Study the Potential Protective Effect of Ethanolic Extract of Coriander *(Coriandrum sativum)* Leaves and Seeds Against Lead Toxicity in Rats

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Abstract

Bioactive compounds found in natural sources have the potential to act as oxygen free cleaners or metal chelators, enabling their use as natural antidote for heavy metal toxicity. So, in this research , the ethanolic extract of *Coriandrum sativum* leaves and seeds was evaluated for its potential effect in reducing the harmful effect of lead in rats. Thirty rats were randomly divided into 6 groups.Group1 set as a negative control group. Group 2 received a daily dose of lead acetate (40 mg/kg body weight orally) for 7 days for induction of oxidative stress then reclassified into 5 groups . Group 2 was left as a positive control group .Group three and four received an oral dose of coriander leaves extract (100 and 200 mg /kg), respectively.While the fifth and sixth group received an oral dose of coriander seeds extract (100 and 200mg /kg), respectively. The content of coriander leaf and seed extracts of phenolic and flavonoid substances was estimated. Also, the effect of these treatments on lead concentration in serum, liver and brain, kidney and liver function markers,lipid profile, oxidative stress markers, glucose level , and histopathological changes in liver and brain was evaluated .The results showed an increase in indicators of liver and kidney function ,lipid profile, glucose level and in the signs of oxidative stress in rats treated with lead acetate ,while the effect was mitigated by leaf and seed coriander extract. Also, extract improved the tissue structure of the liver and brain. The effect of coriander leaves

was more pronounced than that of the seeds. From the previous results it was shown that coriander possesses antioxidant activity and thus can be used as a natural chelating agent for lead toxicity.

Key words: oxidative stress, hepatotoxicity, metal chelators, lead acetate

Introduction

The discharge of water resulting from industrial processes that contain toxic heavy metals into rivers and aquifers leads to an increase in environmental pollution and poses a threat to human and animal health. The most abundant heavy metals in wastewater are chromium , lead, zinc, nickel and copper (**Tagharobiyan and Poozesh, 2015).**

Lead (Pb) is a bluish , thin heavy metal that is ubiquitous. It is considered a popular reason of pet poisoning in worldwide, and is reputed to cause a numerous physiological, behavioral and biochemical imbalances in both humans and laboratory animals **(Kansal *et al.*, 2012 and Goto *et al.*, 2020),** including the central nervous system **(Velaga *et al.*, 2014)** , kidney, liver, hematopoietic system , reproductive system and cardiovascular system **(Al-Rubaye , 2016 and Al-Snafi, 2016).** Also , **Ning *et al.*, (2021)** reported that Pb can lead to dysfunction and anemia of immune members.

One of the important mechanisms explaining the toxicity of heavy metals is due to oxidative stress. Toxic metals cause an elevation in the formation of free radicals and also reduce the amount of antioxidants , which work to reduce the severe damage caused by free radicals. Numerous data indicated that metals have the ability to react with DNA and nucleoproteins, leading to oxidative degradation in biological macromolecules **(Bedi *et al.*, 2016).**

Currently, lead toxicity is considered one of the critical and important problems in various parts of the world and so far there is no effective, safe and reliable treatment for this problem, but many metal chelators such as ethylenediaminetraacetic (EDTA) , dimercaptosuccinic acid (DMSA) and diethylenetriaminepentaacetate (DTPA) have been used to reduce lead toxicity but it was found that these substances are useless in reducing the burden of lead in the body. Moreover, these substances may be poisonous **(Sears, 2013).**

The use of many plants that have many chelating features has attracted great interest from scientists and researchers at the present time, and it has been found that these plants have the ability to mitigate lead induced neurotoxicity, hepatic and renal toxicity in rats, and prevent cadmium induced mitochondrial injury and programmed cell death in tissue culture models **(Sharma *et al.*, 2010, Sadeghi *et al.*, 2013 and**

Nicula *et al.*, 2016). Therefore, in this research we used *Coriandrum sativum* that is a fast growing herb whose seeds and leaves are used as one of the best spices in the world and a famous ingredient in the Middle East, India, Mediterranean and Latin America **(**Al-**Rubaye , 2016).**

