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Cytotoxic effects of Albendazole, antiparasitic drug, on the liver of the rat: Sub-chronic study

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ABSTRACT

Albendazole is one of the most important antiparasitic drugs. The present study was undertaken to evaluate the metabolic changes that could be encountered in response to Albendazole administration. Albendazole was administered orally (400 mg/kg body wt). Liver and blood samples were obtained from the control group as well as from the treated groups after 3, 6, 12, 24, 48, 96 and 192 hours post-treatment. Liver tissue was used for the determination of glutathione (GSH) content, the level of lipid peroxidation and total proteins content. The level of blood GSH was also determined, while serum samples were used for the determination of the activities of gamma glutamyl transferase (GGT), aspartate aminotransferase (AST) and alanine aminotransferase (AST). The results showed that hepatic and blood GSH content decreased significantly after 24, 48 and 96 hours post-treatment. The level of hepatic lipid peroxidation decreased significantly at 12 and 24 hours post-Albendazole administration followed by significant increase after 192 hours. Treatment with vitamin E (200 mg/kg body wt) 24 hours before Albendazole administration decreased the level of hepatic lipid peroxidation at 192 hours. This may be due to the ability of vitamin E to scavenge free radicals that might be induced by ABZ metabolites. Hepatic total protein content did not exert any significant effect. The activities of GGT increased significantly during the whole time course of the experiment. On the other hand, the activities of both AST and ALT increased significantly at 24, 48 and 96 hours after Albendazole treatment. Accordingly, it could be suggested that the depletion in hepatic glutathione (GSH) in the period from 24 to 96 hours may be due to the conjugation between ABZ and hepatic GSH and/or its involvement in the elimination of the toxic effect of ABZ metabolites. The decrease in the level of hepatic TBA-reactants at 12 and 24 hours post-treatment of ABZ could be attributed to the decrease in the metabolic rate while the increase in lipid peroxidation after 192 hours could be related to the depletion of hepatic glutathione. The significant increase in the activity of GGT could be correlated to the depletion of hepatic glutathione content. Moreover the elevation of AST and

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ALT levels could be attributed to partial cellular injury to the hepatocytes caused by Albendazole. In conclusion, although Albendazole is one of the most important antiparasitic drugs with high margin of safety, the present investigation revealed some unwanted side effects, which cannot be ignored.

KEYWORDS: Albendazole, GSH, lipid peroxidation, liver enzymes.

INTRODUCTION

Parasitic diseases caused by helminth infestation have been recognized as a major problem facing the human health and animal production especially in the developing countries. Parasites absorb the host food, suck the host blood, and damage the host tissues. Worms pathogenic for animal and human being are Metazoa conventionally classified into nematodes, trematodes, and cestodes. This biological diversity vary with respect to life cycle, structure, development, physiology, localization within the host, and susceptibility to chemotherapy.

Chemicals that can be used to remove endoparsites without undesirable effects on host animals or man are difficult to discover and develop (Prichard 1990). Various compounds have been used since the beginning of this century, in an attempt to control helminth parasites. The limited antiparasite efficacy and the large number of side effects were among the main limitations of earlier compounds (Lanusse & Prichard 1993). All drugs are capable of producing harmful as well as beneficial effects. The nature of these harmful effects falls into two mechanistic categories: (1) effects related to the principal pharmacological action of the drug, and (2) effects unrelated to the principal pharmacological action of the drug, which often involving a chemically reactive metabolite of the drug rather than the parent compound. Effects of this kind are often much more serious than unwanted effects in the first category, and include such reactions as liver, kidney damage, bone marrow suppression, carcinogensis and disordered foetal development (Rang & Dale 1991).

Anthelmintics are drugs that act either locally to expel worms from the gastrointestinal tract or systemically to eradicate adult helminths or developmental forms that invade organs and tissues (Adams 1995). The process of anthelmintic discovery and development has been particularly intensive since the introduction of Thiabendazole in 1961 (Brown *et al.* 1961). This was the first broad-spectrum anthelmintic and was the breakthrough that opened a new area in the treatment of the parasitic disease. Since then, many new drugs, in particular, those of the Benzimidazole family, have been introduced.

