# Biomarkers Of Aflatoxin B1 Oxidative Damage And The Role Of Curcumin As An Antidotal Therapy

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## ABSTRACT

This study was carried out to spot light on the different biomarkers caused by aflatoxin B1 oxidative damage, in order to get an early diagnosis, and study the effect of curcumin as a model used as an antidotal therapy to reduce or even ameliorate the oxidative damage induced by aflatoxin B1. Forty apparently healthy male adult albino rats weighing 120-150 gm were divided into four equal groups, the 1st group was orally administered 250 µg/kg Body weight aflatoxin B1 using stomach gavage, the 2nd group was orally administered 250 µg/kg body weight in combination with 200 mg/kg body weight Curcumin, the 3rd group was orally administered 200 mg/kg body weight Curcumin, while the fourth group was administered distilled water and kept as negative control group. Rats in all groups were administered 10 oral doses for two weeks (5 successive doses /week). Serum samples were obtained to estimate different biochemical parameters including antioxidant enzymes (CAT, GSH, GRH, SOD) ,liver markers enzymes (GOT, GPT, and ALT) , MDA a marker of lipid oxidative damage, and carbonyl and thiol groups of protein a marker of protein oxidative damage.

The results revealed that aflatoxin B1 induced a significant decrease of serum antioxidant enzymes, and significant increase of liver markers enzymes, MDA level, and carbonyl and thiol groups of protein. Generally, Curcumin administration caused significant alteration on all parameters toward nearly normal level, although Curcumin administration alone caused no significant changes in all parameters level when compared to the control group.

## INTRODUCTION

Aflatoxin B1 is the most prevalent and carcinogenic form of the aflatoxins, and classified as a Group I carcinogen *(1)*.Several reports have suggested that aflatoxin B1-mediated toxicity may be due to production of intracellular reactive oxygen species (ROS) during the metabolic processing of aflatoxin B1 by cytochrome P450 in the liver *(2)*. Negative effects of aflatoxin B1 include cell damage, release of free radicals and lipid peroxidation which plays a major role in the toxicity of aflatoxin B1 *(3)*.

Aflatoxin B1-treated rats by dose of 25 µg /rat (150-180gram) /day orally for 90 days showed significant increase in the activities of serum ALT and AST enzymes, while GSH, SOD, CAT and GSH-Px enzymes were significantly decreased, when compared with the control group *(4)*.

SGOT, SGPT and SALP levels were elevated, while hepatic GSH was significantly lowered, with an increase in the tissue malondialdehyde (MDA) level, an indirect index of lipid peroxidation after AFB1 I/P injection in rats with a single dose of 1.5 mg/ kg *(5)*.

Iron-induced liver injury in rats after daily i.p. injections of ferric nitrilotriacetate (FeNTA) in the dose of 9 mg Fe for 2 days and 12 mg Fe for the following 2 days resulted in remarkable increase in liver MDA. Treatment with Curcumin (100 mg/kg b.w 3 days before and concurrently with iron administration) for 8 days succeeded to normalize the elevated hepatic MDA level *(6)*.

Turmeric, a spice common to India and its surrounding regions, is derived from the rhizome of *Curcuma Longa*. The use of turmeric as a medicinal compound dates back to around 2000 B.C. when it was used as an anti-inflammatory

agent. Fractions of turmeric known as curcuminoids (curcumin, demethoxycurcumin, and bisdemethoxycurcumin) are considered the active compounds and possess a yellowish orange color *(7)*. Most of curcumin's cellular effects are an outcome of its redox characteristics; the phenolic OH groups seem to be the most important moiety in curcumin. Replacement of this group inhibits or eliminates lipid peroxidation and scavenging free radical *(8)*.

A wide variety of effects of curcumin are mediated by its capability to act as a free radical scavenger, to alter gene expression of various stress protein and genes involved in angiogenesis, and to inhibit activity of many important transcription factors such as nuclear factor κ-light-chain-enhancer of activated B cells (NF-κB) and activator protein 1 (AP-1) *(9)*.

Rats treated with curcumin (200 mg/kg BW) along with Aflatoxin B1 (25 µg /rat (150-180gram) /day orally for 90 days), revealed that the activities of serum ALT and AST enzymes were significantly decreased, while GSH, SOD, CAT and GSH-Px activities were increased when compared with AFB1 treated group *(4)*. Administration of Curcumin (50mg/kg b.w.) orally for 10 days after or before paracetamol administration tends to bring the GSH, SOD , GPx, CAT, GR level and serum and hepatic Pr-SH (protein thiol) to near normal *(10)*.

AST and ALT activities in rats treated with *curcuma longa linn.* extract (100 mg/kg intragluteally.) every day for 2weeks followed by carbon tetrachloride treatment three hours after the final treatment , were lowered than that of the non-treated group *(11)*.

Treatment of mice (6-7 weeks, 30 gram body weight) by with Phenytoin as hepatotoxic drug (300 mg/kg body weight) orally for 3 weeks, increased the level of malondialdehyde due to lipid peroxidation. This induction was significantly decreased by the use of curcumin 200 mg/kg body weight in combination with Phenytoin *(12)*.

## MATERIAL AND METHODS

### Material:-

**Aflatoxin B1** pure powder from *Aspergillus Flavus* was purchased from Sigma-Aldrich (USA) the compound is soluble in water and polar organic solvents.

**Curcumin** was purchased from BIO BASIC INC. Company is a water soluble yellow colored polyphenol; it is the active principle of *Curcuma longa.*

### Experimental animals

In this study a forty apparently healthy male adult albino rats weighing 120-150 gm were used .They were obtained from Lab. animal colonies –ministry of public health, Helwan, Animals were housed in metallic cages (10 rats/cage) and acclimatized for 2 weeks to the laboratory condition before starting the experiment. The hygienic condition was kept constant throughout the experimental period; Food and water were offered *ad libtium.* The normal day light was only used.