Coriander can be used in the food industry to act as a preservative in the form of seeds, leaves, crushed or all of its parts (**Singletary 2016)** and it has also been added to food to hide the taste of some foods such as meat, fish and bread recipes **(Mahendra and Bisht 2011)**. Coriander is also used in traditional medicine to treat a variety of disease states **(Prachayasittikul *et al.*, 2018) .**

Studies have shown that coriander contains many different chemical compounds in every part of the plant including leaves, roots, seeds, and fruits, and these compounds have a great therapeutic benefits **(Mandal and Mandal 2015).** For example, these compounds include thymol , bornyl acetate and gallic acid which are expected to exert autonomic relaxation induction, anticancer and anti-inflammatory effects, respectively **(Riella *et al.*, 2012 and Sun *et al.*, 2016)**. Research has proven that Linalool, a terpene alcohol found in coriander, is the major compound that is responsible for some therapeutic effects of coriander because it has anticonvulsant, neuroprotective, analgesic, and anxiolytic effects **(deLucena *et al.*, 2020 and Li *et al.*, 2016) .** Also, HPLC analysis confirmed that rutin camphor, luteolin, quercetin, apigenin, catechin, chlorogenic acid, caffeic acid, gallic acid and ferulic acid were the most important and active compounds of *Coriandrum sativum* leaves (**Anita *et al.*, 2014 and Ashika *et al.*, 2018**).

It is worth noting that coriander was used in India to treat respiratory and urinary problems and to relieve stomach and intestinal disorders. It is also used in some areas of Pakistan in folk medicine to treat dysentery, diarrhea, flatulence, and vomiting **(Laribi *et al.*, 2015).**Coriander also plays an important role in strengthening memory, this is because it contains antioxidants and essential oils **(Ulutas *et al.*, 2018).**

On the other hand, coriander is widely used in many diets to rid the body of toxins, as it helps in removing toxic metal residues such as lead and mercury by excreting them in urine or feces **(Kansal *et al.*, 2012) .**

Some studies in rats poisoned with several doses of lead showed amazing results results in chelation and reduced toxicity in these animal models when treated with coriander **(Velaga *et al.*, 2014 and Tellez- lopez *et al.*, 2017) .** Therefore, this experiment was carried out to find out the role of coriander leaves and seeds in reducing the harmful effect of lead in the body.

Material and methods

Plants: Coriander leaves and seeds powder was obtained from a private herbalist.

Chemicals: Lead acetate was purchased from El-Gomhoria Company for Drugs and Medical Equipments, Cairo, Egypt . All other chemicals used in the research were obtained from Bio-Diagnostic Company, El-Dokki , Giza , Egypt .

Diets: Diet consists of sucrose, corn oil, casein , choline chloride, mineral mixture, cellulose, vitamins mixture and corn starch were brought from El-Gomhoria Company for Drugs and Medical Equipments, Cairo, Egypt.

Preparation of coriander seeds ethanolic extract

Dried coriander seeds (200 g) were placed with (800 ml) of ethanol in the soxhlet device for 48 hours at a temperature of 60 ° C. After this period ,The extract was evaporated and dried at 50–55 °C using a rotary evaporator and was stored at 4 °C.The extract was dissolved in distilled water when starting the experiment **(Donia, 2019) .**

Preparation of coriander leaves ethanolic extract

Dried coriander leaves (1 kg) were soaked with 10 L ethanol, twice. Filter paper was used to filter the mixture and the filtrate was concentrated by a rotary vacuum evaporator at a temperature of 60°C **(Aligita *et al.*, 2018).**

Experimental design

Thirty male albino rats were divided into 2 main groups as follows:

Group (1) : Untreated group **(**control) received distilled water.

Group (2) : Lead acetate treated group, received lead acetate (Pb (CH3COO)2) at a dose of 40 mg/ kg body weight (b.w.) / day for 7 day to induce lead toxcity according to **Donia , (2019)** then reclassificied into 5 groups :

Group (2) was left as a positive control group.