Benzimidazoles are anthelmintic drugs with wide range of antiparasitic action, high degree of efficacy, good margin of safety (Adams 1995). Of several hundred synthesized compounds, the few selected for further development on the basis of overall safety and effectiveness include Albendazole (ABZ) and other related compounds (Marriner *et al.* 1986).

ABZ is a nematocidal drug, used for pinworm infection, ascariasis, and trichuriasis. It is also the drug of choice in treatment of hydatid disease and an alternative drug in cysticercosis. Albendazole is unique in having therapeutic activity against adult forms of *Fasciola hepatica* and *Fasciola magna*. However, ABZ may affect the normal biochemical and physiological parameters of the treated host

(Marriner *et al.* 1986). Following oral administration, ABZ is oxidized to sulphoxide (ABZ-SO) which has an asymmetric sulphur centre and it is the main active metabolite of ABZ. Another metabolite of ABZ is the sulphone (ABZ-SO_2) that has been suggested to have no antiparasite activity (Chinnery & Morris 1986; Velebny *et al.* 1997). However, recently Ingold *et al.* (1999) reported that ABZ-SO_2 induces extensive ultrastructural alterations and leads to the death of *Echinococcus multiocularis* metacestodes *in-vitro* in a way similar to that for ABZ-SO. Plasma ABZ was not detectable after oral administration to rabbits, indicating that rapid biotransformation to sulfoxide and/or very rapid distribution from blood into other tissues occurred (Li *et al.* 1995). The same authors mentioned that the parent drug, Albendazole, and its two metabolites were detected in liver, heart, kidney and muscle tissues over the 48 hours sampling period. On the other hand, the sulfoxide and the sulfone concentrations were high in plasma.

Since the discovery of Albendazole, some scattered reports have been published about its toxicity and side effects on the experimental animals and humans, such as hepatocellular toxicity (Morris & Smith 1987), embryolethality, teratogenicty and fetotoxicity (Delatour *et al.* 1984; Mantovani *et al.* 1995). In 1996, Deliguoro *et al.* published a very interesting paper. They reported that ABZ metabolites (sulphoxide and sulphone) were found in high levels (1-4 mg/kg) in milk collected from sheep within 24 hours after treatment. Products derived from such milk also contained high concentrations of the two oxidized metabolities. They also confirmed the need for careful control to ensure adherence to the prescribed withdrawal time (3 days) after the use of ABZ in lactating sheep owing to the known toxicity of the ABZ-SO. Cristofol *et al.* (1997) mentioned that a significant correlation was found between rate of developmental toxicity and ABZ metabolite concentration, and ABZ-SO embryo concentrations could be the main factor accounting for toxicity. In the same respect, Sotelo & Jang (1998) reported that when ABZ is given orally, it is rapidly and extensively metabolised to ABZ-SO, which is considered to be the metabolite directly or indirectly responsible for both toxicity and efficacy outside the gastrointestinal tract.

The increasing usage of Albendazole as a broad spectrum anthelmintic drug in both humans and domestic animals show the need of more studies about its pathophysiological effects. The rational of this study is to investigate the possible side effects (cytotoxicity) of ABZ on the liver of the rat. Measuring some specific enzymes for 8 days following oral administration of the drug into rats monitored liver function, the main site of ABZ metabolism. Also, the possibility of formation of free radicals in the hepatocytes that induced by the reactive metabolites of the drug have been investigated through the measurement of the levels of lipid peroxidation and glutathione (GSH) contents.

MATERIALS AND METHODS

Drugs

Albendazole (Methyl 5 -propylthio-1 H -benzimidazol-2-YL carbamate) is a broad spectrum anthelmintic developed as a veterinary product in 1975. It was obtained from Pfizer Egypt Company as 1.9 % suspension (Valbazen)®. Vitamin E (100 mg) gelatine capsules, was purchased from Pharco Pharmaceuticals Company, Egypt.

