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Protective Effects of Vitamin E on Albendazole Adverse Effects

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Abstract

The present study was conducted to determine the effect of albendazole alone or in combination with vitamin E on antioxidant activity and histopathological, changes on the liver and kidney. Following oral administration of albendazole of 0.25 mg/kg body weight and Vitamin E of 0.01 mg/kg body weight used for 21 successive days to broiler chicken, the experiment was done on fifteen broiler chickens divided into three groups: group one was non-treated, group two was treated with albendazole of 0.25 mg/kg body weight and group three was treated in combination with vitamin E of 0.01 mg/kg body weight. The blood sample and tissue were taken at the end of experiment 12 hrs after the last dose. The experimental result revealed that the significant decrease of liver enzymes caused by albendazole like serum Alanine Aminotransferase (ALP), Aspartate Aminotransferase (AST), Alkaline Phosphatase (ALT), when compared with the control group, the experimental result significant decrease in kidney parameters like urea creatinine level caused by albendazole and finally there was a significant increase in antioxidant enzymes activity like CAT, SOP, GPX and a significant decrease in MDA. Histopathology results in liver-treated animals with albendazole in combination with vitamin E showed dilated, congested Portal Blood Vessels (PBV, arrow), mild to moderate Biliary Proliferation (BP, arrow), portal Round Cells Aggregation (RCA, arrow), and focal Hepatocellular Degeneration (HCD, arrow). Histopathology results of kidney-treated animals with albendazole in combination with vitamin E showing a mild Per Tubular Edema (PTE arrow), focal Tubular Degeneration (TD arrow), Tubular Regeneration (TR, arrow), glomerular lobulation and atrophy (GL arrow), and beside interstitial cells aggregation (RCA arrow), H & EX 200. Therefore, vitamin E should be taken by albendazole to decrease its effect.

Keywords

Albendazole, Vitamin E, Antioxidant Enzymes

1. Introduction

Oxygen is an indispensable element for the sustenance of living beings and many biological systems. Cells reduce oxygen and generate Adenosine Triphosphate (ALP) in the mitochondria. By-products known as free radicals are created during this process. These free radicals are beneficial in moderate levels but at higher concentrations can damage tissue by oxidative stress [1]. Antioxidants have been defined as substances that prevent that the genesis of Reactive Oxygen Species (ROS) or other oxidants, and repaired the damage they cause [2]. Antioxidant defense systems act as a stable and symmetrical framework and each depends on the activity of the other. In health, the stability lies somewhat in support of the reactive species so that they can accomplish their biological roles. Repair systems protect against damage which happens at a low level in healing individuals (Hallowell, 1995). Antioxidants are molecules that prohibit the oxidation of other molecules. Oxidation reaction means that a chemical reaction transports electrons or hydrogen from a substance to an oxidizing agent. Oxidation reactions can output free radicals and in turn, these radicals can begin a chain reaction by removing free radical intermediates and prohibiting other oxidation reactions. Antioxidants are often reducing agents such as anthills, ascorbic acid or polyphenols, tocopherols and thoils [3]. The antioxidant defenses consist of a low molecular mass antioxidant such as vitamin E and enzymes, e.g., SOD, CAT, GPX. The mission of antioxidant enzymes is to protect tissues and body fluids from damage by ROS and RNS, whether produced physiologically or as a response to inflammation, infection or disease [4]. Vitamin E is an important antioxidant in biological systems that decreases the peroxidation of unstructural lipids by a chain-breaking Free Radical (FR), so it shares in the stability of cellular membranes [5]. Vitamin E (α-tocopherol) is the most important lipid-phase antioxidant. Albendazole is one of the most widely used as the anthelmintic in poultry. It is too active against most gastrointestinal and respiratory nematodes of cestodes and trematodes in poultry [6]. The metabolism of AB generates several metabolites including two major ones: Albendazole Sulfoxide, which is active, and Albendazole Sulfone, which is inactive. Albendazole Sulfoxide, the active metabolite, causes selective degeneration of cytoplasmic microtubules in intestinal and tegmental cells of intestinal helminths and larva. The metabolites bind to the β-tubulin subunit of helminths microtubules polymerization. Albendazole also causes impaired glucose utilization and causes a decrease in parasite glycogen stores. At high concentration, albendazole inhibits parasite metabolic pathways such as the Krebs cycle by inhibiting key enzymes such as malate dehydrogenase. The subsequent decrease in Alp production occurs which cause energy depletion which leads to immobilization of parasite and subsequent death [7]. This review covers key studies of the effect of albendazole in combination with vitamin E on antioxidant, then tissue and blood samples were collected and the protective effect of vitamin E on the liver and kidney appreciated through measuring biochemical constituents is sera, such as serum creatinine level, liver biomarkers

like serum Alanine Aminotransferase (ALT), Alanine Phosphatase (ALP), total proteins, albumin and oxidative stress biomarkers such as Catalase (CAT), Superoxide Dismutase (SOD) and Malondialdehyde (MDA). The obtained results show that vitamin E has protection through prohibiting the raise in liver and kidney injury biomarkers, and the current pathological result also enhances this effect.

