ملخص البحث

الدور المحتمل لبذور الكتان على ارتفاع دهون الدم ، الاجهاد التاكسدى والتسمم المحدث بواسطه خلات الرصاص فى ذكور الفئران البالغه

يعتبر الرصاص من المواد التى تؤدى الى حدوث الاكسده ويظهر تاثيره الضار خاصه على الكلى والكبد . تحتوى بذور الكتان على تركيز عالى من الاحماض الدهنيه الغير مشبعه (n–3) واللجنين الذين يعتبروا من مضادات الالتهاب ولهما خصائص مضاده للاكسده . وتهدف هذه الدراسه الى تقييم دور بذور الكتان كمضاد للتاكسد على خلات الرصاص التى تؤدى الى احداث ارتفاع بدهون الدم وكذلك احداث تلف تاكسدى فى الكبد والكلى لذكور الفئران. تم اجراء الدراسة على 30 فار من نوع ذكور الالبينو وقد تم تقسيمهم الى مجموعتين المجموعة الاولى والتى تغذت على الغذاء المثالى الغير محتوى على خلات الرصاص (المجموعه الضابطه السالبه). بينما باقى المجموعات فقد تغذت على الغذاء المحتوى على خلات الرصاص بنسبه (200 ملجم/كجم غذاء) وتم معاملاتها بثلاث جرعات من بذور الكتان (2.5 ، 5 ، 10 جم/كجم طعام) . وقد اظهرت النتائج ان المجموعات التى تناولت خلات الرصاص وتم معاملاتها ببذور الكتان فقد اظهرت تغير معنوى بمستويات دهون الدم ، مضادات الاكسده وكذلك فى وظائف الكبد والكلى . كذلك تمكنت بذور الكتان من احداث تحسن بالمعاملات الخاصه بالكبد والكلى فقد اقتربت من المجموعه الضابطه السالبه . حيث ادى تناول بذور الكتان الى انخفاض بمعدل السيرم من الكرياتينين ، نيتروجين اليوريا ، يوريك اسيد ، اكسده الدهون وكذلك اوكسيد النيتريك . كما انه ادى الى ارتفاع مستوى الجلوتاثيون ، كتاليز ، سوبراوكسيد ديسماتيز ، وكذلك نشاط الجلوتاثيون بيروكسيديز . وبذلك يظهر التاثير الايجابى لبذور الكتان والتى تقلل من التاثير التسممى المحدث بواسطه المعادن الثقيله بالبيئه وخاصه خلات الرصاص ، كما ان له تاثير جيد فى تقليل ضرر السميه واكسده الدهون المحدثه بواسطه خلات الرصاص . ونتيجة للتأثير الإيجابي لبذور الكتان على القياسات المختلفة التى تمت دراستها لذلك توصى هذه الدراسه بزياده استهلاك بذور الكتان الذى يقى من التسمم وذلك لما تحتويه من تركيز عالى من الاحماض الدهنيه الغير مشبعه (n–3) وكذلك اللجنين ، كما ينبغي تدعيم المنتجات ببذور الكتان وكذلك التشجيع على عمل برامج التوعية التغذوية لتوعية الافراد باهمية بذور الكتان فى الحماية وتقليل خطر التسمم وكذلك ارتفاع دهون الدم.

الكلمات المفتاحية : خلات الرصاص – التسمم – بذور الكتان – الاجهاد التاكسدى – الكبد – الكلى – ارتفاع دهون الدم .

Abstract

The potential role of flaxseeds on hyperlipidemia, oxidative stress and toxicity induced by lead acetate in adult male albino rats

The current study was carried out to evaluate the antioxidant activity of flaxseeds against lead acetate-induced hyperlipidemia and oxidative damage in the liver and kidney of male rats. Thirty adult male albino rats were divided into two main groups, the first group (n=6) was kept on the basal diet as negative control (-ve), while the second group (n=24) was received lead acetate in basel diet at (200 mg/kg diet) and divided into four groups and treated with three doses of flaxseeds at 2.5 , 5 and 10 g / kg diet . The results showed that groups received lead acetate and treated with flaxseeds had significant enhance in plasma lipid levels, the antioxidant status and the liver and kidney functions. In the same line , flaxseeds lead to improve the biochemical parameters of the liver and kidney functions towards the normal values of the control group . Flaxseeds decreased the levels of serum creatinine, blood urea nitrogen, uric acid, lipid peroxidation and nitric oxide production with concomitant elevation in glutathione, catalase, superoxide dismutase, glutathione reductase and glutathione peroxidase activities. Thus, this study concluded that , the flaxseeds had beneficial effects in decreasing toxication induced by environmental heavy metals especially lead acetate, and had good effect in reducing the toxic , lesion and lipid peroxidation induced by lead acetate. Flaxseeds is recommended due to their role in preventing lead toxicity and hyplipidemia. Encouraging food stuff fortification with flaxseeds and nutrition education programs are needed to inform the public about the importance of flaxseeds in protective and decreasing the risk of toxicity and hyperlipidemia .

Key words: Lead acetate , toxicity , flaxseeds , oxidative stress , liver , kidney, hyperlipidemia .

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histological changes in lead acetate hepatotoxicity **(Abdou and Newairy, 2006) .** Moreover, **El-Dakhakhny et al. (2000)** showed that, flaxseeds displayed protective role against hepatotoxicity induced by lead acetate, that marked improvement in liver represented by normal portal vein surrounded by some healthy hepatocytes, whereas, small aggregations of lymphocytes were present in addition to the appearance of Kupffer cells.