Animals and Experiments

Male Sprague-Dawly rats (175-200 g) were obtained from the breeding unit of National Research Center, Dokki, Giza, Egypt. Rats were housed six per cage in a well ventillated room (25 ± 2°C) and 12 hours light / dark cycle at the animal house of Zoology Department, Suez Canal University, Ismailia, Egypt. Animals were regularly fed on a standard diet *ad-libitum*.

A total of 84 animals were divided randomly into 14 groups (6 rats/group). The first seven groups were administered Albendazole (400 mg/kg body wt) orally using gastric tube. The other seven groups were considered as their corresponding controls and injected with the vehicle (distilled water) orally at the same times as Albendazole treated groups. Blood samples were collected using orbital sinus technique (Sanford, 1954) from the seven treated and seven control groups after 3, 6, 12, 24, 48, 96 and 192 hours post-treatment respectively. Heparinized blood was used in the determination of blood glutathione according to the method of Beutler *et al.* (1963). On the other hand the activities of the specific liver enzymes: gamma glutamyl transferase (GGT), aspartate amino transferase (AST) and alanine amino transferase (ALT) were measured in serum using kits obtained from Biomerieux kits (Laboratory reagent and instrument, France) and UV-Visible spectrophotometer (Shimadzu-1601-PC, Japan).

After collection of blood samples rats were decapitated then the livers were rapidly removed after the same time points (3, 6, 12, 24, 48, 96 and 192 hours) and perfused with cold 0.15 M KCl, then blotted between filter papers. Liver was homgenized with 5ml of 0.15 M KCl on ice using glass homogenizer and the homogenate was used for the determination of liver glutathione (Beutler *et al.* 1963), lipid peroxidation which was based on the measurement of thiobarbituric acid (TBA) reactants according to the method of Sharma & Wadhwa (1983) and total proteins content using Biomeriux kit (Laboratory reagent and instrument, France).

The present study aimed to use one of the most important exogenous antioxidant, vitamin E, in combination with ABZ to get more information about the cytotoxic effects of the drug. For studying the effect of Albendazole in rats pre-treated with vitamin E, 36 rats were divided into two main groups. Each group was subdivided into 3 sub-groups (6 rats/group). The first three sub-groups were only treated with vitamin E (200 mg/kg) orally using gastric tube and considered as positive control. The second three sub-groups were orally given vitamin E (200 mg/kg) 24 hours before the oral administration of ABZ (400 mg/kg Body wt). All rats were killed after 24, 48 and 192 hours from injection. Liver lipid peroxidation level was measured in the liver homogenate for all animals as described above.

Statistical analysis

Data represented as mean ± SEM of 6 animals for each group. Applying Student's unpaired *t*-test according to Snedecor (1956) did statistical comparison of the tested parameters between the control and the drug treated groups. Groups differences were considered statistically significant at the level of $P < 0.05$.

RESULTS

Liver and blood glutathione (GSH)

Liver and blood glutlathione (GSH) content in control and Albendazole treated groups are represented in Tables (1 & 2). After 24, 48 and 96 hours of Albendazole treatment,

liver GSH content was significantly decreased with percentage of change equal to 50.0, 50.1 and 41.7 respectively. Also, blood GSH level was significantly fall with percentage values of 29, 36.8 and 28.2 at the same time intervals as compared to their corresponding controls. It was observed that the lowest GSH levels were recorded after 48 hours in both liver and blood of the treated animals and it was returned back to almost the same values of the control after 192 hours post- treatment.

Table (1): Effect of oral administration of Albendazole (400 mg/kg) on rat's liver glutathione content (nmol/g fresh tissue).