2. Material and Methods

2.1. Drugs and Chemicals

1) Vitamin E (vitamin E. Capsule) was supplied by PHARCO pharmaceutical CO., Alex., Egypt, and vitamin E is dissolved in corn oil.

2) Albendazole 2% - 5%pharm sweet Egypt.

2.2. Animals

Fifteen broiler chickens, whose ages are about twenty-one days old, weighting about (400 gm) used in this study. All chickens were maintained under similar conditions—the chickens were housed in batteries in a post-graduate research laboratory in the faculty of veterinary medicine. Zagazig University and a balanced ration with free access to water chicken were kept for one week for accommodation conditions before beginning of Experimental.

2.3. Experimental Design

2.3.1. Chicken were Classified to 3 Group Each One Group 5 Chicken

- The first group served as control non-tread;
- The second group received the therapeutic dose of albendazole 2 - 5 mg/kg orally for 21 day following the suction of the manufacturing company;
- The third group received albendazole in combination with vitamin E in therapeutic dose orally for 21 day.

2.3.2. Preparation of Serum Sample and Tissue Sampling

Preparation of serum sample and tissue sampling was at the end of the experiment (12 hrs). After the last dose chicken was sacrificed and the following samples were collected. Blood collected from all chicken blood was taken on EDTA Coated tubes for hematological study serum separation to other samples for biochemical determination of liver function and kidney function test following necropsy tissue S specimens from liver and kidney for histopathological examination.

Biochemical markers of liver and kidney injury

Determination of serum Alanine Aminotransferase (ALT) Aspartate Aminotransferases (AST) activities was established according to the principles described previously [8], also evaluation of activity of serum Alkaline Phosphatase (ALP) was determined according to the principles mentioned before [9]. Evaluation of createnine, urea and uric acid has been done according to the method previously [10]. Determination of these parameters was carried out through commercial kits from

spectrum diagnostics.

2.3.3. Hepatic and Nephron Histopathological Evaluation

Liver and kidney tissues were fixed in 10% neutral buffered for the main solution for 24 hrs. Then, the tissue processing and paraffin blocks preparations were done. Masson's trichrome and hematoxylin eosin stains were used to evaluate circulatory disturbances, inflammation, degeneration, apoptosis, necrosis and any other pathological changes in the examined tissues according to method of [8].

2.3.4. Biochemical Markers of Antioxidant Activity

Determine the Catalase (CAT) activity, Superoxide Dismutase (SOD) activity, Glutathione Peroxidase (GPX) activity and Malondialdehyde (MDA) activity by method according to previous principles [5] [11].

2.4. Statistical Analysis

The data were analyzed using prism version 6, statistical evaluation of the result except as one way, Analysis of Variance (ANOVA).

3. Results and Discussion

Effect of albendazole on RBCs, Hb, PCV, WBCs

It was showed clearly from Table 1 that the oral administration of albendazole alone or in combination with Vitamin E in therapeutic dose for three week to broiler chicken induced significant increase in RBcs, Hb, PCV, WBcs level when compared with albendazole group (Table 1).

Effect of albendazole on serum AST, ALT, ALP

It was clearly evident from Table 2 that the oral administration of albendazole alone or in combination with vitamin E in therapeutic dose for three week to broiler chicken induced significant decrease in AST, ATP, ALT level when compared with albendazole group (Table 2).

Effect on serum Creatinine, Uric acid, it was clearly evident from Table 2 that the oral administration of albendazole alone or in combination with vitamin E in therapeutic dose for three week to broiler chicken induced significant decrease in serum Creatinine, Uric acid, level when compared with albendazole group (Table 3).

Table 1. Effect of oral administration of albendazole and its combination with vitamin E once daily for 21 successive days on serum, RBCs, Hb, PCV and WBC in broiler chickens post treatment (mean ± SE) n = 5.

Groups	RBCs (10^6/µl)	Hb (g/dl)	PCV (%)	WBC (10^3/µl)
Control	4.29 ± 0.24^c	8.13 ± 0.22^c	47.0 ± 0.31^c	152.0 ± 4.2^c
Albendazole	4.00 ± 0.36^b	7.00 ± 0.18^b	42.00 ± 0.35^b	149.00 ± 7.9^b
Albendazole + Vitamin E	5.49 ± 0.24^a	10.73 ± 0.17^a	50.00 ± 0.32^a	167.00 ± 7.8^a

*Means with the same column carrying different superscripts are significantly different at $P < 0.05$, effect of albendazole on RBcs, Hb, PCV, WBcs.