The flaxseeds have increased attention for their potential role in preventing lipid disorders **(Upasani & Balaraman , 2003 ; Abdou and Newairy, 2006 ; Farrag et al., 2007 and Abdel-Moneim et al., 2010)**. The phenolic lignans and other phytoestrogens have antioxidant activity **(Kitts et al., 1999 ; Farrag et al., 2007 ; Skerfving and Bergdahl , 2007 and James et al., 2008)**. The more striking finding in this study is that the presence of flax lignans with lead acetate alleviated its harmful effects on the levels of GSH and on the activities of GPx, GR, SOD and GST enzymes. The corrected levels of these parameters were observed likely to near normal values of the control group. Flaxseeds is the richest source of lignans, which have also been reported to have antioxidant and hypolipidemic effects **(Neal et al., 1999 ; MacDonald-Wicks & Garg 2002 ; Rendón-Ramirez et al., 2007 ; Ho & Lin (2008 ; Navarro-Moreno et al. 2009 ; Newairy & Abdou, 2009 and Tan et al., 2011) .**

Flaxseeds significantly reduced lipid peroxidation, and it can be suggested that the active flaxseeds peptide fractions may have altered the pathway for lipid peroxidation synthesis in the macrophages. Polyunsaturated fatty acid and α –linolenic acid has shown that the activity of potential therapeutic agents of flaxseeds is responsible for the inhibition of lipid peroxidation production **(Ho and Lin 2008; Pan et al., 2008).**

In conclusion, this study conclude that the dietary supplementation with flaxseeds caused improvement and potential role against the toxicity induced by lead acetate . In this study, co-treatment of lead acetate and flaxseeds resulted in a significant improvement in the most treated parameters and histopatholigical examination of the liver and kidney. Therefore, the flaxseeds may play a protective role against lead acetate , that induced liver , kidney injury and hyperlipidemia . Collectively, it is clear that flaxseeds had maximum protective effects on lead acetate-induced damage, and that the effects are associated with the high concentrations of (n-3) fatty acids , lignans and antioxidant effect of flaxseeds . So that , this study recommends increase the consumption of flaxseeds due to their high concentrations of (n-3) fatty acids and lignans, to prevent the lead toxicity. Encouraging food stuff fortification with flaxseeds and nutrition education programs are needed to inform the public about the importance of flaxseeds in protective and decreasing the risk of toxicity and hyperlipidemia .

stress (**Newairy and Abdou , 2009) .** The possible explanation could be related to the proposed role of GSH in the active excretion of lead through bile by binding to the thiol group of GSH and then being excreted. A decrease in GSH levels could lead to oxidative stress and a consequent increase in LIP (**Reglero et al., 2009 and El-Nekeety et al., 2009**) . In the same line , lead is known to adversely affect many organs, where the kidney is another of the important targets (**Garçon et al., 2007**) . Lead produces oxidative damage in the kidney, by enhancing LIP (**Farrag et al., 2007 and El-Nekeety et al., 2009**) . In this study, treatment with lead acetate resulted in a significant increase lipid peroxidation as indicated by the significant increase of MDA levels and the significant decrease of GSH levels. Similar results have been reported by **Upasani & Balaraman ,(2003) ; Farrag et al., (2007) and Navarro-Moreno et al., (2009)** . The lead induced oxidative damage by causing formation of reactive oxygen species (**Jin et al., 2006**) .

Concerning , the effect of lead on histopathological examination of the tested organs results were agreed with **Upasani & Balaraman , (2003) ; Farrag et al., (2007**) **and Navarro-Moreno et al., (2009)** , they reported that lead induces oxidative damage to the membranes by the accumulation of oxidant metabolites (such as free protoporphyrins, heme and iron ions) and by direct or indirect ; by inhibition of antioxidant enzymes, reducing the total antioxidant protection of the cell, affecting membrane structure and function and altering physiological processes of organs and tissues . These damages are reflected in cellular structural changes and explain the close relationship between the morphological changes found in the kidneys of lead exposed animals with the molecular and physiological changes .

Lead poisoning cause adverse effects to hepatic cells because after lead exposure, liver is one of the major organs involved in the storage, biotransformation and detoxification **(Sivaprasad et al., 2004).** The results of the present study run in full agreement of previous studies that lead is a very toxic agent which affects many vital organs, such as the liver and kidney. **Abdou and Newairy (2006)** showed that histological analysis of livers of rats treated with lead acetate showed hepatocytes damage, abnormal localization and infiltration of hepatocytic nuclei. Results of the present study agreed with the previous results that dramatically alterations appeared in liver and kidney sections of rats were received lead acetate. The degeneration in the cells, cytoplasmic vacuolization appeared besides the appearance of Kupfer cells, largenecrotic areas appeared and great dilatation in sinusoids, dilatation in blood vessels with congestion was present. Histological examination of liver tissue in rats received lead acetate and treated with flaxseeds showed minimal alterations with reduced fat deposition compared to the lead acetate treated rats. These findings confirmed the protective effect of flaxseeds against the

The liver plays a major role in lead's metabolism, and it is in special risk due to the oxidative action of lead , that induced lipid peroxidation of cellular membranes and plays a crucial role in the mechanisms of hepatotoxic action **(Rahman & Sultana , 2006 and El-Nekeety et al., 2009)** . On the other hand, lead is known also to affect the kidney, which is another important target (**Ponce-Canchihuam et al., 2010)**. Lead produces oxidative damage in the kidney as evidenced by enhancing lipid peroxidation (LIP) (**Farrag et al., 2007 and Ademuyiwa et al., 2009**) . In vivo and in vitro studies it has been suggested that lipid metabolism is altered both in acute and chronic exposure to lead (**Bolin et al., 2006**) .