Time (hours)	Control	Treated	% of change
3 hr.	2551±43.1[a]	2710±19.0	+ 6.20
6 hr.	2551±42.2	2320±47.1	- 9.10
12 hr.	2550±43.0	2538±47.5	- 1.00
24 hr.	2548±42.8	1262±22.4*	- 50.0
48 hr.	2547±43.0	1269±79.1*	- 50.1
96 hr.	2547±43.8	1486±22.4*	- 41.7
192 hr.	2550±43.8	2632±88.9	+ 3.20

[a] Represents the mean values ± S.E. from 6 rats/group.
* Significantly different compared to the control animals, student's unpaired t-test ($P<0.05$).

Table (2): Effect of oral administration of Albendazole (400 mg/kg) on the level of blood glutathione (nmol/ml) of rat.

Time (hours)	Control	Treated	% of change
3 hr.	3622±82.3[a]	3885±82.1	+ 7.30
6 hr.	3619±83.9	3342±72.9	- 7.70
12 hr.	3619±82.8	3638±96.1	+ 0.50
24 hr.	3620±82.9	2577±11.2*	- 29.0
48 hr.	3617±81.8	2285±73.2*	- 36.8
96 hr.	3570±87.6	2560±19.4*	- 28.2
192 hr.	3600±70.2	3724±105	+ 3.40

[a] Represents the mean values ± S.E. from 6 rats/group.
* Significantly different compared to the control animals, student's unpaired t-test ($P<0.05$).

Liver lipid peroxidation (LP)

Results in Table (3) illustrate the level of liver LP in control and Albendazole-treated groups at different time intervals of the experiment. It was noticed that the level of LP was significantly decreased with values equal to 34.9% and 34.3% after 12 hours and 24 hours post-treatment respectively as compared to the control values. However, LP level was elevated significantly with a percentage of change equal to 130 higher than the control animals after 192 hours of Albendazole treatment.

To study more the mechanism underlying the observed changes in the LP values as a result of Albendazole administration an exogenous antioxidant, vitamine E, have been injected 24 hours before the drug. Data in Table (4) show the comparison between the effects of oral administration of Albendazole alone and the combination of the drug and vitamin E on the level of liver LP after 24, 48 and 192 hours post-treatment. Vitamin E pre-treatment caused a significant decrease in the level of LP and the most

significant change (- 53.2%) was recorded after 192 in comparison with Albendazole-treated group only. It is very important to mention that there was no significant differences in the LP values of rats treated with vitamin E alone (200 mg/kg) compared to the control animals (injected with the vehicle).

Table (3): Effect of oral administration of Albendazole (400 mg/kg) on the level of lipid peroxidation (thiobarbituric acid reactants TBA) in rat's liver.

Time (hours)	TBA Control	TBA Treated	% of change
3 hr.	0.065±0.005[a]	0.060±0.005	- 7.70
6 hr.	0.064±0.005	0.062±0.002	- 3.10
12 hr.	0.063±0.004	0.041±0.008*	- 34.9
24 hr.	0.064±0.005	0.042±0.006*	- 34.3
48 hr.	0.065±0.005	0.064±0.005	- 1.50
96 hr.	0.065±0.004	0.059±0.005	- 9.50
192 hr.	0.066±0.004	0.152±0.013*	+ 130

[a] Represents the mean values ± S.E. from 6 rats/group.
* Significantly different compared to the control animals, student's unpaired t-test (P<0.05).

Table (4): Effect of oral administration of Albendazole (400 mg/kg) on the level of liver lipid peroxidation in rats pre-treated with vitamin E (200 mg/kg).

Time (hours)	Control	Treated (Alb.)	% of change	Treated (Vit. E + Alb.)	% of change
24 hr.	0.064±0.005[a]	0.042±0.006*	- 34.3	0.052±0.002	+ 23.8
48 hr.	0.065±0.005	0.064±0.005	- 1.50	0.035±0.004 **	- 45.3
192 hr.	0.066±0.004	0.152±0.013*	+ 130	0.071±0.010 **	- 53.2

[a] Represents the mean values ± S.E. from 6 rats/group.
* Significantly different compared to the control animals, student's unpaired *t*-test (P<0.05).
** Significantly different compared to Albendazole treated group, student's unpaired *t*-test (P<0.05).