Group (3) and (4) were administered with ethanolic coriander leaves extract at a dose of 100 and 200 mg/ kg b.w. orally, respectively.
Group (5) and (6) were administered with ethanolic coriander seeds extract at a dose of 100 and 200 mg/ kg body weight orally , respectively.

Tissue sample collections:

The liver and brain of each rat were splitted into two pieces , the first piece was homogenized to use for biochemical assay (determination of lead concentration) according to **Combs *et al.*, (1987)** . The second piece of liver and brain was washed in saline and then in 10% formalin to perform a histopathological examination .

Determination of total phenolic and flavonoid content

The total phenolic (µg GAE /g) and flavonoid (µg CE /g) contents of the coriander leaves and seeds extract were quantified according to **Bakari *et al.*, (2018)**

Biochemical analysis

Lead concentration in serum was measured according to **Parsons *et al.*, (1998) .** The lead residue in brain and liver was estimated according to **Ruhling and Tyler, (1973)**.Serum glucose level was determined according to **Kaplan, (1984).**

Alkaline phosphatase (ALP) , Alanine amino transferase (ALT) and Aspartate amino transferase (AST) , were measured according to **Moss , (1982), Henry, (1974) and Tietz , (1976) ,** respectively. Serum uric acid , urea and creatinine, were determined according to **While *et al.*, (1970) , Schirmeister *et al.*, (1964)** and **Patton and Crouch (1977) .** Cholesterol, triglycerides (T.G) , high density lipoprotein cholesterol (HDL-c) were estimated according to **Richmond, (1973)** , **Fossati and Principe (1982)** and **Allain , (1974) ,** respectively . Low density lipoprotein cholesterol (LDL-c) was estimated according to **Castelli *et al.*, (1977)**

LDL Concentration mg/dl =Total Cholesterol- HDL -VLDL

Very low density lipoprotein cholesterol (VLDL-c) was calculated according to **Lee and Nieman, (1996)** equation:

VLDL-C concentration mg/dl = T.G / 5

Malondialdehyde (MDA) , catalase (CAT) and glutathion transferase (GTF) were assayed according to **Ohkawa *et al.*, (1979)** , **Diego, (2011)** and **HU, (1994)**, respectively.

Statistical analysis

The data was analyzed using the statistical program COSTAT according to **Snedecor and Cochran (1986) .**

Results and discussion

Table (1) : Total phenolic and total flavonoids content in coriander leaves and seads ethanolic extract

Coriander extract	Total phenolics (µg of GAE /g) Mean ± SD	Total flavonoids (µg of CE/g) Mean ± SD
Ethanolic coriander leaves extract	14.3 ± 0.2	54.7± 2.3
Ethanolic coriander seeds extract	7.5± 2.6	18.8 ± 0.5

GAE=Gallic acid **CE**= Catechin

Data in table (1) shows total phenolic (equivalent to gallic acid) and total flavonoids (equivalent to catechin) content in coriander leaves and seeds ethanolic extract . Regarding to the total phenolics in coriander leaves and seeds ethanolic extract , the mean values were 14.3 ± 0.2 and 7.5± 2.6 (µg of gallic acid /g), respectively. While the mean values of total flavonoids in coriander leaves and seeds ethanolic extract were 54.7± 2.3 and 18.8 ± 0.5 (µg of catechin /g) , respectively . From the previous results, it is clear that coriander leaves are rich in flavonoids and phenolic substances compared to seeds. The present study is in accordance with **Wangensteen *et al.*, (2004)** they showed that the coriander seeds reported lower antioxidant effect than the leaves

Usually, high content of flavonoids and total phenol contents lead to better DPPH (2,2-Diphenyl-1-picrylhydrazyl) scavenging activity **(Felhi *et al.*, 2017) .** it is known that , polyphenols have a metal chelating ability and their redox activity can be confirmed by their chemical composition **(Schvab *et al.*, 2016).** For this reason , the great antioxidant activity of coriander leaves and seeds is due to the high content of the high polyphenolic components .