Lead inhibits antioxidant enzyme activity, such as superoxide dismutase and catalase, and also decreases the level of glutathione, increases lipid peroxidation (**Newairy & Abdou , 2009 and Karadeniz et al., 2009**) , which harms proteins, cell membranes and DNA **(Farrag et al., 2007)**. Significant increase in lipid peroxidation as indicated by the significant increase in MDA and the significant decrease in GSH with the antioxidant enzymes (GR, GPx, CAT, SOD and GST) **(Acharya et al., 2003 ; Gurer-Orhan et al., 2004 and Abdel-Wahhab & Aly, 2005)**. The stimulation of lipid peroxidation, presumably caused by lead treatment, could be due to the formation of free radicals through an exhaustion of antioxidants **(Harlan et al. 1984 ; Jindal & Gill, 1999 ; Shabani & Rabbani, 2000 ; Abdel-Wahhab & Aly, 2005 ; Abdel-Wahhab et al., 2006 ; Abdel-Wahhab et al., 2007)** and subsequently to oxidative stress **(Abdel-Wahhab et al., 2007 and El-Nekeety et al., 2009)**. Heavy metal poisoning like lead causes adverse effects to hepatic cells because after lead exposure, liver is one of the major organs involved in the storage, biotransformation and detoxification. Lead also, affects the kidney, which is another important organ that participates in the detoxification **(Herman and Geraldine , 2009**) .

Moreover , lead is a heavy metal that produces oxidative damage in the liver by enhancing lipid peroxidation (LIP **) (Can et al., 2008 and El-Nekeety et al., 2009) .** Lead toxicity leads to free radical damage by two separate, pathways: (1) the generation of reactive oxygen species (ROS), including hydroperoxides, singlet oxygen, and hydrogen peroxides, evaluated by MDA levels as the final products of lipid peroxidation , and (2) the direct depletion of antioxidant reserves (**Newairy and Abdou , 2009)** . The results of our study found that , received lead acetate had the significant increase of lipid peroxidation as indicated by the significant increase of MDA levels and the significant decrease of GSH levels. Our results are in agreement with other studies (**Upasani & Balaraman , 2003** ; **Newairy & Abdou , 2009 and Reglero et al., 2009)** . The presence of LIP that observed in the current study was also due to decreased SOD and CAT activities, both indicators of oxidative

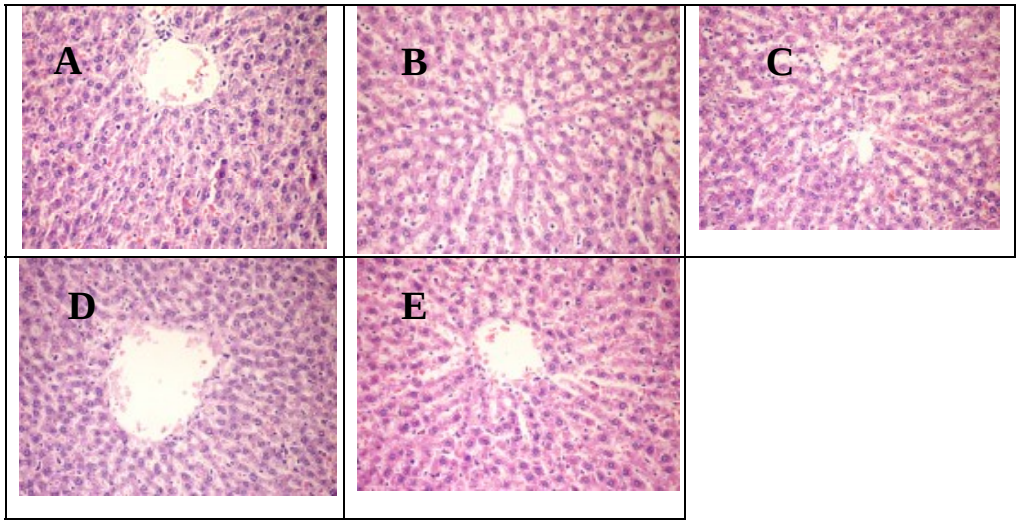

Photo (1) : Histopathological changes detected in the liver of (A) negative control, (B) positive control, (C) *2.5 g / kg diet* of flaxseeds , (D) *5 g / kg diet* of flaxseeds , (E) *10 g / kg diet* of flaxseeds . (H and E X 400) .