Liver total protein content

The data obtained from Table (5) indicated that liver total proteins content changed non-significantly during the whole time course of experiment in the treated animals.

Table (5): Effect of oral administration of Albendazole (400 mg/kg) on the liver total proteins content (mg/g tissue) of rat.

Time (hours)	Control	Treated	% of change
3 hr.	0.353±0.011[a]	0.353±0.017	0.0
6 hr.	0.353±0.011	0.294±0.015	- 5.9
12 hr.	0.353±0.011	0.339±0.030	- 1.4
24 hr.	0.353±0.011	0.348±0.030	- 0.5
48 hr.	0.353±0.011	0.359±0.013	+ 0.6
96 hr.	0.352±0.011	0.405±0.011	+ 5.3
192 hr.	0.352±0.011	0.445±0.021	+ 9.3

[a] Represents the mean values ± S.E. from 6 rats/group.

DISCUSSION

The widespread development of drug resistance, particularly in parasites of some domestic animals, is a major factor responsible for the overwhelming and extensive use of some broad-spectrum anthelmintic drug to overcome the therapeutic failure in parasite control. However, this requires sustainable and more careful investigations related to the main aspects of this important subject, and one of them of course is the pathophysiological effects of such drugs.

Albendazole is a benzimidazole anthelmintic drug used in the treatment of helminthiases in animals and man. The present study was undertaken to investigate and monitor the effects of ABZ on liver glutathione content, the level of liver lipid peroxidation, liver total proteins content and the activities of GGT, AST and ALT in rat's serum, for 8 days following oral treatment with a single dose (400 mg/kg).

The high levels of GSH in many animal and plant cells suggest that it may have important biological functions. GSH participates in a variety of biosynthetic and detoxification reactions (Jocelyn 1972; George & Calvin 1983). The toxicity of numerous chemicals are associated with the depletion of liver GSH or may become enhanced after depletion of GSH by pre-treatment with other xenobiotics (Gary *et al.* 1987). GSH plays a critical role in many cellular processes, including the metabolism and detoxification of oxidants, metals, and other reactive electrophilic compounds of both endogenous and exogenous origin (Lee *et al.* 1998).

The protective role of GSH against the effect of ABZ has not been evaluated before. The results of the present study showed a significant decrease in hepatic GSH content after 24, 48 and 96 hours from ABZ administration. These results correlate well with the data obtained for blood GSH which is decreased significantly at the same time points. Depletion of liver GSH and/or involvement of blood GSH as a nucleophilic scavenger of the reactive metabolites of ABZ might be the main causes for the significant fall in blood GSH values. Ballatori & Rebbeor (1998) mentioned that the liver is the major site of GSH synthesis, and GSH released at high rates into both blood plasma and bile. They also added that nearly half of the GSH released by rat hepatocytes is transported across the canalicular membrane into bile. It functions as a driving force for bile secretion and plays an important role in hepatic detoxification of drugs, metals, and other reactive compounds of both endogenous and exogenous origin, The reminder of the GSH is released across the sinusoidal membrane into blood plasma for delivery to other tissues. As mentioned before that ABZ is biotransformed rapidly to its active metabolite (ABZ-SO) which might cause an oxidative stress state in the host's liver leading to depletion of GSH in the first four days following treatment. The results also showed that GSH was returned back to almost the same value of the control after 8 days in Albendazole-treated rats. This could be attributed to the capability of mammalian cells to resynthesize GSH after the depletion of GSH. This finding was in agreement with Lertratanangkoon *et al.* (1997).

