared to vitamin E and control group [Figure 6].

Effects of Diazinon and Vitamin E on Serum Total Proteins and Albumin level

This study on serum total proteins showed significant decrease ($p < 0.001$) in diazinon (7.5 mg or 10 mg/kg) exposed rats when compared with control and 6 mg groups [Figure 7]. There was a significant ($p < 0.05$) increase in diazinon plus vitamin E groups when compared to control groups [Figure 8].

Albumin level significantly ($p < 0.05$) reduced in all rats exposed to diazinon when compared to control [Figure 9]. There was no statistical significant change in vitamin E plus

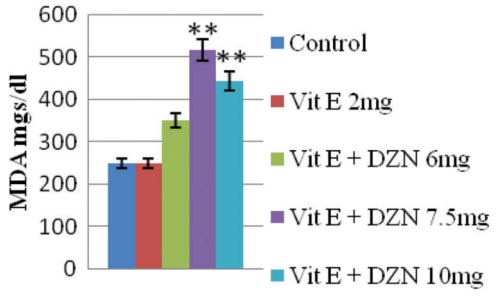

Figure 2: Effect of vitamin E and diazinon on serum MDA (mg/dl) level. Control vs Vit E + DZN (7.5 mg or 10 mg/kg) = $^{**}p < 0.001$. Vit E vs Vit E + DZN (7.5 mg or 10 mg/kg) = $p < 0.001$.

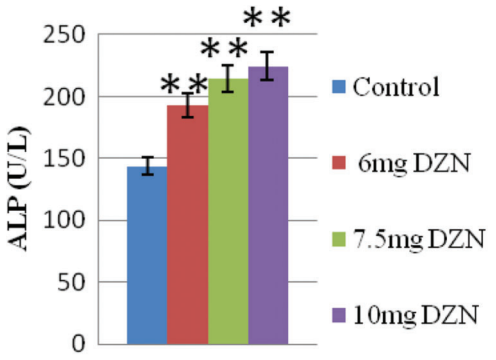

Figure 3: Effect of diazinon on serum ALP (U/L) level. Control vs 6 mg/kg or 7.5 mg, or 10 mg/kg = $^{**}p < 0.001$. 6 mg/kg vs 7.5 mg, 10 mg/kg = $p < 0.001$.

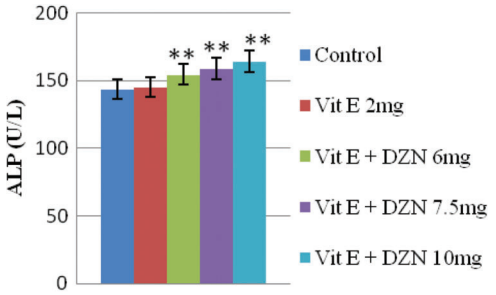

Figure 4: Effect of diazinon and vitamin E on serum ALP (U/L) level. Control vs Vit E + DZN (6 mg, 7.5 mg, or 10 mg/kg) = $^{**}p < 0.001$. Vit E vs Vit E + DZN (7.5 mg or 10 mg/kg) = $p < 0.001$.

diazinon-treated groups when compared with control or vitamin E-treated groups [Figure 10].

Effects of Diazinon and Vitamin E on Aminotransferase (ALT, AST) enzymes

Administration of diazinon for 30 days resulted in increase in the values of serum ALT and AST, which were significantly different from control group. The ALT level increased sig-

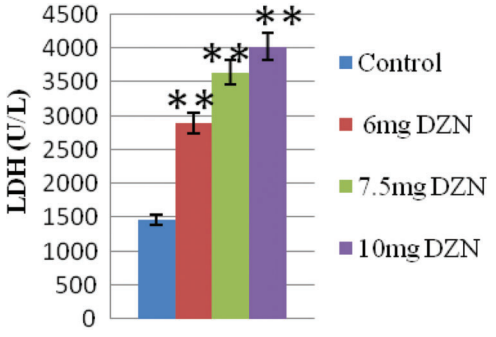

Figure 5: Effect of diazinon on serum LDH (U/L) level ($n = 6$). Control vs 6 mg or 7.5 mg or 10 mg = $^{**}p < 0.001$. 6 mg vs 10 mg/kg = $p < 0.001$.

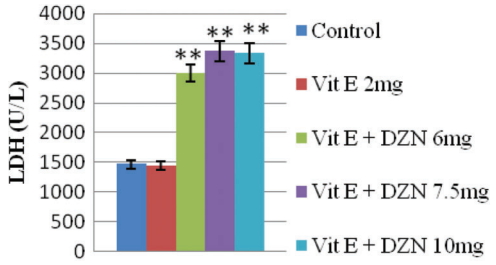

Figure 6: Effect of diazinon and vitamin E on serum LDH (U/L) level (n = 6). Control vs Vit E + DZN (6 mg, 7.5 mg, or 10 mg/kg) = **$p < 0.001$. Vit E vs Vit E + DZN (6 mg, 7.5 mg, or 10 mg/kg) = $p < 0.001$.