Effect of albendazole on serum protein, albumin, globulin

It was clearly evident from Table 4 bellow that the oral administration of albendazole alone or in combination with vitamin E in therapeutic dose for three week to broiler chicken induces significant decrease in serum protein, albumin, globulin, level when compared with albendazole group (Table 4).

Effect of albendazole on Serum SOD, CAD, GPX, MDA

It was clearly evident from Table 2 that the oral administration of albendazole alone or in combination with vitamin E in therapeutic dose for three week to broiler chicken induced significant decrease in SOD, CAD, GPX, and MDA levels when compared with albendazole group (Table 5).

Histopathology Result in Liver

Figure 1 showed dilated portal blood vessels (PBV), portal round cells aggregations

Table 2. Effect of oral administration of albendazole and its combination with vitamin E once daily for 21 successive days on serum AST, ALT and ALP in broiler chickens post treatment (mean ± SE) n = 5.

Groups	AST (U/L)	ALT (U/L)	ALP (U/L)
Control	35.33 ± 1.58^{c}	37.60 ± 2.70^{c}	33.00 ± 2.20^{b}
Albendazol	75.33 ± 11.40^{a}	62.36 ± 6.47^{a}	44.70 ± 2.51^{a}
Albendazol + Vitamin E	68.35 ± 3.08^{b}	42.55 ± 5.12^{b}	30.6 ± 2.70

*Means with the same column carrying different superscripts are significantly different at $P < 0.05$.

Table 3. Effect of oral administration of albendazole and its combination with vitamin E once daily for 21 successive days on serum creatinine and uric acid in broiler chickens post treatment (mean ± SE) n = 5.

Groups	Creatinine (mg/dl)	Uric acid (mg/dl)
Control	0.79 ± 0.07^{b}	3.900 ± 0.32^{b}
Albendazol	1.52 ± 0.07^{a}	4.87 ± 0.63^{a}
Albendazol + Vitamin E	0.89 ± 0.01^{c}	3.00 ± 0.33^{c}

*Means with the same column carrying different superscripts are significantly different at $P < 0.05$.

Table 4. Effect of oral administration of albendazole and its combination with vit. E once daily for 21 successive days on serum total proteins, albumin and globulins in broiler post treatment (mean ± SE) n = 5.

Groups	Total proteins (g/dl)	Albumin (g/dl)	Globulins (g/dl)
Control	7.73 ± 0.39^{c}	4.10 ± 0.35^{c}	3.21 ± 0.22^{c}
Albendazol	8.72 ± 0.63^{a}	$5.30\ 0.51^{a}$	4.10 ± 0.21^{a}
Albendazol + Vitamin E	8.11 ± 0.55^{b}	4.90 ± 0.51^{b}	3.75 ± 0.22^{b}

*Means with the same column carrying different superscripts are significantly different at $P < 0.05$.

(RCA) and biliary proliferation hyperplasia (BP). Marked interstitial round cells aggregation, hepatocellular degeneration (HCD) and individual cellular apoptosis (HCA), H&E X200, 400.

Figure 2 phtomicrograph of liver (A) (B), (G3) showed dalited, congested portal blood vessels (PBV, arrow), mild to moderate biliary proliferation (PB, arrow), portal round cells aggregation (RCA, arrow), and focal hepatocellular degeneration (HCD, arrow). H&E X200.

Histopathology Result in Kidney

Figure 3 of kidney (A) (B) (G2) showing peritubular edema (PTE, arrow), marked glomerular lobulation and atrophy (A G, arrow) interstitial round cells aggregation (RCA, arrow) and renal tubular degeneration (RTD, arrow) with focal early

Table 5. Effect of oral administration of albendazole and its combination with vitamin E once daily for 21 successive days on serum SOD, CAT, GPX and MDA in broiler chickens post treatment (mean ± SE) n = 5.

Groups	SOD (U/ML)	CAD (U/ML)	GPX (U/ML)	MDA (U/ML)
Control	33.68 −069[a]	256.21 −6.62[a]	120.33 −1.50[a]	7.45 −0.41[b]
Albendazol	27.21 −021[b]	200.00 −7.10[b]	1110.21 −2.30[b]	20.32 −0.11[b]
Albendazol + Vitamin E	30.31 −0.21[c]	240.11 −3.30[c]	118.21 −2.10[c]	9.11 −0.21[c]

*Means with the same column carrying different superscripts are significantly different at $P < 0.05$.