Badee *et al.*, (2020) emphasized that coriander leaves are natural sources that are full of phenolic and flavonoid substances. The phenolic

content in coriander leaves extract was (6.87mg GAE/g) while total flavonoid was (21.83 mg CE/g) , Some other scientists **(Pillay, 2017; Jangra *et al.*, 2018 and Ashika *et al.*, 2018)** have also showed the same results . In this context , **Ergün , (2022)** also reported that coriander leaves and seeds are rich in their content of antioxidants, which prevent human body from the harmful activity of free radicals , and the leaf extract was rich in its content of flavonoids compared to seed extract .

Table (2): Effect of coriander leaves and seeds ethanolic extract on lead in rats serum, brain and liver of negative control and lead groups

Groups	Serum lead (µg/dl) Mean ± SD	Liver lead (µg/g) Mean ± SD	Brain lead (µg/g) Mean ± SD
(1) Control (-)	3.9^{e} ± 0.2	0.75^{e} ± 0.194	$o.3^{c}$ ± 0.2
(2) Control (+)	65.13^{a} ± 2.66	28.86^{a} ± 1.56	5.5^{a} ± 1.802
(3) Coriander leaves extract (100 mg / kg body weight)	22.73^{c} ±2.71	13.36^{bc} ± 2.95	2.2^{bc} ± 0.9
(4) Coriander leaves extract (200 mg / kg body weight)	12.73^{d} ± 2.47	8.5^{d} ± 1.5	1.5^{c} ± 0. 3
(5) Coriander seeds extract (100 mg / kg body weight)	27.53^{b} ± 2.61	15.8^{b} ± 2.19	3.73^{b} ± 0.642
(6) Coriander seeds extract (200 mg / kg body weight)	14.93^{d} ± 2.76	11.16^{cd} ± 1.75	1.73^{c} ± 0.208
L.S.D	4.308	3.355	1.565

Values are mean ± SD. Values in the same column sharing the same superscript letters are not statistically significantly different (p≤ 0.05)

Effect of coriander leaves and seeds ethanolic extract on lead in rats serum, brain and liver of negative control and lead groups presented in table (2). Data showed that exposure of rats to lead acetate can increase lead levels in serum, brain and liver compared to negative control group .These results are in the same line with **Dupler,(2001)** who emphasized that the exposure of rabbits to lead negatively affects on

brain development and causes neurological defects in the brain. Also, **Rheman, (2016)** observed an increase in lead concentration in the fish brain when exposed to lead and this percentage increased with the increase in lead exposure time compared to the negative control group. Treating rats with ethanolic extract of coriander leaves and seeds led to a decrease in lead levels in the serum, brain and liver of rats.

The coriander chelating activity has been evaluated in aquatic environments alone or in combination with other compounds. Fortification of *Oncorhynchus mykiss* diet with 2% coriander powder reduced cadmium concentration in kidney and liver by 20-30% **(Ren *et al.*, 2006)**. Also, coriander assists in the removal of cadmium chloride from rainbow trout (**Ren *et al.*, 2009)** .

These results are in the same line with **Winarti *et al.*, (2018)** who reported that coriander leaf extract can reduce the toxicity of heavy metals (Pb, Hg and Cu) present in contaminated *lorjuk* meat from Kengiran Beach, Surabaya without affecting on the protein content . Increasing the soaking time increases the effectiveness of the extract in reducing the bad signs caused by heavy metals . Also, **Donia, (2019)** reported that the alcoholic and aqueous extract of coriander seeds contains many antioxidants so it can be used as a natural lead chelator.

Ahmed *et al.*, (2020) proved that the addition of alcoholic extract of coriander to the diet at a dose of 30 mg / kg resists the immunotoxic effects of exposure to lead by improving the immune response to *O. niloticus.*In addition , it was confirmed that fortification of the *Carassius gibelio* diet with 2% of each of coriander , chlorella and garlic protected against kidney damage caused by exposure to cadmium **(Nicula *et al.*, 2016). Bahrekazemi *et al.*, (2020)** also observed that feeding on coriander powder at a dose of 10 or 15 g / kg led to a decrease in the concentration of heavy metals in *Huso huso* carcasses because coriander contains many antioxidants compounds such as thymol, gallic acid and bornyl acetate which reduce the toxicity of lead .