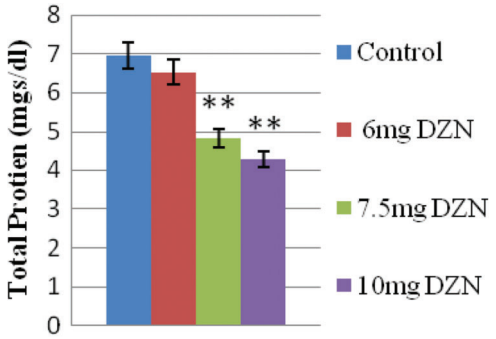

Figure 7: Effect of diazinon on serum total protein (mgs/dl) level. Control vs 7.5 mg, 10 mg/kg =** $p < 0.001$. 6 mg v/s 7.5 mg, 10 mg/kg = $p < 0.001$.

nificantly ($p < 0.05$) in all rats treated with diazinon (7.5 mg) and marked increase ($p < 0.001$) in rats exposed to 10 mg/kg diazinon. Additionally, the ALT activity statistically increased ($p < 0.001$) in diazinon (10 mg/kg)-exposed rats when compared to 6 mg or 7.5 mg/kg body weight group [Figure 11].

In comparison with control group, significant increase ($p < 0.05$) of ALT level was recorded in diazinon (6 mg and 7.5 mg) plus vitamin E rats, while this parameter was markedly elevated ($p < 0.001$) in 10 mg/kg diazinon plus vitamin-treated

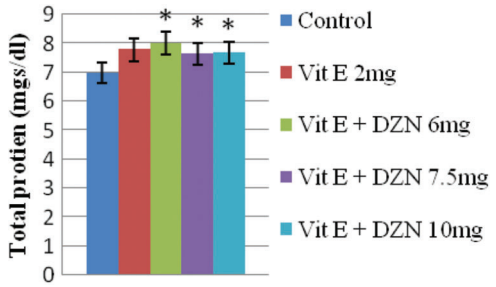

Figure 8: Effect of diazinon and vitamin E on serum total protien (mgs/dl) level. Control vs Vit E + DZN (6 mg, 7.5 mg, or 10 mg/kg) = *$p < 0.05$.

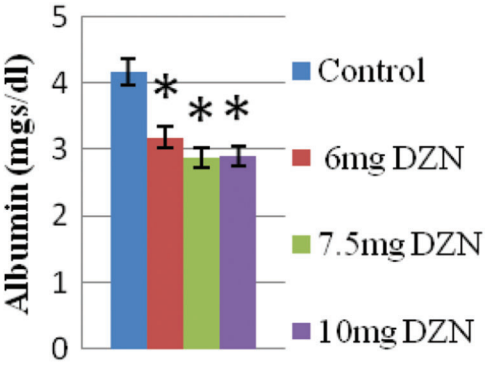

Figure 9: Effect of diazinon on serum albumin (mgs/dl) level. Control vs DZN (6 mg, 7.5 mg, or 10 mg/kg) = *$p < 0.05$.

rats [Figure 12].

AST level was significantly increased ($p < 0.05$) with diazinon (7.5 mg or 10 mg) when compared to control. Rats treated with vitamin E plus diazinon (10 mg/kg) showed significant increase ($p < 0.05$) in AST level when compared with control and vitamin E [Figures 13 and 14].

Effects of Diazinon and Vitamin E on Serum cholesterol and Triglyceride level

Exposure of rats to low doses of diazinon was also shown by this study to cause alteration in the levels of serum cholesterol and triglyceride. The cholesterol level significantly ($p < 0.001$) decreased after 30 days exposure of diazinon (6 mg or 7.5 mg or 10 mg) when compared to control group [Figure 15].

Rats treated with vitamin E plus diazinon observed significant decrease ($p < 0.001$) in cholesterol level when compared with control and vitamin E [Figure 16].

There was a significant increase ($p < 0.001$) in triglyceride level in 10 mg/kg diazinon-treated rats when compared with diazinon (6 mg or 7.5 mg)-treated rats [Figure 17]. Rats treated with vitamin E plus diazinon did not show any significant changes [Figure 18].

Effect of Diazinon and Vitamin E on Histology of Liver

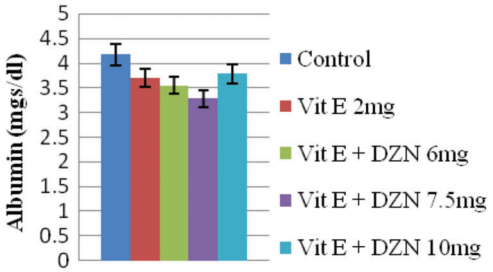

Figure 10: Effect of diazinon and vitamin E on serum total protien (mgs/dl) level. Control vs Vit E + DZN (6 mg, 7.5 mg, or 10 mg/kg) = *$p < 0.05$.