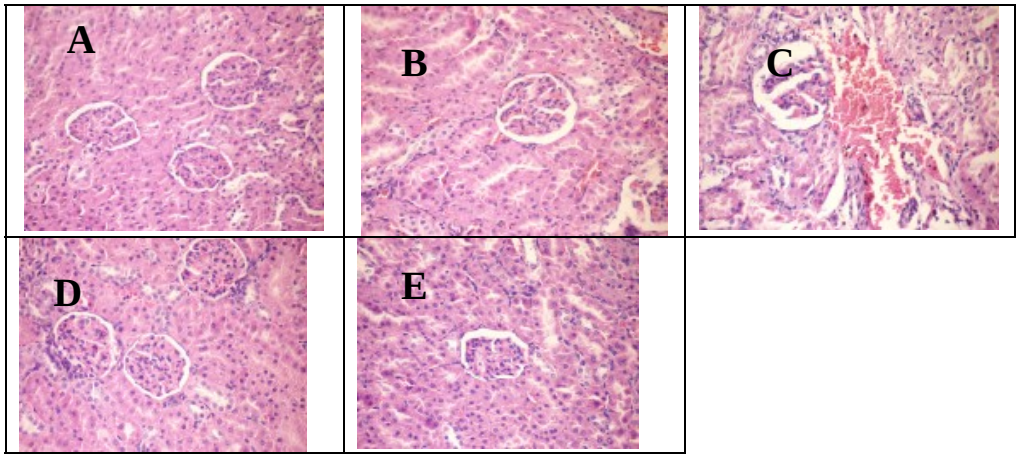

Photo (2) : Histopathological changes detected in the kidneys of (A) negative control, (B) positive control, (C) *2.5 g / kg diet* of flaxseeds , (D) *5 g / kg diet* of flaxseeds , (E) *10 g / kg diet* of flaxseeds. (H and E X 400) .

Disscution :

Lead (Pb+2) is a heavy metal that can be toxic when introduced into the human and animal bodies by ingestion or inhalation in sufficient quantities. It causes various destructive effects **(Neathery and Miller, 1975**). In human, increased levels of lead causes many serious diseases and dysfunction of organs **(Gennart et al., 1992; McGregor and Mason, 1990)** and reduction in body weight gain; similar observations were reported by **El-Nekeety et al., (2009)** and **Ponce-Canchihuam et al., (2010) .**

CAT , GSH and GPX , but significant decrease in serum concentrations of MDA compared to the positive control group .

Table 8 : The Effect of flaxseeds On Antioxidant enzymes and lipid peroxidation

Treatments	Superoxide dismutase **(mg /dl)**	Catalase **(mg /dl)**	Glutathione **(mg /dl)**	Glutathione peroxidase **(mg /dl)**	Malondialdahyde **(mg/dl)**
Negative control	74.70 ± 2.98 ^{a}	710.11 ± 1.02 ^{a}	8.00 ± 1.54 ^{a}	35.91 ± 2.01 ^{a}	16.86 ± 1.12 ^{c}
Positive control	45.81 ± 2.00 ^{c}	291.50 ± 1.06 ^{d}	4.48 ± 1.52 ^{b}	28.52 ± 1.95 ^{b}	24.33 ± 1.95 ^{a}
Flaxseeds at 2.5 g / kg diet	60.73 ± 1.84 ^{b,c}	385.32 ± 1.00 ^{c}	4.87 ± 0.99 ^{b}	30.18 ± 1.87 ^{a,b}	20.44 ± 2.25 ^{a,b}
Flaxseeds at 5 g / kg diet	67.33 ± 2.01 ^{b}	417.10 ± 1.45 ^{b}	6.18 ± 1.87 ^{a,b}	34.71 ± 1.94 ^{a,b}	19.48 ± 1.84 ^{b}
Flaxseeds at 10 g / kg diet	72.51± 3.52 ^{a}	709.40 ± 0.99 ^{a}	7.59 ± 1.99 ^{a}	35.17 ± 2.00 ^{a}	17.31± 1.41 ^{c}

Values are mean ± SD. Values in the same column sharing the same superscript letters are not statistically significant.

Histopathological examination :

Histopathological examination of liver for rats fed basal diet (negative control) showed normal histological structure of hepatic lobule as shown in (Photo1- A) . The liver of rats received lead acetate in the diet (positive control group) showed kupller cells activation , dilatation of hepatic sinusoids with few leucocytes in hepatic sinusoids as shown in (Photo1-B) . While Photo (1-C) showed the liver of toxic rats treated with level 1 (2.5 g / kg diet) of flaxseeds showed kupller cells activation and small vacuoles in the cytoplasm of hepatocytes , while the group treated with level 2 (5 g / kg diet) of flaxseeds showed dilatation of central vein as shown in Photo (1-D) . Moreover , Photo (1-E) showed the liver of toxic rats treated with level 3 (10 g / kg diet) of flaxseeds showed no histopathological changes (Photo 1-F).

This study showed that the kidneys of the negative control group (fed on basal diet) had the normal histological structure of renal parenchyma as shown in (Photo 2- A) , on the other hand the kidneys of rats received lead acetate in the diet (positive control group) showed coagulative necrosis of renal tubular epithelium (Photo 2- B) , while the toxic rats treated with level 1 (2.5 g / kg diet) of flaxseeds showed congestion of renal blood vessels as shown in Photo (2- C) . Moreover , Photo (2- D and E) showed at kidneys of the toxic rats treated with level 2 and level 3 of flaxseeds at (5 and 10g / kg diet , respectively) had no histopathological changes.