Table (3): Effect of coriander leaves and seeds ethanolic extract on liver rats functions of negative and lead groups

Groups	GOT (U/L) Mean ± SD	GPT (U/L) Mean ± SD	ALP (U/L) Mean ± SD
(1) Control (-)	$66.03^{d} \pm 2.21$	$70.83^{e} \pm 2.02$	$148^{d} \pm 2.64$
(2) Control (+)	$98.96^{a} \pm 2$	$117.86^{a} \pm 2.47$	$182.73^{a} \pm 2.41$
(3) Coriander leaves extract (100 mg / kg body weight)	$82.23^{b} \pm 2.79$	$98^{b} \pm 2.64$	$174^{b} \pm 3.60$
(4) Coriander leaves extract (200 mg / kg body weight)	$74.66^{c} \pm 2.13$	$82.33^{d} \pm 2.51$	$161.5^{c} \pm 3.5$
(5) Coriander seeds extract (100 mg / kg body weight)	$84.3^{b} \pm 3.63$	$98^{b} \pm 2.64$	$179.43^{a} \pm 2.37$
(6) Coriander seeds extract (200 mg / kg body weight)	$80.73^{bc} \pm 6.13$	$88^{c} \pm 2.64$	$165.9^{c} \pm 2.02$
L.S.D	6.16	4.451	5.022

Values are mean ± SD. Values in the same column sharing the same superscript letters are not statistically significantly different ($p \leq 0.05$)

Table (3) shows the effect of coriander leaves and seeds ethanolic extract on liver rats functions of negative and lead groups. Data showed that exposure of rats to lead acetate can increase liver function markers (GOT, GPT and ALP) in positive control group compared with negative group . The same results were obtained by **ELmenoufy , (2012)** who showed that lead acetate can increase liver functions of lead groups compared with negative control group . All treated groups with coriander seeds and leaves showed significant decrease in liver function markers when compared to the positive control group . On the other hand, liver function markers decreased gradually with increasing the level of coriander extract .

It is noteworthy that the liver and kidneys are the most organs affected by lead poisoning as a result of lead storage in these organs. In this study, the high level of liver enzymes in the blood may be due to the damage of liver cells caused by lead acetate and this is consistent with the results of **Obafemi *et al.*, (2019).**

This result is in complete agreement with **Iqbal *et al.*, (2018)** who indicated that coriander seeds and leaves have an effective role in mitigating lead toxicity in the liver, and the effect of the leaves was more pronounced than that of the seeds. **Donia , (2019)** came to the same conclusion, noting that coriander seeds had the ability to significantly improve liver function in rabbits exposed to lead acetate . Coriander extract has the ability to decrease TNF-α , caspase 3, nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) and necrosis in hepatic ischemia reperfusion injury (**Kukner *et al.*, 2021).**

The previous results were in agreement with those of **Gazwi *et al.*, (2022)** who confirmed that fortifying the diet of broiler chicks with coriander extract did not effectively affect the level of albumin and globulin but the level of liver enzymes (AST and ALT) was significantly affected when the diet was supplemented with the extract.

In contrast, **Al-Rubaye, (2017)** confirmed that consumption of aqueous coriander leaves extract at a dose of 250 mg/kg has a toxic effect on the liver of rats , It was also noted that the weight of the liver decreased, and the levels of its enzymes increased, with a marked degeneration of the liver cells by treatment with this dose but rats treated with a dose of 125 mg / kg of coriander leaf extract showed signs of moderate toxicity despite the relative weights of the liver and biochemical parameters were in the normal range.

Table (4) : Effect of coriander leaves and seeds ethanolic extract on kidney function markers of negative control and lead groups