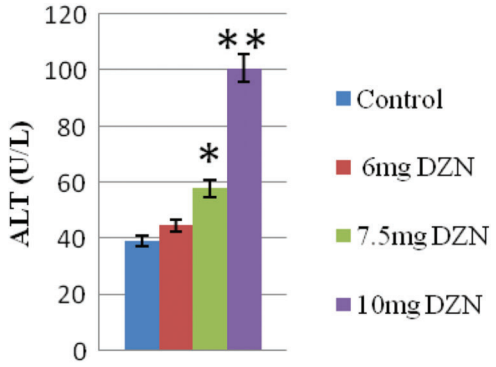

Figure 11: Effect of diazinon on serum ALT (U/L) level. Control vs 7.5 mg/kg = $*p < 0.05$; control vs 10 mg/kg = $**p < 0.001$. 6 mg vs 10 mg/kg = $p < 0.001$; 7.5 mg vs 10 mg/kg = $p < 0.001$.

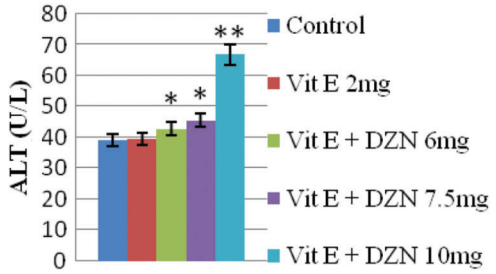

Figure 12: Effect of diazinon and vitamin E on serum ALT (U/L) level. Control vs 6 mg or 7.5 mg = $*p < 0.05$; 10 mg/kg = $**\ p < 0.001$. Vit E vs Vit E + DZN (10 mg/kg) = $p < 0.001$.

Diazinon induced pyknotic changes in nucleus, ballooning degeneration (fatty changes), periportal inflammation, and Kupffer cells hyperplasia [Figures 18, 19 and 22]. Several serial sections showed development of large fat globules, which occasionally displaced the nucleus of the hepatocytes [Figure 21] and bile stasis within biliary canaliculi [Figure 20]. These effects were seen in a dose dependent pattern.

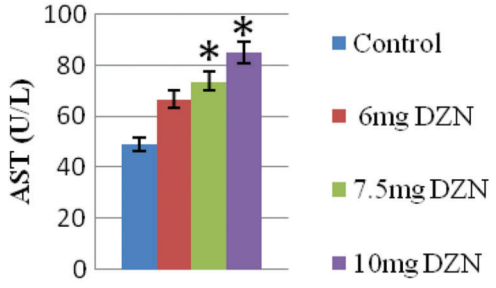

Figure 13: Effect of diazinon on serum AST (U/L) level. Control vs 7.5 mg and 10 mg/kg = $*p < 0.05$.

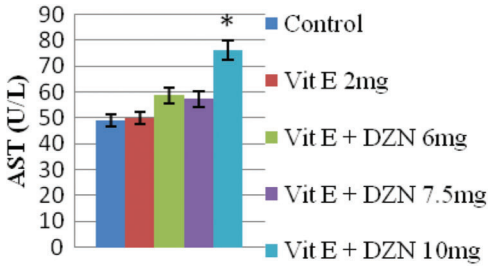

Figure 14: Effect of diazinon and vitamin E on serum AST (U/L) level. Control vs Vit E + 10 mg/kg DZN = $*p < 0.05$.

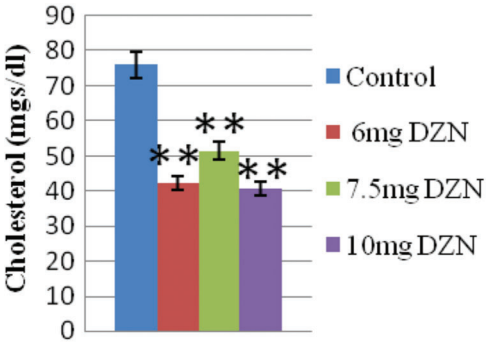

Figure 15: Effect of diazinon on serum cholesterol (mg/dl) level. Control vs 6 mg, 7.5 mg, and 10 mg/kg DZN = $**p < 0.001$.