### Grouping, dosing, and samples

Rats were divided into four groups each of 10 rats, the 1st group was orally administered 250 µg/kg Body weight Aflatoxin B1 using stomach gavage, the 2nd group was orally administered 250 µg/kg (1/4 LD50) body weight in combination with 200 mg/kg body weight Curcumin (**13**), the 3rd group was orally administered 200 mg/kg body weight Curcumin administration with either Curcumin , AFB1 or both was 5 successive doses /week for two weeks. While the fourth group was administered distilled water only and kept as a control group.

Blood samples were taken 24 hours after the last treatment from the orbital venous plexuses using a capillary tube the collected samples were left to clot at room temperature then centrifuged for about 20 minutes at 3000 r.p.m to obtain clear serum. The sera were labeled and stored in deep freezer at -20C until used for the biochemical analysis.

## Methods

**1.Determination of serum antioxidant enzymes (Superoxide Dismutase, Glutathione Peroxidase, Glutathione Reductase, Catalase).**

Superoxide Dismutase *(14),* glutathione Peroxidase *(15),* glutathione reductase *(16),* and catalase *(17)* were determined spectrophotometrically using ready-made kits of molecular probes company, Egypt.

**2.Determination of serum alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase level.**

Alanine aminotransferase (glutamate pyruvate transaminase) *(18),* aspartate aminotransferase (glutamate oxaloacetate transaminase) *(19),* and alkaline phosphatase *(20)* were determined colorimetrically using readymade kits of Vitro Scient Company, Egypt.

**3.Determination of serum malondialdhyde.**

Serum Malondialdhyde was determined spectrophotometerically using ready-made kits of molecular probes company, Egypt *(21).*

**4.Determination of serum thiol and Carbonyl groups of protein.**

Serum thiol *(22)* and carbonyl groups *(23)* were determined spectrophotometerically using readymade kits of molecular probes company, and Cayman chemical company, Egypt.

**5.Statistical analysis**

The results are expressed as mean±standard deviation (SD). Differences between groups were assessed by one-way ANOVA analysis using the SPSS software package for Windows. Significance at P-values $\leq 0.001, \leq 0.01, \leq 0.05$ have been given respective symbols in the tables.

## RESULTS

Serum antioxidant enzymes (Superoxide dismutase, Glutathione reductase, Glutathione peroxidase, and Catalase) were significantly reduced after oral administration of aflatoxin B1 (250µg/kg body weight) for 2 weeks, this reduction was significantly decreased when curcumin was administered in a dose of 200 mg /kg body weight orally for 2 weeks in combination with aflatoxin B1, but the decrease did not reach the level of the control group. Although curcumin administration alone caused no significant changes in antioxidant enzymes level when compared to the control group (Table 1).

**Table 1. Effect of AFB1 (250 µg /kg body weight), AFB1 with Curcumin (250 µg /kg and 200 mg /kg body weight), and Curcumin alone (200 mg /kg body weight) for 2 weeks (5 successive doses /week) on serum antioxidant enzymes of adult male albino rats.**

| Group / Parameter | Control | 1st group | 2nd group | 3rd group |
|---|---|---|---|---|
| | | Aflatoxin B1 | Aflatoxin B1 with Curcumin | Curcumin |
| Superoxide Dismutase (IU/ml) | 0.17 [a] ±0.006 | 0.05 [d] ±0.005 | 0.11 [c] ±0.006 | 0.13 [b] ±0.01 |
| Glutathione Reductase (nmol/min/ml) | 170.20 [a] ±4.22 | 75.60 [d] ±3.47 | 94.80 [c] ±1.715 | 153.80 [b] ±8.85 |
| Glutathione Peroxidase (nmol/min/ml) | 255.20 [a] ±6.52 | 75.60 [d] ±1.81 | 136.60 [c] ±3.44 | 230.40 [b] ±4.82 |
| Catalase (IU/ml) | 128.60 [a] ±1.21 | 57.40 [c] ±3.08 | 88.00 [b] ±1.58 | 126.20 [a] ±2.85 |

Means carrying different superscripts within the same row are highly significant from each other's ($P \leq 0.001$).

**Figure 1. Effect of AFB1 (250 µg /kg body weight), AFB1 with Curcumin (250 µg /kg and 200 mg /kg body weight), and Curcumin alone (200 mg /kg body weight) for 2 weeks (5 successive doses /week) on serum superoxide dismutase enzyme (IU/ml) of adult male albino rats.**

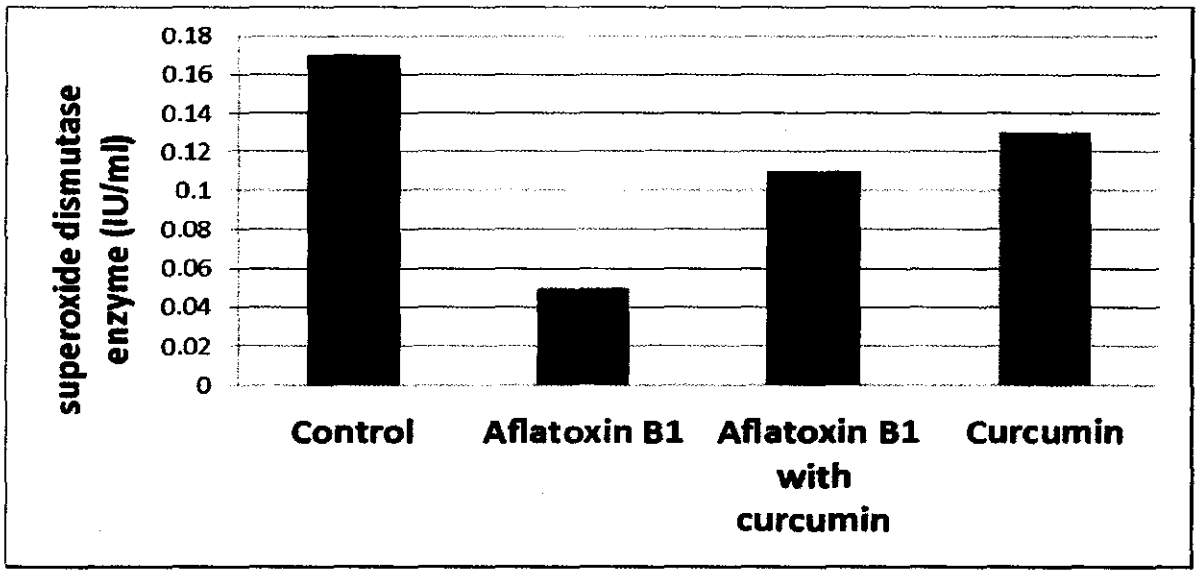



**Figure 2. Effect of AFB1 (250 µg /kg body weight), AFB1 with Curcumin (250 µg /kg and 200 mg /kg body weight), and Curcumin alone (200 mg /kg body weight) for 2 weeks (5 successive doses /week) on serum glutathione reductase enzyme (nmol/min/ml) of adult male albino rats.**