Groups	Urea (mg/dl) Mean ± SD	Creatinine (mg /dl) Mean ± SD	Uric acid (mg/dl) Mean ± SD
(1) Control (-)	$47^{I} \pm 2.64$	$0.61^{c} \pm 0.11$	$1.63^{c} \pm 0.208$
(2) Control (+)	$82.73^{a} \pm 2$	$1.5^{a} \pm 0.3$	$3.76^{a} \pm 0.251$
(3) Coriander leaves extract (100 mg / kg body weight)	$65.96^{c} \pm 2.15$	$1^{bc} \pm 0.1$	$2.83^{b} \pm 0.306$
(4) Coriander leaves extract (200 mg / kg body weight)	$54^{e} \pm 2.64$	$0.76^{c} \pm 0.152$	$2.06^{c} \pm 0.208$
(5) Coriander seeds extract (100 mg / kg body weight)	$78^{b} \pm 2.64$	$1.3^{ab} \pm 0.2$	$3.13^{b} \pm 0.152$
(6) Coriander seeds extract (200 mg / kg body weight)	$60.83^{d} \pm 2.28$	$0.9^{c} \pm 0.1$	$2.6^{b} \pm 0.360$
L.S.D	4.29	0.312	0.457

Values are mean ± SD. Values in the same column sharing the same superscript letters are not statistically significantly different (p≤ 0.05)

Data in table 4 show the effect of coriander leaves and seeds on rats kidney functions of negative and lead groups. The results illustrated that the levels of uric acid, creatinine and urea in positive control group were significantly increased after administration with lead acetate compared with negative control rats. The results are in agreement with **Obafemi *et al.*, (2019)** who concluded that high levels of creatinine and urea in the blood appeared in the group treated with lead, and this may be due to the fact that lead makes cells impermeable to urea and creatinine, which leads to this. Therefore, an elevated level of urea and creatinine in the blood indicates a defect in renal function and it is a functional evidence of lead-induced nephrotoxicity. All rats fed on coriander seeds and leaves had lower levels in uric acid , urea and creatinine compared with positive control group .

The results of the present research agreed with **Singh *et al.*, (2019)** who proved that treatment with the ethanolic extract of coriander leaves or with fresh leaf juice leads to a clear decrease in blood urea level and may protect the kidney from toxicity in rats with gentamicin-induced nephrotoxicity. Also, **Thuraisingam *et al.*, (2019)** referred to the diuretic activity of coriander leaf extracts as the aqueous and alcoholic extract of the leaves increases urinary sodium excretion more than potassium so it can be said that coriander extract has effective blood pressure lowering properties. On the other hand , **Petrina *et al.*, (2021)** proved that coriander leaf extract at a dose of 100 mg/kg BW have not the ability to protect the kidney from the harmful effect of mercury chloride, while the dose of 200 mg/kg BW showed clear positive results and protected the kidney to a large extent **.**

Also**, Gazwi *et al.*, (2022)** showed that the concentration of uric acid and urea in broiler chicks was reduced when treated with a diet fortified with coriander extract. Also, the addition of coriander extract to the diet did not lead to a negative result on the indicators of kidney function and it was found that the extract did not contain any toxic components.

Table (5) : Effect of coriander leaves and seeds ethanolic extract on rats lipid profile of negative and lead groups

Group	T.C (mg/dl) Mean ± SD	T.G (mg/dl) Mean ± SD	HDL (mg/dl) Mean ± SD	LDL (mg/dl) Mean ± SD	VLDL (mg/dl) Mean ± SD
(1) control (-)	147.76^{d} ± 2.61	133^{e} ± 3.60	95.66 ^{a} ± 2.08	25.5^{e} ± 0.81	26.6 ^{e} ± 0.721
(2) control (+)	173.33 ^{a} ± 2.08	186.43^{a} ± 3.12	36.76^{f} ± 2.41	99.28^{a} ± 3.11	37.34^{a} ± 0.593
(3) Coriander leaves extract (100 mg / kg body weight)	165.53^{b} ± 3.56	160^{c} ± 2	53.43^{d} ± 2.64	80.1^{b} ± 5.52	32^{c} ± 0.4
(4) Coriander leaves extract (200 mg / kg body weight)	151.66^{d} ± 3.05	142.43^{d} ± 2. 50	88^{b} ± 2.64	35.18^{d} ± 4.04	28.48^{d} ± 0.50
(5) Coriander seeds extract (100 mg / kg body weight)	172^{a} ± 2.64	172.86^{b} ± 2.55	42.76^{e} ± 2.57	94.66^{a} ± 3.29	34.57^{b} ± 0.51
(6) Coriander seeds extract (200 mg / kg body weight)	159.33^{c} ± 3.05	155.76^{c} ± 3.15	64.8^{c} ± 3.60	63.38^{c} ± 2.87	31.43^{c} ± 0.579
L.S.D	5.114	5.109	4.681	6.34	1.002