Discussion

In this study, Figure 1 has shown that diazinon treatment at low doses for 30 days results in a significant increase in serum MDA concentration. Levels of MDA, a major oxidation product of peroxidized polyunsaturated fatty acids, have been considered as an important indicator of lipid peroxidation.[11] Generation of oxidative stress and consequent lipid peroxidation by pesticides is reported in many species. Several drugs, xenobiotics, and environmental pollutants are known to cause imbalance between formation and removal of free radicals. An elevation of lipid peroxidation in serum, as evidenced by increased production of MDA in this study, suggests participation of free

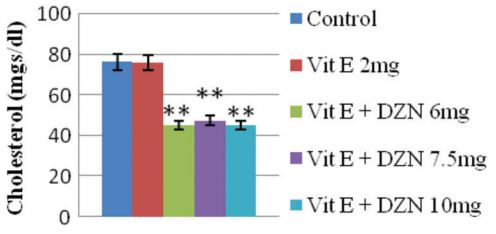

Figure 16: Effect of vitamin E and diazinon on serum cholesterol (mg/dl) level. Control vs Vit E + DZN (6 mg, 7.5 mg, and 10 mg/kg) = $**p < 0.001$. Vit E vs Vit E + DZN (6 mg, 7.5 mg, or 10 mg/kg) = $p < 0.001$.

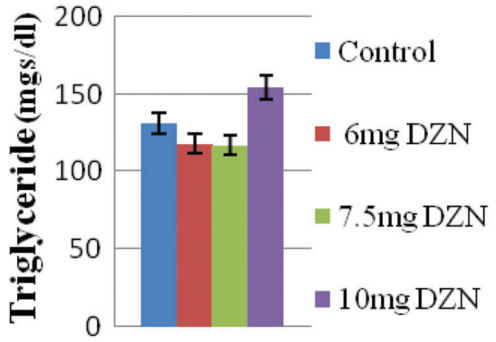

Figure 17: Effect of diazinon on serum triglyceride (mg/dl) level. 6 mg vs 10 mg/kg = $p < 0.001$; 7.5 mg vs 10 mg/kg = $p < 0.001$.

radical-induced oxidative cell injury in mediating the toxicity of diazinon. Our results are in agreement with the studies of El-Shenawy et al.,[12] Ogutcu et al.,[13] Altuntas et al.,[14] and Gokalp et al.,[15] who demonstrated a significant increase in lipid peroxidation level of rat liver, erythrocytes, pancreas, and heart by diazinon treatment. An elevation in lipidperoxidation caused by other pesticides in different experiments has also been reported; Methoxychlor,[16] endosulfan,[17] and 2,3,7,8-tetrachlorobenzo-P-dioxin(TCDD),[18] malathion, and dimethoate.[19]

Liver is a target organ and primary site of detoxification and is generally the major site of intense metabolism and is therefore prone to various disorders as a consequence of exposure to the toxins of extrinsic as well as intrinsic forms. Liver plays an important role in metabolism to maintain energy level and structural stability of body.[20] It is also the site of biotransformation by which a toxic compound transforms into a less harmful form to reduce toxicity. However, this will damage the liver cells and produce hepatotoxicity.

Liver function tests are a group of blood tests that can help to show how well a liver is working. The liver function tests include measurements of total protein, albumin, and various hepatic-specific enzymes such as ALT, AST, ALP, and levels of cholesterol, triglycerides, etc.

The present investigation indicates that oral administration of sublethal doses of diazinon to rats caused significant alterations in haematobiochemical and histopathological parameters. The levels of total protein and albumin statistically decreased, while the activities of AST, ALT, ALP, and LDH

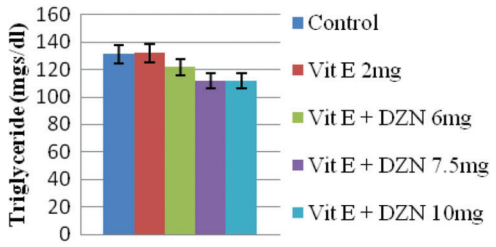

Figure 18: Effect of vitamin E and diazinon on serum triglyceride (mg/dl) level.

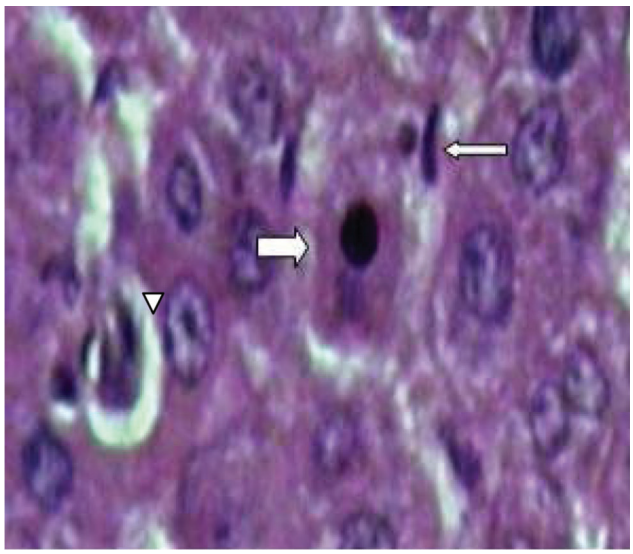

Figure 19: Hepatocytes showing Pyknotic Nucleus (Thick Arrow), hyperplasia of Kupffer cells (Thin Arrow) and fatty degeneration (Triangle) (original magnification X40).