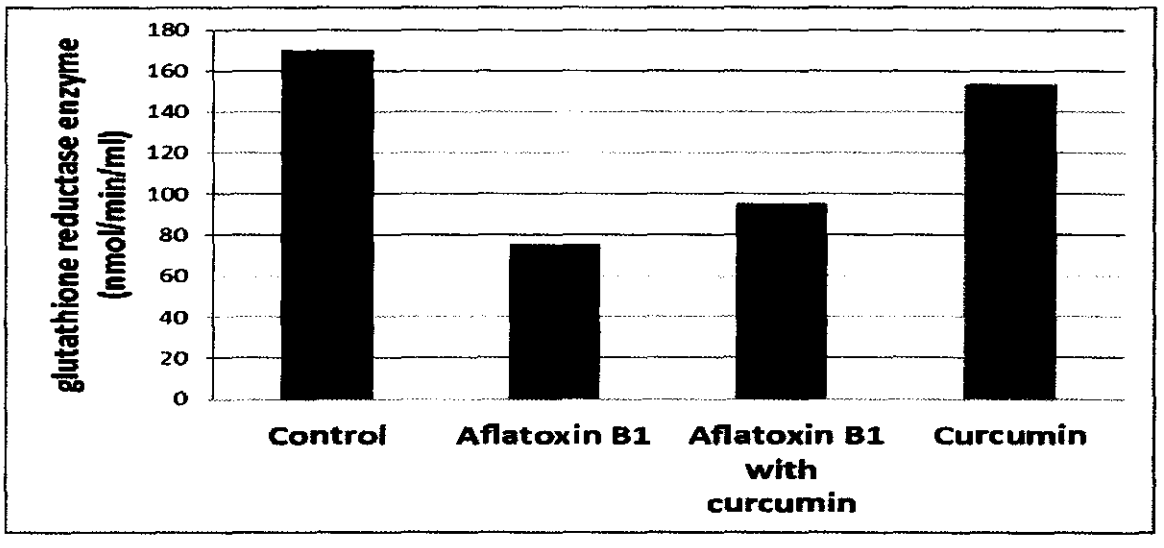


**Figure 3. Effect of AFB1 (250 µg /kg body weight), AFB1 with Curcumin (250 µg /kg and 200 mg /kg body weight), and Curcumin alone (200 mg /kg body weight) for 2 weeks (5 successive doses /week) on serum glutathione peroxidase enzyme (nmol/min/ml) of adult male albino rats.**

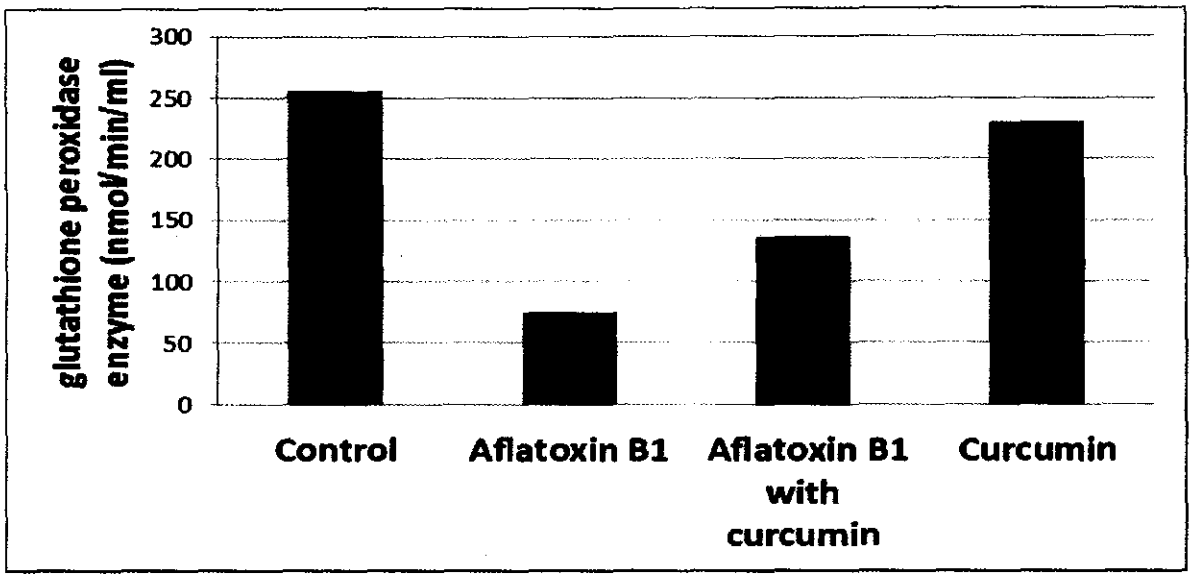
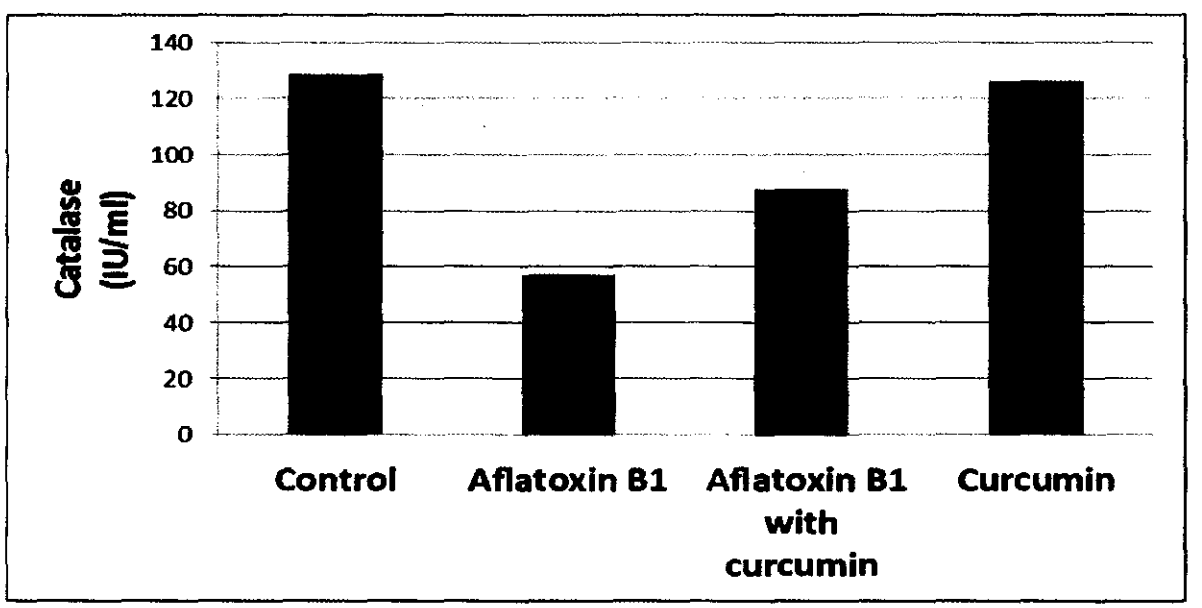