Glutathione depletion renders the animal more susceptible to free radicals-mediated damages, especially the damage induced by cellular lipid peroxidation. It has been observed that glutathione depletion is accompanied by an increase in the amount of TBA- reactants (lipid peroxidation) in experimental animals (Mellaro *et al.* 1990; Moustafa 1998). In contrast, there was a significant decrease in the level of hepatic lipid peroxidation after 12 and 24 hours from ABZ administration, which could be related to the reduction in the metabolic rate as one of the defense mechanisms against free

radicals. This finding was in agreement with Misra & Gorsky (1981) and Allen *et al.* (1984). Alternately, ABZ may have an effect similar to that exerted by paraquat as described by the same authors. These studies postulated that paraquat produces oxygen free radicals but does not stimulate lipid peroxidation since it diverts electrons from the pathways that are involved in lipid peroxidation. However, after 192 hours from ABZ administration the level of hepatic TBA-reactants increased significantly. This increase may be due in part to the recorded depletion in the hepatic glutathione content in the period from 12 to 96 hours post Albendazole-treatment and/or due to vitamin E deficiency in the biological membranes (Goldstein *et al.* 1970; Block 1979; Casini *et al.* 1982; Combs & Peterson 1983; Konings 1986; Burton & Traber 1990).

Vitamine E is potent natural antioxidant and it protects phospolipids of cell membrane, endoplasmic reticulum membrane and mitochondrial membrane from peroxidation damage by reacting with free radicals or reactive oxygen species (Summerfield & Tappel 1984; Dean & Cheeseman 1987). Alpha-tocopherol (vitamin E) reacts with a lipid radical to yield the alpha-tocopherol radical and a harmless fatty acid. The alpha-tocopherol radical can then be reduced to alpha-tocopherol by glutathione (Wefers & Sies 1988). In an attempt to find out the role of this natural antioxidant in minimising the harmful effect of ABZ, vitamin E (200 mg/kg) was given 24 hours pre-treatment with ABZ. The level of hepatic TBA-reactants decreased significantly in vitamin E-ABZ treated rats when compared to rats administered ABZ alone after 192 hours of treatment. The decrease in the level of hepatic TBA-reactants could describe the ability of vitamin E to scavenge free radicals induced by ABZ (especially ABZ metabolities) and thus assists in maintenance of the structure and integrity of cell membrane (Tsen & Collier 1960; Mengel 1972; Recknegal & Glende 1973; Smith *et al.* 1983; Niki *et al.* 1984; Cadenas *et al.* 1984; Fukuzawa *et al.* 1985; Liebler *et al.* 1986; Jewell *et al.* 1986).

Gamma glutamyl transferase (GGT) regulates the transport of amino acids across cell membranes by catalyzing the transfer of a glutamyl group from glutathione to a free amino acid (Rajpert *et al.* 1988). ABZ treatment induced significant increase in the activity of GGT during the whole time course of the experiment (8 days). The increase in the activity of GGT could be attributed to the depletion in hepatic glutathione content. John (1991) reported that adaptive increase in GGT occurred to restore glutathione used in the metabolism of drugs which accounts for the elevated activity assayed.

The effects of Albendazole on the levels of serum AST and ALT were also studied. There are significant increases in the activity of both enzymes after 24, 48 and 96 hours from ABZ administration. This moderate increase in the values of AST and ALT could be ascribed to the mild damage in the hepatocyte plasma membrane due to ABZ treatment leading to the release of the cytoplasmic AST and ALT into the circulation (Nalpas *et al.* 1986). The present results were also in agreement with Davis *et al.* (1989) who stated that the most common side effect of ABZ is the increase in the serum aminotransferases (AST, ALT) activities and the drug is not recommended for patients with hepatic cirrhosis. However, it was observed that the activities of (GGT, AST and ALT) almost returned to the control range after 192 hours post-treatment with ABZ. This suggests that the effect of ABZ could be temporary and transient on the host's liver.

In conclusion, although Albendazole is one of the most important antiparasitic drugs with high margin of safety, the present investigation revealed some unwanted side

effects, which cannot be ignored. Also, it can be suggested that further investigations are needed to establish the possible role of vitamin E as an exogenous antioxidant in mitigating the oxidative stress induced by ABZ metabolites.