significantly increased. These results are in agreement with different previous researches, which indicated that exposure to diazinon and other organophosphates induces severe physiological and biochemical disturbances in experimental animals.[21,22]

Exposure to an organophosphate insecticide, such as diazinon, may disturb total protein and albumin metabolism. Albumin is synthesized by the liver. Albumin level might decrease according to liver function disorders after diazinon treatment.[23] As a matter of fact, free radicals can damage DNA and proteins, either through oxidation of DNA bases (primarily

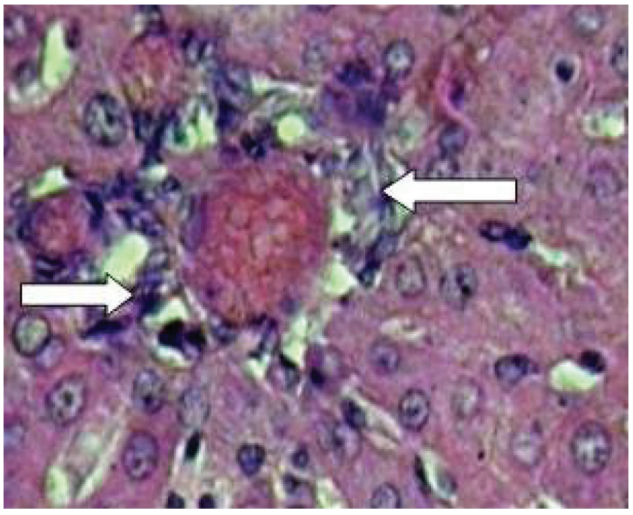

Figure 20: Dilated central vein and focal area of inflammatory cell infiltrate (arrow) (original magnification X40).

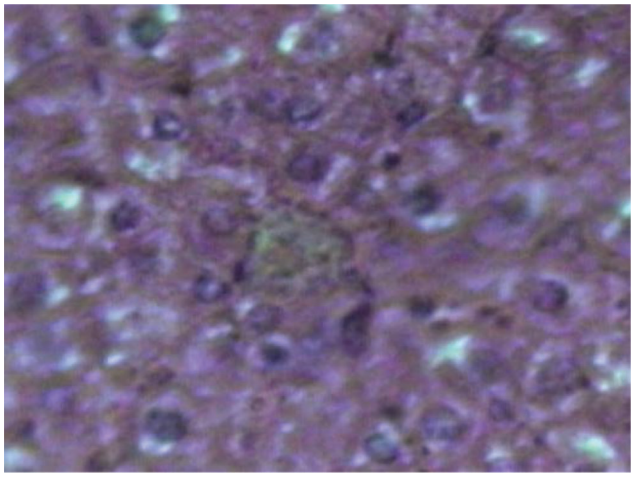

Figure 21: Showing hepatocytes and bile stasis within bile canaliculi (original magnification X40)

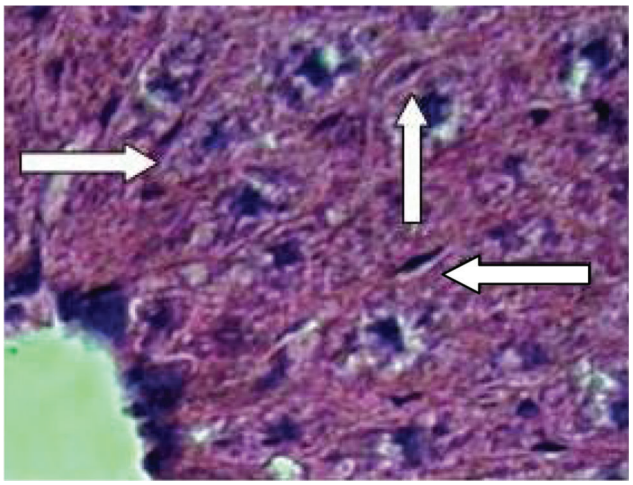

Figure 23: Effect of vitamin plus diazinon on liver showing extensive Kupffer cell hyperplasia changes (arrow) (original magnification X40)

guanine via lipid peroxyl or alkoxyl radicals) or through covalent binding to DNA resulting in strand breaks and cross linking. ROS can also induce oxidation of critical Sulfhydril (SH) groups in proteins and DNA, which will alter cellular integrity and function.[24] Exposure to organophosphorus has been shown to inhibit all the cytoplasmic proteases and some of the lysosomal proteases in the liver tissues.[25]