**Figure 4. Effect of AFB1 (250 µg /kg body weight), AFB1 with Curcumin (250 µg /kg and 200 mg /kg body weight), and Curcumin alone (200 mg /kg body weight) for 2 weeks (5 successive doses /week) on serum catalse enzyme (IU/ml) of adult male albino rats.**



Serum marker enzymes (ALT, AST, and AP) were significantly increased after oral administration of aflatoxin B1 (250µg/kg body weight) for 2 weeks, this elevation was significantly decreased when curcumin was administered in a dose of 200 mg /kg body weight orally for 2 weeks in combination with aflatoxin B1, Although curcumin administration alone caused no significant changes in level of ALT, AST, and AP when compared to the control group (Table 2).

**Table 2. Effect of AFB1 (250 µg /kg body weight), AFB1 with Curcumin (250 µg /kg and 200 mg /kg body weight), and Curcumin alone (200 mg /kg body weight) for 2 weeks (5 successive doses /week) on serum alanine transaminase, aspartate transaminase, and alkaline phosphatase enzyme of adult male albino rats.**

| Group / Parameter | Control | 1st group Aflatoxin B1 | 2nd group AFB1 with Curcumin | 3rd group Curcumin |
|---|---|---|---|---|
| GOT (nm/ml) | 5.00 $^{c}$ ± 0.45 | 16.20 $^{a}$ ± 0.58 | 16.80 $^{b}$ ± 0.37 | 5.20 $^{c}$ ± 0.37 |
| GPT (nm/ml) | 5.40 $^{c}$ ± 0.51 | 19.40 $^{a}$ ± 0.51 | 13.00 $^{b}$ ± 0.45 | 6.60 $^{c}$ ± 0.51 |
| ALP (nm/ml) | 20.60 $^{c}$ ± 0.71 | 40.40 $^{a}$ ± 1.03 | 27.20 $^{b}$ ± 0.86 | 19.60 $^{c}$ ± 0.87 |

**Figure 5. Effect of AFB1 (250 µg /kg body weight), AFB1 with Curcumin (250 µg /kg and 200 mg /kg body weight), and Curcumin alone (200 mg /kg body weight) for 2 weeks (5 successive doses /week) on serum alanine transaminase enzyme (nm/ml) of adult male albino rats.**

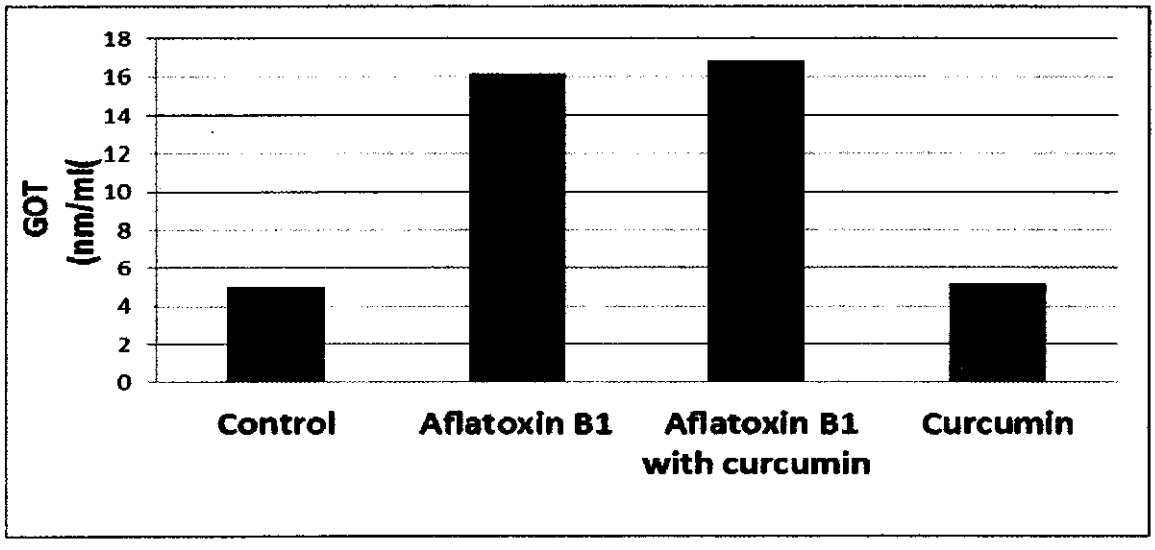


**Figure 6. Effect of AFB1 (250 µg /kg body weight), AFB1 with Curcumin (250 µg /kg and 200 mg /kg body weight), and Curcumin alone (200 mg /kg body weight) for 2 weeks (5 successive doses /week) on serum aspartate transaminase enzyme (nm/ml) of adult male albino rats.**