Table 6 : The Effect of flaxseeds on Serum kidneys functions (Creatinine, Urea and Urea nitrogen)

Treatments	Creatinine (mg/dl)	Urea (mg/dl)	Urea nitrogen (mg/dl)
	Mean ±SD	Mean ±SD	Mean ±SD
Negative control	0.97 ± 1.84 [b]	20.33 ± 1.95 [b]	9.70 ± 1.50 [b]
Positive control	1.38 ± 1.87 [a]	37.08 ± 1.57 [a]	15.90 ± 1.74 [a]
Flaxseeds at 2.5 g / kg diet	1.29 ± 1.95 [a]	28.00 ± 1.85 [a,b]	14.13 ± 1.54 [a]
Flaxseeds at 5 g / kg diet	1.16 ± 1.74 [a,b]	23.00 ± 1.41 [b]	13.20 ± 1.99 [a,b]
Flaxseeds at 10 g / kg diet	1.08 ± 1.45 [a,b]	20.66 ± 2.06 [b]	9.93 ± 1.79 [b]

Values are mean ± SD. Values in the same column sharing the same superscript letters are not statistically significant.

Table 7 : The Effect of flaxseeds on Serum kidneys functions (Uric acid and Total protein)

Treatments	Uric acid (mg/dl)	Total protein (mg/dl)
	Mean ±SD	Mean ±SD
Negative control	2.46 ± 0.99 [c]	6.20 ± 1.85 [c]
Positive control	4.46 ± 1.02 [a]	8.43 ± 1.25 [a]
Flaxseeds at 2.5 g / kg diet	3.73 ± 1.65 [a,b]	7.83 ± 2.00 [a,b]
Flaxseeds at 5 g / kg diet	3.10 ± 1.99 [b]	6.86 ± 1.99 [b]
Flaxseeds at 10 g / kg diet	2.86 ± 1.85 [b,c]	6.43 ± 2.01 [b,c]

Values are mean ± SD. Values in the same column sharing the same superscript letters are not statistically significant.

Antioxidant Enzymes and Lipid Peroxidation:

Data presented in Table (8) showed that the positive control group showed significant decreased in the values of serum levels of superoxide dismutase (SOD) , catalase (CAT) ; glutathione (GSH) and glutathione peroxidase (GPX) compared with the negative control group with mean values of 45.81 ± 2.00 ; 291.50 ± 1.06 ; 4.48 ± 1.52 and 28.52 ± 1.95 mg /dl , (respectively) vs. 74.70 ± 2.98 ; 710.11 ± 1.02 ; 8.00 ± 1.54 and 35.91 ± 2.01 mg /dl , (respectively) . However , these parameters were increased when rats were received lead acetate in diet with flaxseeds at *2.5* , 5 and 10 *g / kg diet* . The highest levels of serum SOD , CAT , GSH and GPX were observed in group treated with flaxseeds at 10 *g / kg diet* . In addition positive control group showed significant increase in the values of serum malondialdehyde (MDA) concentration than the negative control group 24.33 ± 1.95 mg /dl, vs. 16.86 ± 1.12 mg /dl. Groups of rats fed on diets containing flaxseeds at different levels , showed significant decreased in the values of serum MDA . The lowest value of the MDA concentration in serum were shown when toxic rats were fed flaxseeds at 10 *g / kg diet* . Results revealed that the highest level of flaxseeds in the diet (10 *g / kg diet*) showed significant increase in serum levels of SOD ,

Liver Functions:

Results in Table (5) revealed that positive control group had significant increases in serum levels of AST and ALT at $p<0.05$ (31.66 ± 2.62 IU/L and 11.00 ± 0.48 IU/L, respectively) compared to the normal control group (8.66 ±2.01 IU/L and 4.83 ± 0.95 IU/L , respectively). However , groups fed on different levels of flaxseeds at (2.5 , 5 and 10 *g / kg diet*) had significant decreases in serum levels of AST and ALT compared to the positive control group. The lowest values of AST and ALT in serum were showed in groups treated with flaxseeds at 10 *g / kg diet as* 9.00 ± 2.99 IU/L and 5.33 ± 0.78 IU/L , respectively .

Table 5 : The Effect of Flaxseeds on Serum liver enzymes (AST and ALT)

Treatments	AST (IU/L)	ALT (IU/L)
	Mean ±SD	Mean ±SD
Negative control	8.66 ±2.01[c]	4.83 ± 0.95 [b]
Positive control	31.66 ± 2.62 [a]	11.00 ± 0.48 [a]
Flaxseeds at 2.5 g / kg diet	21.00 ± 3.51 [b]	8.00 ± 0.98 [a,b]
Flaxseeds at 5 g / kg diet	16.66 ± 3.04 [b]	7.66 ± 1.06 [a,b]
Flaxseeds at 10 g / kg diet	9.00 ± 2.99 [c]	5.33 ± 0.78 [b]

Values are mean ± SD. Values in the same column sharing the same superscript letters are not statistically significant.

kidneys Functions :

Data in Table (6) showed that the positive control group (toxicated rats) had significant increase in serum levels of creatinine , urea and urea nitrogen (1.38 ± 1.87 mg/dl ; 37.08 ± 1.57 mg/dl and 15.90 ± 1.74 mg/dl , respectively) compared with the negative control group with a mean value 0.97 ± 1.84 mg/dl ; 20.33 ± 1.95 mg/dl and 9.70 ± 1.50 mg/dl , respectively . Animals fed on different levels of flaxseeds had significant decrease in serum level of creatinine , urea and urea nitrogen compared to the positive control group . In addition, data in Table (7) showed that , the toxicated rats induced by lead acetate (positive control group) showed highly significant increase of serum uric acid and total protein compared to the negative control group with mean values of 4.46 ± 1.02 mg/dl and 8.43 ± 1.25 mg/dl , respectively vs. 2.46 ± 0.99 mg/dl and 6.20 ± 1.85 mg/dl , respectively . However , the toxicated rats treated with different levels of flaxseeds had significant decrease in serum level of serum uric acid and total protein compared to the positive control group . The highest values of serum uric acid concentration and total protein were showed in group treated with flaxseeds at 10 *g / kg diet as* 2.86 ± 1.85 mg/dl and 6.43 ± 2.01 mg/dl, respectively.