Diazinon caused prominent increase in AST, ALT, ALP, and LDH enzymes activities as reported by Gomes et al.,[21] Gokcimen et al.,[26] and El-Shenawy et al.[27] These enzyme level alterations might differ dependent on exposure time, dose, mode, and form of test compound (pure, technical or formulated preparations) of administration.[28] These observations suggest that increased serum hepatic-specific enzyme activities are associated with hepatic degeneration and are secreted into the blood after hepatocellular injury.[26] The liver cells are the sites of toxic action of diazinon,[24] which affect mitochondrial membrane transportation in liver[29,30,18] and cause swelling of mitochondria in hepatocytes,[23] resulting in increase of liver enzymes. The present increases of serum ALT, AST, and ALP in rats exposed to diazinon could be taken as an index of liver damage. Liver histopathological examination in our study also confirms these findings. However, several studies showed that these enzymes increased in human and experimental animals subjected to different pesticides including diazinon.[31–33] Lactate dehydrogenase (LDH) is an enzyme present in a wide variety of organisms, including plants and animals. It catalyzes the interconversion of pyruvate and lactate with concomitant interconversion of NADH and NAD+. As it can also catalyze the oxidation of hydroxybutyrate, it is occasionally called hydroxybutyrate dehydrogenase (HBD). Lactate dehydrogenase is a widespread cytosolic enzyme present in almost all body tissues. The LDH estimation serves as a good indicator of cytotoxicity.[34]

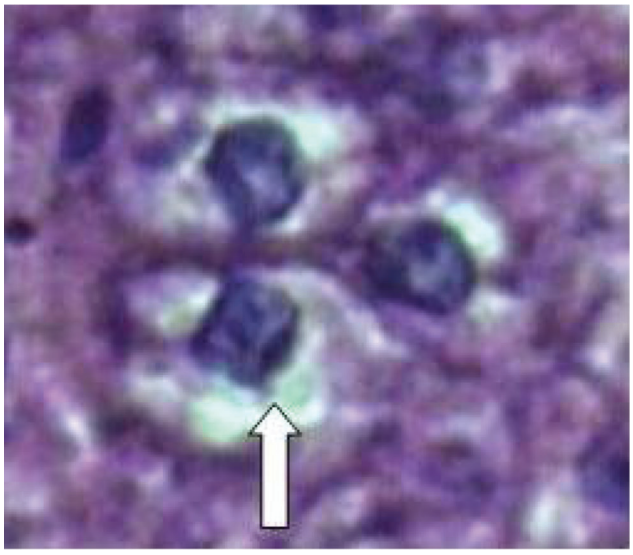

Figure 22: Hepatocytes Showing ballooning and fatty degeneration with nucleus of few cells pushed to the periphery (Arrow) (original magnification X40)

Generally, high concentrations of LDH are found in the liver, testes, skeletal muscles, and kidneys. Consequently, toxicity to those organs associated with significant elevation in serum LDH activity.[35] Additionally, high-serum LDH activity has also been reported in a variety of cancers.[36] The present increase in LDH level could be attributed to the injury induced by diazinon in vital organs such as liver of rats. These results are consistent with several previous experimental studies.[31,37]

In this study, serum total cholesterol was significantly decreased with all three doses (6 mg, 7.5 mg, 10 mg/kg) of diazinon treated for 30 days. Similar hypocholesterolaemia was previously reported in the serum of experimental animals that were treated with various insecticides, including acephate,[38] dichlorvos,[39] and diazinon.[40] These results are also

coincident with those of El-Zayat et al.[41] who reported significant reduction in cholesterol level in rats treated with deltamethrin. On the other hand, other insecticides have been reported to produce a rise in serum total cholesterol. These included methomyl[42] dialdrin,[43] and furadon.[44]

This study also showed a slight but insignificant change in the plasma levels of triglyceride. This finding is similar to Nagi et al.[40] Many earlier studies confirmed an increase in the level of plasma triglyceride in the experimental animals that were exposed to different insecticides including dichlorvos,[39] and carbamate furadon.[44] This increased level of plasma triglyceride has been attributed to an inhibition of the lipase enzyme activity of both the hepatic triglyceride and plasma lipoproteins.[45,46] On the other hand, the decrease in plasma triglyceride that was observed previously in rats treated with acephate may be a reflection of the organophosphate-induced reduction of this lipid fraction in all lipoprotein classes, particularly LDL.[38] It is therefore possible to suggest that the present insignificant change in plasma triglyceride could possibly be due to the absence of an interaction of the insecticides in the previously mentioned mechanisms.

Organophosphorus insecticides are known to induce various histopathological changes in the liver tissues.[26,47]. Confirming to the literature, indeed we found by light microscopic analyses that diazinon induced pyknotic changes in nucleus, ballooning degeneration (fatty changes), periportal inflammation, and Kupffer cells hyperplasia (Figure). Several serial sections showed development of large fat globules, which occasionally displaced the nucleus of the hepatocytes. These effects were seen in a dose-dependent pattern. These changes are entirely consistent with the changes in various biochemical parameters that were also observed such as oxidative stress markers. Such liver damage may arise from the toxic effects of diazinon, which disturbs the detoxification mechanism of liver causing, thereby, a disturbance in metabolic activity. In addition, it is possible that like other insecticides, diazinon adversely affects the cytochrome P450 system or the mitochondrial membrane transport system of hepatocytes.[26] Prominent fatty changes with necrosis in portal areas indicated that some toxic metabolites may be transported from intestine to liver, resulting in these changes. The presence of definite necrosis indicated capability of the toxic metabolites causing cell death.[48] Lipid accumulation is a common hepatic response to toxic agents such as carbon tetrachloride,[54] phosphorous,[50] and chlorinated hydrocarbon insecticides.[51] It has reported that increase in ROS can cause the destruction of all cellular structures including membrane lipid.