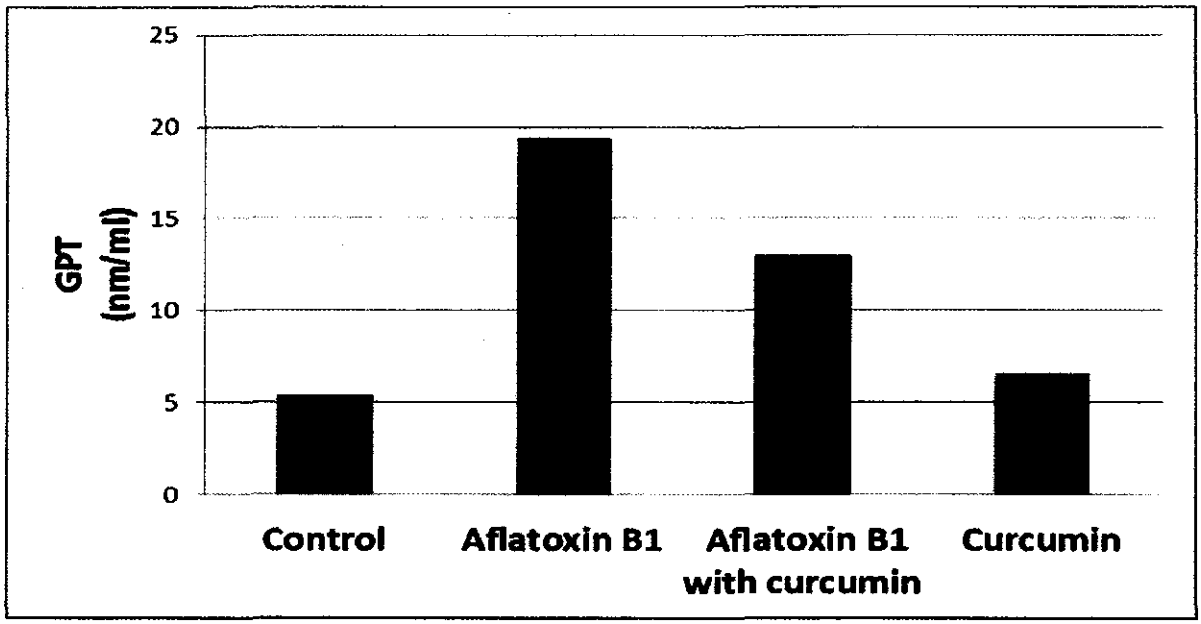
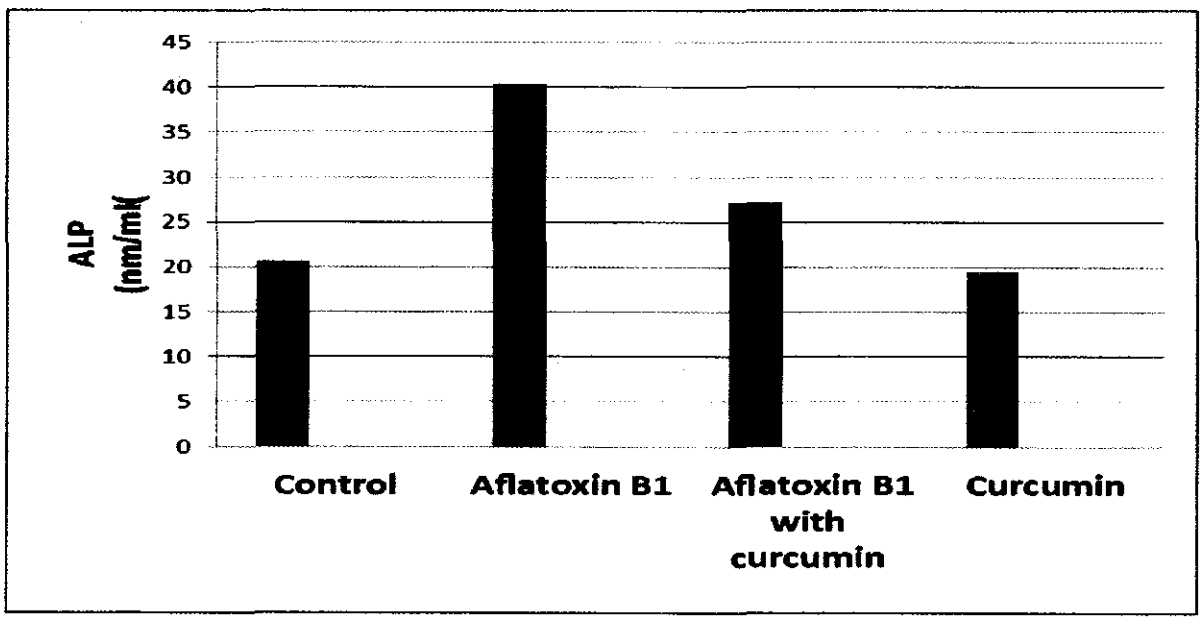



**Figure 7. Effect of AFB1 (250 µg /kg body weight), AFB1 with Curcumin (250 µg /kg and 200 mg /kg body weight), and Curcumin alone (200 mg /kg body weight) for 2 weeks (5 successive doses /week) on serum alkaline phosphatase enzyme (nm/ml) of adult male albino rats.**