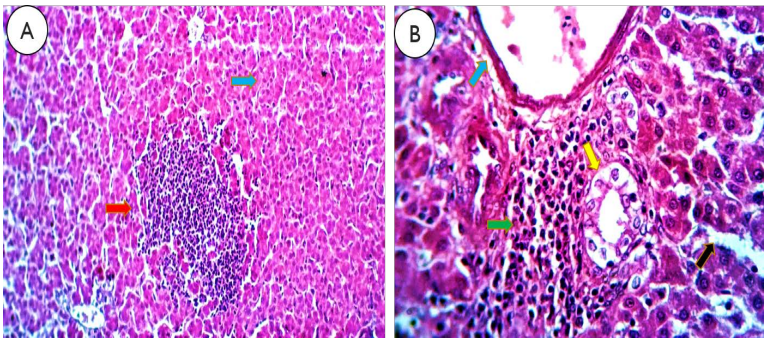

Figure 1. Livers of albendazole treated animals 21-day sacrifice.

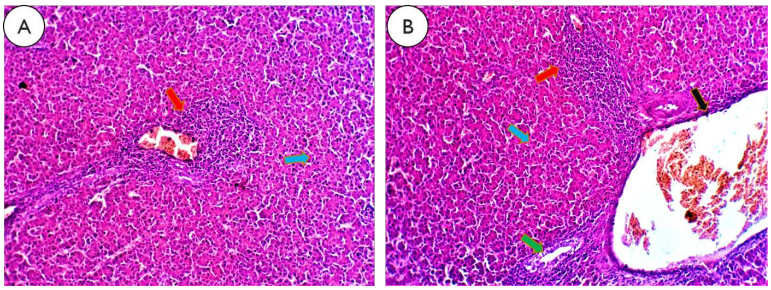

Figure 2. Livers of albendazole + Vitamin E treated animals 21-day sacrifice.

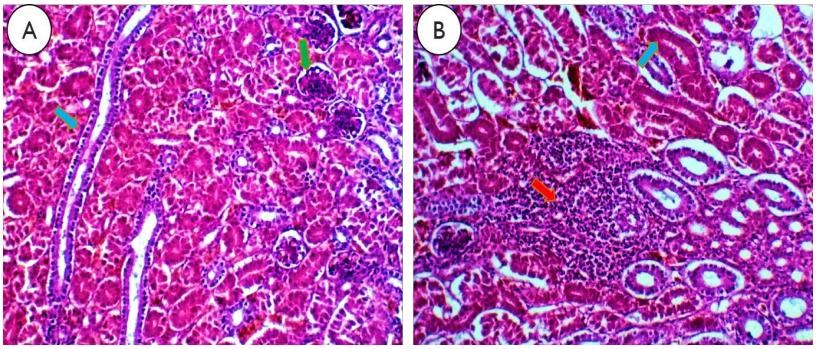

Figure 3. Kidney of albendazole treated with albendazole animals 21-day sacrificed.

necrotic changes .HXE X100, 400.

Albendazole + Vitamin E treated animal 21 day sacrifice showing Amid Peritubular Edema (PTE, arrow), focal Tubular Degeneration (TD, arrow), Tubular Regeneration (TR, arrow), Glomerular Lobulation and atrophy (GL, arrow) beside interstitial Round Cells Aggregations (RCA, arrow). H&E X200, 400.

4. Discussion

The present study conducted to investigate the effects of albendazole alone or in combination with vitamin E on broiler chicken and evaluate its impact on antioxidant enzymes and on some biochemical parameters as well as histopathological changes. The study result reported that the level of liver enzymes ALT, ATP, AST, were significant decrease when compared with albendazole group the study finding were in agreement with some previous study who reported that the antioxidant mainly using natural and synthetic. Antioxidant performs asinsible therapeutic approach for prevention and treatment of liver disease due to role of oxidative stress in contributing to initiation and progression of hepatic damage. The result reported that the level of urea and creatinine were significant decrease when compared with albendazole group. The result reported that the significant increase in antioxidant enzymes like CAT, SOD, GPX activities with significant decrease in MDA when compared with albendazole group. These results are in agreement with [9] who found that the antioxidant enzymes SOD, CAT, GPX activities in chicken were increased as lipid peroxidation levels were reduced upon supplementation with vitamin E.

5. Conclusion

It could be concluded that Vitamin E has a protective effect against hepatonephrotoxicity of albendazole which contributes to decreasing the harmful effect of albendazole by inhibiting the free radical formation and by restoration of the antioxidant system. The combination of Vitamin E and albendazole showed a better result than albendazole alone.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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