Lipid Profile:

Data in Table (3) demonstrated that toxicated rats fed on lead acetate in the diet (positive control group) had significant increase in serum concentrations of total cholesterol (TC) and triglyceride (TG) (93.33± 0.98 mg/dL and 108.33 ± 2.05 mg/dL , respectively) compared to the negative control group (70.17 ± 1.87 mg/dL and 80.33 ± 2.87 mg/dL, respectively). The groups of rats were treated with flaxseeds at different levels (2.5 , 5 and 10 *g / kg diet*) had significant decrease in serum concentrations of TC and TG compared to the positive control rats. Treated groups fed on flaxseeds at 10 *g / kg diet* had significant lower mean values of TC and TG in serum (71.67 ± 1.00 mg/dL and 81.33 ± 1.88 mg/dL, respectively) compared to the other treated groups.

Table 3 : The Effect of Flaxseeds on Serum Total Cholesterol and Triglyceride

Treatments	Total Cholesterol (mg/dl)	Triglyceride (mg/dl)
	Mean ±SD	Mean ±SD
Negative control	70.17 ± 1.87 [b]	80.33 ± 2.87 [c]
Positive control	93.33± 0.98 [a]	108.33 ± 2.05 [a]
Flaxseeds at 2.5 g / kg diet	84.67 ± 1.05 [a,b]	91.33 ± 1.99 [b]
Flaxseeds at 5 g / kg diet	81.33 ± 1.87 [a,b]	85.00 ± 1.09 [b,c]
Flaxseeds at 10 g / kg diet	71.67 ± 1.00 [b]	81.33 ± 1.88 [c]

Values are mean ± SD. Values in the same column sharing the same superscript letters are not statistically significant.

Data in Table (4) show that induced toxicity in rats using lead acetate had significant increase in serum concentration of VLDL-C and LDL-C (21.68 ± 0.77 mg/dL and 47.67 ± 1.35 mg/dL) compared to the negative control group (16.07 ± 1.98 mg/dL and 18.00 ± 1.87 mg/dL). Animals fed different levels of flaxseeds had significant decrease in serum level of VLDL-C and LDL-C as compared to the positive control group . With regard to serum levels of HDL-C , results revealed that the positive control group had significant reduction in serum level of HDL-C (24.00 ± 1.95 mg/dL) compared to the animal fed basal diet (36.100 ± 1.84 mg/dL). Feeding groups with different levels of flaxseeds caused significant increase in serum level of HDL-C (29.00 ± 1.95 , 34.00 ± 1.87 and 35.00 ± 1.99 mg/dL, respectively) compared to the positive control group (24.00 ± 1.95 mg/dL).

Table 4 : The Effect Of flaxseeds On Serum Lipid Profiles (VLDL , LDL and HDL)

Treatments	VLDL	LDL	HDL
	Mean ±SD	Mean ±SD	Mean ±SD
Negative control	16.07 ± 1.98 [b]	18.00 ± 1.87 [c]	36.100 ± 1.84 [a]
Positive control	21.68 ± 0.77 [a]	47.67 ± 1.35 [a]	24.00 ± 1.95 [c]
Flaxseeds at 2.5 g / kg diet	18.26 ± 1.25 [a]	37.40 ± 1.87 [a,b]	29.00 ± 1.95 [b,c]
Flaxseeds at 5 g / kg diet	17.00 ± 1.85 [a,b]	30.33 ± 1.96 [b]	34.00 ± 1.87 [a,b]
Flaxseeds at 10 g / kg diet	16.26 ± 1.02 [b]	20.40 ± 1.76 [c]	35.00 ± 1.99 [a,b]

Values are mean ± SD. Values in the same column sharing the same superscript letters are not statistically significant.

Results :

The results in Table (1) showed the lead acetate-induced rats exhibited a very highly significant decreased of feed intake , body weight gain and feed efficiency ratio as compared to the negative control group . The experimental groups were be supplemented with flaxseeds in their diet were showed significant increase of feed intake , body weight gain and feed efficiency ratio compared to the positive control group. The highest values of feed intake, body weight gain and feed efficiency ratio where showed in group of rats received lead acetate and supplemented with flaxseeds at 5 g / kg diet .

Table 1: Effect Of flaxseeds On Feed Intake , Body Weight Gain and Feed Efficiency Ratio

Treatments	Feed intake (g / day)	Body weight gain (g)	Feed efficiency ratio
	Mean ±SD	Mean ±SD	Mean ±SD
Negative control	15.40 ± 0.58 [a]	9.20 ± 0.48 [a]	0.024 ± 0.15 [a]
Positive control	10.60 ± 0.98 [c]	-5.80 ± 0.74 [c]	-0.020 ± 0.99 [c]
Flaxseeds at 2.5 g / kg diet	13.40 ± 0.25 [b]	3.60 ± 0.91 [b]	0.010 ± 0.18 [b]
Flaxseeds at 5 g / kg diet	14.80 ± 0.87 [a,b]	7.20 ± 0.30 [a,b]	0.018 ± 0.45 [a,b]
Flaxseeds at 10 g / kg diet	14.40 ± 0.85 [a,b]	5.00 ± 0.18 [a,b]	0.012 ± 0.87 [a,b]

Values are mean ± SD. Values in the same column sharing the same superscript letters are not statistically significant.