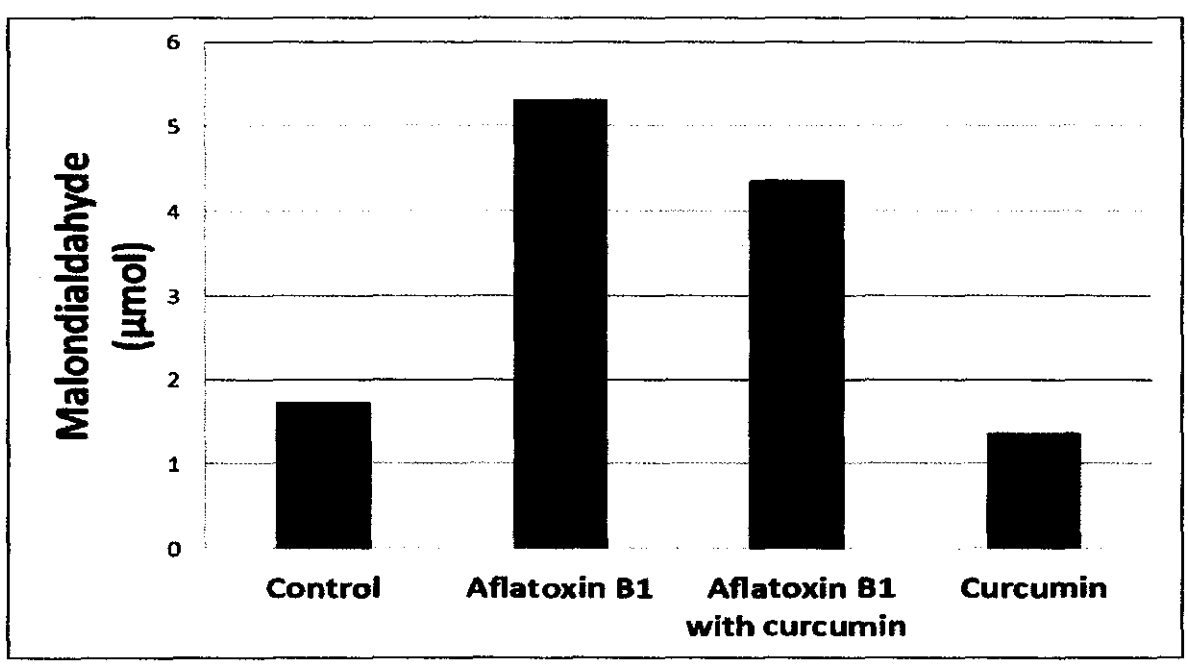
Serum malondialdahyde level was significantly increased after oral administration of aflatoxin B1 (250µg/kg body weight) for 2 weeks, this reduction was significantly decreased when curcumin was administered in a dose of 200 mg /kg body weight orally for 2 weeks in combination with aflatoxin B1, but the decrease was not reach the level of the control group. Although curcumin administration alone caused no significant changes in malondialdahyde level when compared to the control group **(Table 3).**

**Table 3. Effect of AFB1 (250 µg /kg body weight), AFB1 with Curcumin (250 µg /kg and 200 mg / kg body weight), and Curcumin alone (200 mg /kg body weight) for 2 weeks (5 successive doses /week) on serum malondialdahyde (µmol) of adult male albino rats.**

| Group / Parameter | Control | 1st group Aflatoxin B1 | 2nd group Aflatoxin B1 with Curcumin | 3rd group Curcumin |
|---|---|---|---|---|
| **Malondialdahyde** (µmol) | $1.73^{c}$ ± 0.10 | $5.33^{a}$ ± 0.13 | $4.36^{b}$ ± 0.05 | $1.38^{d}$ ± 0.006 |

Means carrying different superscripts within the same row are highly significant from each other's ($P \leq 0.001$).

**Figure 8. Effect of AFB1 (250 µg /kg body weight), AFB1 with Curcumin (250 µg /kg and 200 mg /kg body weight), and Curcumin alone (200 mg /kg body weight) for 2 weeks (5 successive doses /week) on serum malondialdahyde (µmol) of adult male albino rats.**



Carbonyl and thiol groups of protein were significantly increased in serum after oral administration of aflatoxin B1 (250µg/kg body weight) for 2 weeks, this elevation was significantly decreased when curcumin was administered in a dose of 200 mg /kg body weight orally for 2 weeks in combination with aflatoxin B1, Although curcumin administration alone caused no significant changes in level of Carbonyl and thiol groups of protein when compared to the control group **(Table 4).**

**Table 4. Effect of AFB1 (250 µg /kg body weight), AFB1 with Curcumin (250 µg /kg and 200 mg /kg body weight), and Curcumin alone (200 mg /kg body weight) for 2 weeks (5 successive doses /week) on serum carbonyl and thiol groups of protein of adult male albino rats.**

| Group / Parameter | Control | 1st group Aflatoxin B1 | 2nd group AFB1 with Curcumin | 3rd group Curcumin |
|---|---|---|---|---|
| Carbonyl groups (nmol/mg) | 0.13 [c] ± 0.01 | 3.59 [a] ± 0.21 | 2.20 [b] ± 0.16 | 0.18 [c] ± 0.01 |
| Thiol groups (nmol/mg) | 0.22 [c] ± 0.02 | 2.57 [a] ± 0.14 | 1.61 [b] ± 0.07 | 0.31 [c] ± 0.01 |

Means carrying different superscripts within the same row are highly significant from each other's ($P \leq 0.001$).

**Figure 9. Effect of AFB1 (250 µg /kg body weight), AFB1 with Curcumin (250 µg /kg and 200 mg /kg body weight), and Curcumin alone (200 mg /kg body weight) for 2 weeks (5 successive doses /week) on serum carbonyl group of protein (nmol/mg) of adult male albino rats.**