Effect of Vitamin E on Diazinon-Induced Hepatotoxicity

In our study, co-administration of vitamin E with diazinon to rats resulted in insignificant improvement of the liver enzyme activities when compared to that which received diazinon alone. Treatment with vitamin E was not reversed all of examined biochemical indices as well as histopathological changes induced by diazinon. Administration of 2 mg vitamin E produces insignificant antihepatotoxicity effects in diazinon-treated rats. Aldana et al. (2001) Altuntas et al.[8] observed that vitamin E did not show effect on some biochemical indices. Moreover, our light microscopic analyses revealed that the diazinon-treated rats that received vitamin E exhibited the hepatic morphological alterations seen in the liver of the diazinon-treated rats, but to a lesser extent. Kalender et al.[23] and Nahla et al.[27] revealed histopathological changes in liver tissues of rats exposed with diazinon and the severity of the lesions was reduced by the administration of vitamin E. Previously many studies have also shown the protective effect of vitamin E against several organophosphates.[52–54]

Conclusion

From our results, we can assume that hepatotoxic effects of sublethal doses of 99% pure diazinon were mainly attributed to oxidative stress increase since MDA level was largely increased and the effects were not sufficiently prevented by 2 mg/day vitamin E supplementation.

Acknowledgments

Authors acknowledge the help of Prof K.V. Chidananda, Medical Director and Prof Sheela Nayak, Principal of KVG Medical College, Sullia for their constant support and encouragement.

References

1. Lu C, Fenske RA, Simox NJ, Kalman D. Environ Res Sect A. 2000;84:290–302.
2. Quandt SA, Arcury TA, Roa P, Snively BM, Camann DE, Doran AM, et al. Environ Health Perspect. 2004;112(3):382–7.
3. Matsumura SA, Refaie AA, Nada SA. *Toxicology of Insecticides,* 2nd edn. New York: Plenum Press, p. 598.
4. Gallo MA, Lawryk NJ. Organic phosphorus pesticides In: *Handbook of Pesticide Toxicology,* San Diego, CA: Academic Press, pp. 917–1123.
5. Cabello G, Valenzuela M, Vilaxa A. Environ Health Perspect 2001;109(5):471–79.
6. Farag AT, El Okazy AM, El Aswed AF. Reproduct Toxicol 2003; 17(2):203–08.
7. Bomser JA, Quistad GB, Casida JE. Toxicol Appl Pharmacol 2002;178:29–36.
8. Altuntas L, Delibas N. Turk J Med Sci 2002;32:293–7.
9. Yavuz T, Delibas N, Yildrim B, Altuntas L, Chandri O. Arch Toxicol 2004;78:655–9.
10. Verma RS, Mehta A, Srivastava N. Pest Biochem Physiol 2007;88: 191–6.
11. Kalender S, Kalender Y, Ogutcu A, Uzunhisarcikli M, Durak D, Acikgoz F. Toxicology 2004;3:227–35.
12. El-Shenawy NS, El-Salmy F, Al-Eisa RA, El-Ahmary B. Pest Biochem Physiol 2010;96:101–07.
13. Ogutcu A, Uzunhisarcikli M, Kalender S, Durack D, Bayrakdaa F, Kalender Y. Pest Biochem Physiol. 2006;86(2):93–8.