Organs Relative Weight :

Concerning relative weight of the tested organs such as liver , heart , and kidneys (Table 2). The group of rats , that induced by lead acetate were showed non-significant changes of liver , heart and kidneys relative weight compared to the negative control group .While the groups that treated with flaxseeds at different levels were showed a non-significant changes in the organs relative weight (liver , heart and kidneys) compared to the positive control group , except the group was treated with flaxseeds oil at level 10 g / kg diet showed significant decreased in heart and kidneys relative weight when compared with positive control group.

Table 2 : The Effect Of flaxseeds On Organs Relative Weight

Treatments	Liver %	Heart %	Kidneys %
	Mean ±SD	Mean ±SD	Mean ±SD
Negative control	3.04 ±0.16 [a]	0.258 ± 0.87 [a,b]	0.538 ± 0.67 [b]
Positive control	2.69 ± 0.45 [a,b]	0.302 ± 0.98 [a]	0.698 ± 0.18 [a]
Flaxseeds at 2.5 g / kg diet	2.44 ± 0.24 [b]	0.270 ± 0.47 [a]	0.590 ± 0.24 [a,b]
Flaxseeds at 5 g / kg diet	2.60 ± 0.90 [a,b]	0.322 ± 0.47 [a]	0.604 ± 0.49 [a,b]
Flaxseeds at 10 g / kg diet	2.20 ± 0.98 [b]	0.232 ± 0.99 [b]	0.540 ± 0.77 [b]

Values are mean ± SD. Values in the same column sharing the same superscript letters are not statistically significant.

Very low density lipoprotein cholesterol (VLDL-C) was calculated using the following equation:

LDL-Cholesterol = Total cholesterol - (HDL-C + TG/5)

VLDL-C = TG/5

Liver and Kidney Functions Assay:

Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were determined using colorimetric methods as described in the kits instruction (Diamond Co, Hannover, Germany). The absorption of the test samples were read at 505nm for ALT and AST were determined according to **A.A.C.C. (1977).** Serum uric acid (UA), blood urea nitrogen (BUN) creatinine (Cr) , urea , total protein were estimated by the method of **Brod and Sirota (1980) and Marshell et al., (1980)** , respectively .

Determination of lipid peroxidation and antioxidant enzymes :

Malondialdehyde (MDA) was assayed colorimetrically in serum according to the method of **Ohkawa et al. (1979)** . The level of serum antioxidant as catalase (CAT), superoxide dismutase (SOD), glutathione-Stransferase (GST), glutathione peroxidase (GPx) and glutathione reductase (GR) levels were determined by the methods of **(Aebi 1984 ; Nishikimi et al. , 1972 ; Habig et al. , 1974 ; Paglia & Valentine , 1967 and Factor et al. , 1998)** , respectively .

Histopathological Examination:

Liver and kidney of the scarified rats were taken and immersed in 10% formalin solution. The fixed specimens were then trimmed, washed and dehydrated in ascending grades of alcohol. Specimens were then cleared in xylol, embedded in paraffin, sectioned at 4-6 microns thickness and stained with Heamtoxylin and Eosin stain for examination of the liver and kidney as described by **Carleton (1979).**

Statistical Analysis:

The results were expressed as mean ± SD. The differences among means were analyzed through one way analysis of variance (ANOVA) followed by Duncan's post hoc analysis, and the P values ≤ 0.05 were considered significant. SPSS software version 16 was used for the statistical analysis according to **Snedecor and Cochran (1967).**

This group were divided to four sub – groups as followed :
First sub – group : fed on basel diet with lead acetate , from the second to fourth sub – groups they were fed on basel diet with lead acetate in addition flaxseeds after grained and added at 2.5 , 5 and 10 g / kg diet , respectively for the period of experiment (45 days) . Rats were kept for four weeks on the previous experimental diets and then animals were sacrificed for collecting blood and organs such as kidneys , heart and liver.

Blood Samples Collection :

At the end of the feeding trail, animals were fasted over-night, lightly anesthetized under ether . About 7-ml blood was withdrawn from the hepatic portal vein into clean dry centrifuge plastic tubes. Blood samples were centrifuged and sera were obtained then stored at - 20°C in a clean well-stopped vials until biochemical analysis.

Determination of Food Intake, Body Weight Gain and Feed Efficiency Ratio:

Food Intake (FI) was calculated every other day, The biological value of the different diets was assessed by the determination of its effect on body weight gain (BWG) and feed efficiency ratio (FER) at the end of the experimental period were calculated according to **Adron et al., (1976)** and **Stanley et al., (2005) ,** respectively , using the following equation :

BWG = Final body weight (g) - Initial body weight (g)
FER = Weight gain (g) / Feed intake (g) .