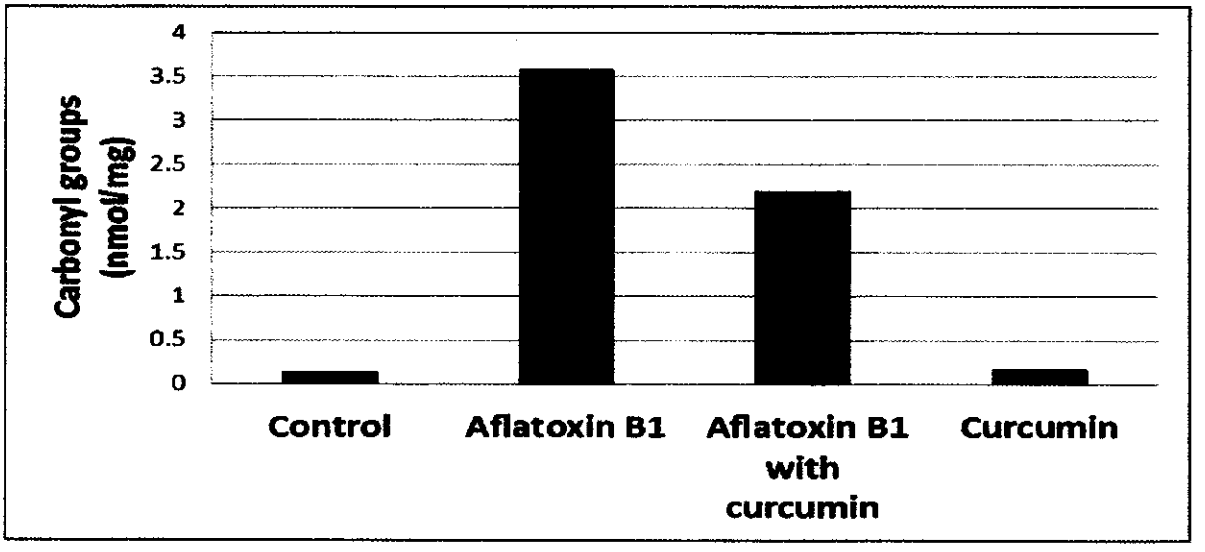
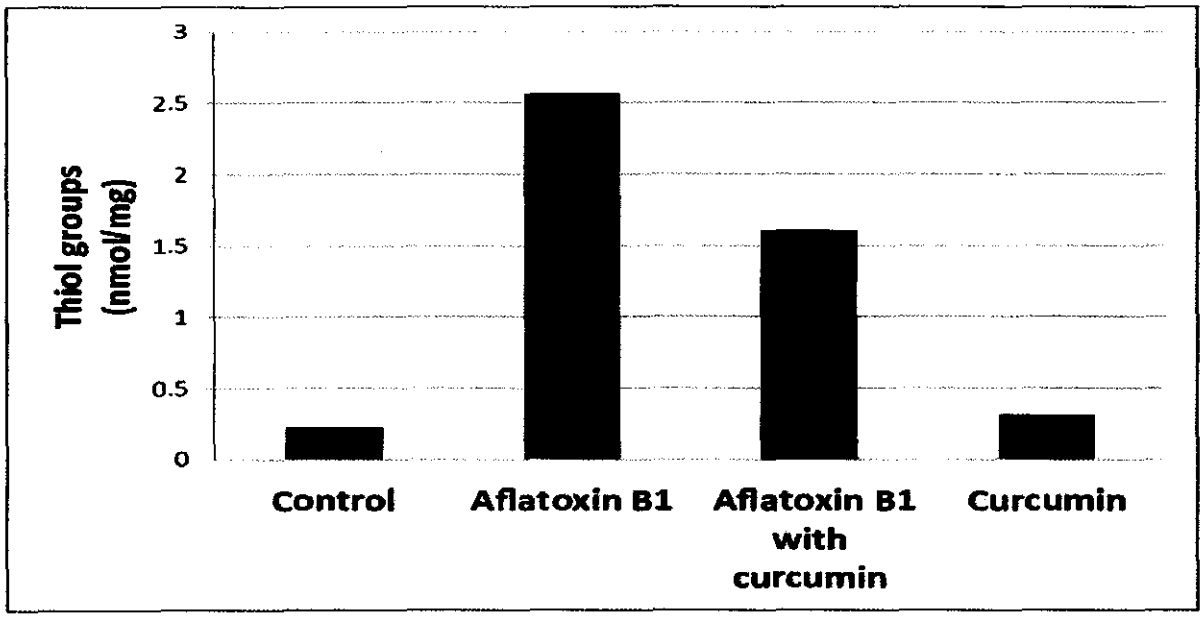


**Figure 10. Effect of AFB1 (250 µg /kg body weight), AFB1 with Curcumin (250 µg /kg and 200 mg /kg body weight), and Curcumin alone (200 mg /kg body weight) for 2 weeks (5 successive doses /week) on serum thiol group of protein (nmol/mg) of adult male albino rats.**




## DISCUSSION

Serum antioxidant enzymes (Superoxide dismutase, Glutathione reductase, Glutathione peroxidase, and Catalase) were significantly reduced after oral administration of aflatoxin B1 (250µg/kg body weight) for 2 weeks, this reduction was significantly decreased when curcumin was administered in a dose of 200 mg /kg body weight orally for 2 weeks in combination with aflatoxin B1 as oxidative stress occurs when the production of ROS exceeds the body's natural antioxidant defense mechanisms, causing damage to macromolecules such as DNA, proteins, and lipids. To counteract the damaging effect of ROS, aerobic cells are provided with extensive antioxidant defense mechanisms. The oxidative damage in a cell or tissue occurs when the concentration of ROS (O2.−, H2O2, and OH·) generated exceeds the antioxidant capability of the cell. Therefore, it could be due to significant decreases in the levels of non-enzymatic antioxidants [e.g., vitamin C, vitamin E, glutathione (GSH)] and enzymatic antioxidants [GSH (glutathione) ,superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT)], which are the main determinants of the antioxidant defense mechanisms of the cell .Antioxidant enzymes form the first line of defense against ROS and a decrease in their activities was observed with AFB1 administration.curcumin is an antioxidant acted as scavenger to ROS and reduced the oxidative stress so increased the level of antioxidant enzymes. These results are in harmony with the findings reported by ***(4,5,10).***

Serum marker enzymes (ALT, AST, and AP) were significantly increased after oral administration of aflatoxin B1 (250µg/kg body weight) for 2 weeks , this elevation was significantly decreased when curcumin was administered in a dose of 200 mg /kg body weight orally for 2 weeks in combination with aflatoxin B1. The enzymes serum aspartate aminotransferase (AST) and serum alanine aminotransferase (ALT) are present in the

cytosol of the hepatocytes. The ALP is also localized in the mitochondria. Whenever liver hepatocytes are damaged, these enzymes are released into the blood. A significant increase in AST, ALT, and ALP activities indicates the damage to the cytosol and also to mitochondria. The results obtained in the present study indicated significant increase in AST , ALT , and ALP activities in the Aflatoxin treated rats .On the other hand, aflatoxin treatment with curcumin showed marked recovery and decreased in the level of theses enzymes due to its antioxidant effect.These results are consistent with the similar effect in CCL4 toxicity *(11)*.