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الملخص العربى

بعض الدلائل على التأثيرات الخلوية السامة لعقار الأبندازول (عقار مضاد للطفيليات) على كبد الفئران

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يعتبر الألبندازول واحداً من أهم العقاقير المضادة للطفيليات. وقد صممت هذه الدراسة لتقييم التغيرات الأيضية التى يمكن أن تحدث فى خلايا كبد الفئران نتيجة لحقن الأبندازول بجرعة واحدة (٤٠٠ مجم/كجم) عن طريق الفم. وقد أخذت عينات الدم والكبد من كل من حيوانات المجموعات الضابطة والموجموعات المعالجة بالعقار بعد ٣ ، ٦ ، ١٢ ، ٢٤ ، ٤٨ ، ٩٦ ، ١٩٢ ساعة من المعالجة. واستخدمت خلايا الكبد فى تعيين محتوى الجلوتاثيون ومستوى أكسدة الدهون وكذلك محتوى البروتين الكلي. وتم أيضا قياس محتوى الجلوتاثيون فى الدم، بينما تم فصل المصل لتعيين نشاطات بعض الإنزيمات الكبدية الهامة مثل الجاما جلوتامين ترانسفيريز والأسبرتيت أمينوترانسفيريز والألانين أمينوترانسفيريز. وقد أوضحت نتائج البحث أن محتوى الجلوتاثيون فى الكبد والدم قد أنخفض إنخفاضاً معنويا بعد ٢٤ ، ٤٨ ، ٩٦ ساعة من المعالجة بالعقار. كذلك إنخفض مستوى أكسدة الدهون فى الكبد بعد ١٢ ، ٢٤ ساعة ولكنه عاد وارتفع إرتفاعا معنويا كبيراً بعد ١٩٢ من المعالجة بالألبندازول. وقد أعطيت مادة طبيعية مضادة للأكسدة وهى فيتامين E (٢٠٠ مجم/كجم) لمجموعة أخرى من الفئران قبل المعالجة بالألبندازول بـ ٢٤ ساعة مما أدى إلى حدوث إنخفاض كبير فى مستوى أكسدة الدهون في الكبد بعد ١٩٢ وذلك مقارنة بالحيوانات المعالجة بالعقار فقط. وهذا التأثير من الممكن أن يكون له علاقة على قدرة فيتامين E على القضاء على نواتج الأكسدة الضارة والتي تنتج من أكسدة الألبندازول

أثناء عملية الأيض الخاصة به والتي تتم في كبد العائل. كما سّجلت زيادة معنوية في نشاط إنزيم GGT طوال فترة التجربة (١٩٢ ساعة) وكذلك إرتفعت مستويات أنشطة إنزيمي AST & ALT ولكن بعد ٢٤ ، ٤٨ ، ٩٦ ساعة من المعالجة بالألبندازول.

مما سبق نستنتج أن الإنخفاض المعنوي في محتوى الجلوتاثيون في الكبد والدم من الممكن أن يكون له علاقة بإستهلاكه في التفاعلات الخاصة بإزالة الآثار السامة للعقاقير والمواد الكيميائية والملوثات والتي يلعب فيها الجلوتاثيون دوراً أساسياً وحيوياً وأن الزيادة الكبيرة في مستوى أكسدة الدهون في الكبد بعد ١٩٢ ساعة من المعالجة يرتبط إرتباطاً وثيقاً بإنخفاض محتوى الجلوتاثيون. كذلك فإن زيادة نشاطات الإنزيمات التي تم قياسها في مصل الفئران المعالجة ربما يرجع إلى إصابة الخلايا الكبدية بنواتج أكسدة الألبندازول مما نتج عنه تحلل جزئي في بعض أنسجة وخلايا الكبد حيث عادت مستويات أنشطة هذه الإنزيمات مرة أخرى إلى قيم المجموعات الضابطة في نهاية زمن التجربة.

وقد أوضحت هذه الدراسة أنه بالرغم من أن عقار الألبندازول أحد أهم العقاقير المضادة للطفيليات إلا أن له بعض التأثيرات الجانبية وبالأخص على مستوى الخلية والتي لا يمكن تجاهلها عند إستخدام هذا العقار.