Calculation of organs relative weight was calculated according to the following equation:

Organs relative weight = (organ weight / animal final weight) x 100

Lipid Profile and Lipoprotein Cholesterol Assay:

Total cholesterol (TC), triglyceride (TG) and high density lipoprotein cholesterol (HDL-C) concentrations were determined using enzymatic methods as described in the instructions provided with the kits (Analyticon® Biotechnologies AG, Germany). The absorbance of the testes samples were read using spectrophotometer adjusted at 546 nm for TG, TC and 500 nm for HDL-C. Low density lipoprotein cholesterol (LDL-C) concentration was calculated by using formula of **Friedwald et al. (1972)** .

evidence that lead induced lipid peroxidation of cellular membranes, plays a crucial role in the mechanisms of hepatotoxic action of these xenobiotics **(Sivaprasad et al., 2004)** . In vivo and in vitro studies suggest that lipid metabolism is altered both in acute and chronic exposure to lead **(Ademuyiwa et al., 2009)**. Lead inhibits antioxidant enzyme activity, such as superoxide dismutase and catalase, and also decreases the level of glutathione, increasing lipid peroxidation **(Newairy and Abdou , 2009)**. Several chelating agents have been used to reduce the toxic effect of lead, but these have also produced a toxic potential . This has necessitated researches into the therapeutic potential of various medicinal plants and herbs (**Senapati et al., 2001 ; Simopoulos , 2002 and Kris-Etherton et al., 2003**).

The study aimed to evaluate the potential role of flaxseeds on hyperlipidemia , oxidative stress induced by lead acetate in adult male rats .

Materials and Methods :

Rats and diet: Male Sprague-Dawley rats weighing 160 ± 10 g were purchased from the Holding Company for Biological Products and Vaccines (VACSERA, Cairo, Egypt). Basal diet constituents and lead acetate were obtained from El-Gomhoria Company for Chemical and Pharmaceutical, Cairo, Egypt. Flax seeds were obtained from local market.

Chemicals : Kits for biochemical analysis of serum total cholesterol, triglyceride, high density lipoprotein Cholesterol (HDL-C), aspartate aminotransferase (AST) , alanine aminotransferase (ALT) , creatinine , uric acid (UA) , blood nitrogen urea (BNU) , urea , total protein , catalase (CAT) , malondialdahyde (MOD) , superoxide dismutase (SOD) , glutathione peroxidase (GPx) and glutathione reductase (GR) were purchased from the Gamma Trade Company for Pharmaceutical and Chemicals, Dokki, Egypt.

Animals and Experimental Design :

Thirty male albino rats of Sprague-Dawley strain weighing approximately 160 - 170 g were placed in a wire bottom cages under hygienic condition and were acsessed to the experimental diets and water (*ad-libitum).* Rats were observed daily, weighed twice a week and feed efficiency ratio were calculated.

All rats were fed on the basal diet , as described by **Reeves et al., (1993) ,** for one week as a period of acclimatization . After acclimatiztion period , rats were randomly assigned to five groups (6 rats / each). The first group was fed on basel diet and served as negative control (- ve). The second group (24 rats) received lead acetate in basel diet at (200 mg/kg diet) according to **Abdou and Newairy (2006)** to induced toxicity .

The potential role of flaxseeds on hyperlipidemia, oxidative stress and toxicity induced by lead acetate in adult male albino rats

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Introduction:

Flaxseeds seemed to be a natural nutritional choice since it is composed of high concentrations of the omega-3 fatty acid precursor, a-linolenic acid, as well as a rich source of lignans **(Prasad , 1997 ; Thompson et al ., 1991 ; Xue et al., 1992 and Prasad , 2000)** . The a-linolenic acid has a wide range of anti-inflammatory and anti-atherosclerotic actions **(Singer et al., 1990 ; Kelley et al ., 1991 and Kitts et al., 1999)** . The lignans produced specific reversible and competitive inhibition of platelet activating factor (PAF) **(Shen & Hussaini , 1990 ; Hall et al., 1993).** Flaxseeds, contains 32 to 45% of its mass as oil of which 51 to 55% is alpha-linolenic acid (18:3 n-3 omega-3 fatty acid), a precursor to eicosapentanoic and docosahexanoic acid and it may have beneficial effects on health and in control of chronic diseases, as well as being a good source of dietary fiber and lignan (**Mantzioris et al., 1994**) . The antioxidant properties of Flaxseeds lignans have been verified in animal models of endotoxic shock (**Pattanaik and Prasad , 1998)** , diabetes , and carbon tetrachloride-induced oxidative stress (**Prasad , 2001 and James et al., 2008**).

Lead acetate , a heavy metal, has continued to pose health hazards in animals and humans in many parts of the world (**Navarro-Moreno et al., 2009**). Many people who are exposed to gasoline, paints and exhaust fumes from automobile through inhalation, oral or dermal route have suffered from lots of health problems (**Ademuyiwa et al., 1994**). Lead is a non-threshold multi-targeted toxicant that causes alterations in different organs of the body, including the kidney (**Jarrar, 2003 and Senapati et al., 2001**). The absorbed lead is conjugated in the liver and passed to the kidney, where a small quantity is excreted in urine and the rest accumulates in various body organs and interferes with their function, specially the kidney as a target site for lead toxicity (**Jarrar, 2003; Garçon et al., 2007 ; Farrag et al, 2007 and El-Nekeety et al., 2009**).

Several reports indicated that lead can cause neurological, hematological, gastrointestinal, reproductive, circulatory, and immunological pathologies, All of them related to the dose and the duration of lead exposure (**Park et al., 2006 ; Patrick , 2006 ; Vega-Dienstmaier et al., 2006 and Ademuyiwa et al., 2007)** . The liver plays a major role in lead's metabolism, and it is in special risk due to the oxidative action of this xenobiotic; given the unquestionable