Serum malondialdahyde level was significantly increased after oral administration of aflatoxin B1 (250µg/kg body weight) for 2 weeks, this increase was significantly decreased when curcumin was administered in a dose of 200 mg /kg body weight orally for 2 weeks in combination with aflatoxin B1. AFB1-induced free radicals production has been referred to as a possible contributor to hepatotoxicity . Lipid peroxidation is one of the main manifestations of oxidative damage initiated by ROS, and it has been linked with altered membrane structure and enzyme inactivation. It is initiated by the abstraction of a hydrogen atom from the side chain of polyunsaturated fatty acids in the membrane . The present data shows that AFB1 administration produced a marked oxidative impact as evidenced from the significant increase in MDA. The increase in lipid peroxides might result from increased production of free radicals and a decrease in antioxidant status. curcumin can act as a non-enzymic antioxidant by direct interaction with ROS or it act as scavenger to ROS and reduce the lipid peroxidatve effect decrease the level of MDA. Similar to that reported in phynotoin *(12)* and iron overloaded toxicity *(6)*.

Carbonyl and thiol groups of protein were significantly increased in serum after oral administration of aflatoxin B1 (250µg/kg body weight) for 2 weeks , this elevation was significantly decreased when curcumin was administered in combination with aflatoxin B1. The serum proteins are invariably secreted by liver, so protein oxidative damage. In cases of hepatotoxicity induced by Aflatoxin B1 and ROS production, there was release of large amount of carbonyl and thiol protein groups in serum .Antioxidant effect of Curcumin caused decrease in the protein oxidative damage induced by Aflatoxin B1 and so decreased the protein carbonyl and thiol groups in serum. These results are in harmony with paracetamol intoxication *(10)*.

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## الملخص العربى
## دلالات التسمم التأكسدى الناتج عن الأفلاتوكسين ب١
## ودور الكوركيومين كترياق علاجي

**كوثر عبد الواحد الهادي ، أيمن كمال عبد الحميد ، عبد العزيز السيد الزفتاوى**
كلية الطب البيطرى –جامعة قناة السويس

أجرى هذا البحث لإلقاء الضوء على الدلالات المختلفة للأعراض الجانبية الناتجة عن الأفلاتوكسين ب١ وهو من أهم السموم الفطرية المؤثرة على الكبد وكذلك دراسة دراسة مادة الكوركيومين واستخدامها كترياق مضاد لتلك الآثار السمية لهذا السم الفطرى على الكبد .وقد تم اجراء هذا البحث على اربعين من ذكور الفئران البالغة والتى قسمت الى اربعة مجاميع كل منها عشرة فئران .

جرعت المجموعة الاولى عن طريق الفم بجرعة تعادل ٢٥٠ ميكروجرام لكل كيلوجرام من وزن الجسم لمدة اسبوعان (خمس جرعات متتالية فى الاسبوع ) وجرعت المجموعة الثانية ايضا عن طريق الفم بنفس الجرعة السابقة من اللأفلاتوكسين بالاضافة الى ٢٠٠ مجم لكل كيلو جرام من وزن الجسم من الكوركيومين لمدة اسبوعان (خمس جرعات متتالية فى الاسبوع ) ايضا.

اما المجموعة الثالثة فقد جرعت عن طريق الفم بجرعة الكوركيومين ٢٠٠ مجم لكل كيلو جرام من وزن الجسم من الكوركيومين لمدة اسبوعان (خمس جرعات متتالية فى الاسبوع ). وكانت المجموعة الرابعة هى المجموعة الضابطة والتى جرعت بالماء المقطر فقط لا غير.

بعد اربع وعشرون ساعة من آخر جرعة فى نهاية اللأسبوعان الخاصة بالتجربة تم أخذ عينات من الدم من كل فأر على حدى فى كل مجموعة وذلك لإجراء بعض التحاليل الكيميائية فى مصل هذه المجاميع من الفئران وقد اسفرت نتائج هذا البحث على الآتى:-

المجموعة الاولى :- وهى التى تجرعت بالأفلاتوكسين ٢٥٠ ميكروجرام لكل كيلوجرام من وزن الجسم على مدار المده الزمنية التى اجرى فيها البحث عن زيادة نسبة المالون داى الديهايد فى المصل وهذا دليل على زيادة نواتج أكسدة الدهون وكان هناك نقص واضح فى نسبة الإنزيمات المضادة للأاكسدة فى المصل Superoxide Glutathione Peroxidase, Catalase, and Glutathione Reductase Dismutase . وكذلك كان هناك انخفاض فى نسبة الكاربونايل والثايول فى المصل وهذا احد نواتج اكسدة البروتينات فى الدم .

وكان تأثير الأفلاتوكسين ب١ واضحاً على الإنزيمات التى تقيس وظائف الكبد واضح ذلك من زيادة مستوى هذه الإنزيمات فى مصل الدم بنسب جوهرية .

اما المجموعة الثانية والتى تجرعت بكل من الأفلاتوكسين بذات الجرعة السابقة مضافاً اليها الكوركيومين ٢٠٠ مجم لكل كيلوجرام من وزن الجسم لمدة اسبوعان (خمس جرعات متتالية فى الاسبوع ) الى تحسين نسب كل النتائج السابقة بنسب متفاوته .

وقد أثبتت نتائج المجموعة الثالثة التى تجرعت بالكوركيومين فقط بنفس ذات الجرعة ٢٠٠ مجم لكل كيلوجرام من وزن الجسم بعدم وجود أى تأثيرات جوهرية على النسب الطبيعية وذلك بالمقارنة بالنتائج التى حصلنا عليها مع المجموعة الضابطة .