14. Altuntas I, Kilinc I, Orhan H, Demirel R, Koylu H, Delibas N. Hum Exp Toxicol. 2004;23:9–13.
15. Gokalp O, Buyukvani E, Cicek K, Ozer K, Koyu A, Altuntas I, Koylu H. Pest Biochem Physiol. 2005;81:123–8.
16. Latchoumycandane C, Mathur PP. Arch Toxicol 2002;76(12):692–8.
17. Kwon GS, Sohn HY, Shin KS, Kin E, Seo BJ. App Microbiol Biol 2005;67(6):845–56.
18. Latchoumycandane C, Chitra KC, Mathur PP. Arch Toxicol. 2003; 77(5):280–4.
19. John S, Kale M, Rathore N, Bhatnagar D. J Nutr Biochem 2001; 12(9):500–04.
20. Guyton AC, Hall JE. *Text Book of Medical Physiology,* 12th edn. WB Saunders, 2011, p. 783.
21. Gomes J, Dawodu AH, Lloyd O, Revitt DM, Anilal SV. Hum Exp Toxicol 1999;18:33–7.
22. Hussain AL, Jakoniuk JM. Pol. J. Environ Stud. 2005;14:199–202.
23. Kalender S, Ogutcu A, Uzunhisarcikli M, Acikgoz F, Durak D, Ulusoy Y, Kalender Y. Toxicology 2005;211:197–206.
24. Fatemeh-Teimouri, Amirkabirian N, Esmaily H, Mohammadirad A, Aliahmadi A, Abdollahi M. Human & Experimental Toxicology 2006;25:697–703.
25. Mansour MK, El-Kashoury AA, Rasheed MA, Koretem KM. Nature and Science 2009;7(2):1–12.
26. Gokcimen A, Gulle K, Demirin H, Bayram D, Kocak A. Pest Biochem Physiol 2007;87(2):103–08.
27. El-Shenawy NS, Al-Eisa RA, El-Salmy F, Salah O. Curr Zool 2009; 55(3):219–26.
28. Sarabia L, Maurer I, Bustos-Obregon E. Ecotoxicol Environ Saf 2009;72(3):938–42.
29. Kappers WA, Edwards RJ, Murray S, Boobies AR. Toxicol Appl Pharmacol 2001;177:68–76.
30. Sams C, Cocker J, Lennerd MS. Toxicol Let 2003;144:146.
31. Manna S, Bhattacharyya D, Mandal TK, Das S. J Vet Sci 2004;5:241–5.
32. Hussain AL, Jakoniuk. Pol J Environ Stud 2005;14:199–202.
33. Hermendez AF, Amparo Gomez M, Perez V, Garcia-lario JV, Pena G, Gil F, Lopez O, Rodrigo L, Pino G, Pla A. Environ Res 2006;102: 70–6.
34. Chenoufi N, Raoul Jl, Lescoat G, Brissot P, Bourguet P. J Nucl Med 1998;39:900–3.
35. Atef M Al Atter. Global J Pharmacol 2009;3(3):171–7.
36. Kanowski D, Clague A. Clin Chem 1994;40:158–9.
37. Sreenivasan P, Vijayan E. Indian J Exp Biol 1996;34:363–5.
38. Choudhari PD, Chakraharti CH. Ind J Exp Biol 1984;22:45–9.
39. Ryhanen R, Herranen J, Karhonen K, Penttila I, Popvilanpi M, Puhakainen E. Int J Biochem 1984;16:687–90.
40. Nagi A Ibrahim, Basiouny A, El-Gamal. J Biochem Mol Biol 2003; 36(5):499–504.
41. El-Zayat E, Elhalwagy MS, Farid M. J Biol Sci 2005;5(2):211–21.
42. Antal M, Bedo M, Constantinovits G, Nagy K Szepvolgyi J. Fd Cosmet Toxicol 1979;17:333–8.
43. Shakoori AR, Rasul YG, Ali SS. Folio Biol 1984;32:213–22.
44. Gupta M, Mukherjee S, Gupta SD, Dolui AK, Dey SN, Roy DK. Toxicol 1986;38:69–79.
45. Ibrahim NA, El-Gamal. J Biochem Mol Biol 2003;36(5):499–504.
46. Goldberg IJ, Paterniti JR, Ginsberg HN, Lindgren FT, Brown WV. J Clin Invest 1982;70:1184–92.
47. Morowati M. Environ Pollut 1997;96:283–8.
48. Benjamin N, Kushwah A, Sharma RK, Katiyar AK. Indian J Exp Biol 2006;44:228–32.
49. Castro JA, De Ferreyra EC, De Castro CR, Diaz Gomex MI, D'Acosta N, DeFenos OM. Toxicol Appl Pharmacol 1973;24:1–19.
50. Jacqueson A, Thevenin M, Warnet JM, Claude JR, Truhart R. Acta Pharmacol Toxicol 1977;4(11):322–9.
51. Ortega P, Hayes WJ, Durham WF. Arch Pathol Lab Sci 1957;64:614–22.
52. Kalender Y, Uzunhisarcikli M, Ogutco A, Acikgoz F, Durak D, Ulusoy Y, Kalender S. Environ Toxicol Pharmacol 2006;22(1):46–51.
53. El-Shenawy NS, Al-Eisa RA, El-Salmy F, Salah O. Curr Zool 2009; 55(3):219–26.
54. Ogutcu A, Suludere Z, Kalender Y. Environ Toxicol Pharmacol 2008;26(3):355–61.

How to cite this article: Damodar D, D'Souza UJ, Bhat S. Protective role of Vitamin E: on diazinon-induced hepatotoxicity by biochemical and histological alterations in Wistar rats. Natl J Physiol Pharm Pharmacol 2015;5:398-406.

Source of Support: Nil, **Conflict of Interest:** None declared.