Values are mean ± SD. Values in the same column sharing the same superscript letters are not statistically significantly different (p≤ 0.05)

Data in table 5 showed that oral administration with lead acetate can led to increase levels of TC,TG,LDL and VLDL in control positive group compared with negative control group while HDL had opposite trend . **Faried *et al.*, (2011**) reported that administration of lead acetate to rats caused increase in TC,TG and LDL in positive control group .The results indicated that treatment with coriander leaves and seeds can decrease LDL,TC,TG and VLDL levels and increase HDL level compared with positive control group .

Several in vivo studies proved that coriander has an effective impact on the level of fat in the body . Coriander has the ability to modulate various enzymes of lipid metabolism pathways and reduce cholesterol and triglyceride levels. For example, the activity of 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase, that turns HMG-CoA into mevalonic acid , was reduced by coriander thus, the availability of cholesterol bound to cells is inhipited . The lecithin-cholesterol acyl transferase (LCAT) enzyme plays an active role in reverse cholesterol transport. Reverse cholesterol transport is a

metabolic process in which surplus cholesterol is transported from the peripheral tissues of the body to the liver for excretion by it. This enzyme plays an active role in the conversion of cholesterol ester to high density lipoprotein cholesterol (HDL) . Coriander improved the activities of tissue lipase and LCAT resulting in further breakdown of lipids **(Dhanapakiam *et al.*, 2008).**

Ramadan *et al.*, (2008) confirmed the previous studies, they showed that seed oil of coriander can reduce TG, LDL and TC and elevate HDL level in rats. Also, dry coriander seed has decreased cholesterol level in the colon , liver and intestine , reduced cholesterol to phospholipid ratio and inhibited intestinal and colon tumors in mice with colon cancer **(Chithra and Leelamma , 2000) .** Hydro-alcohol coriander leaves extract can inhibit DNA damage and peroxidation of lipid **(Harsha and Anilakumar, 2014).**

In the same context **, Sinaga *et al.*, (2022)** showed that coriander leaves can reduce LDL , triglycerides and total cholesterol levels as well as increase serum HDL levels in mice fed on high fat diet . Also, fortify the broiler chicks diet with coriander extract can significantly decrease plasma TG, TC, and LDL because coriander extract contain flavonoids which improve lipid metabolism **(Gazwi *et al.*, 2022).**

Table (6): Effect of coriander leaves and seeds ethanolic extract on rats serum glucose of negative and lead groups

Groups	Serum glucose (mg/dl) Mean ± SD
(1) Control (-)	$99.06^{f} \pm 2.79$
(2) Control (+)	$137.9^{a} \pm 2.66$
(3) Coriander leaves extract (100 mg / kg body weight)	$119.66^{c} \pm 1.52$
(4) Coriander leaves extract (200 mg / kg body weight)	$107.83^{e} \pm 2.37$
(5) Coriander seeds extract (100 mg / kg body weight)	$127.13^{b} \pm 2$
(6) Coriander seeds extract (200 mg / kg body weight)	$115^{d} \pm 2.64$
L.S.D	4.226

Values are mean ± SD. Values in the same column sharing the same superscript letters are not statistically significantly different (p≤ 0.05)

Effect of coriander leaves and seeds ethanolic extract on rats serum glucose of negative and lead groups are shown in Table 6 . These results confirmed that there was an increase in glucose level in positive control group compared to negative and treated groups .These results in accordance with **Ashour , (2006)** who stated that treating rats with lead acetate lead to an increase in glucose level . However administration of coriander leaves and seeds led to a decrease in blood glucose level .The highest reduction in glucose level was observed in rats treated with 200 mg/kg coriander leaves extract .

Coriander affected the metabolism of carbohydrates in the body by increasing the consumption of glucose. Coriander increases the activity of hexokinase , glucose-6-phosphate dehydrogenase, and phosphoglucomutase. Also, it promotes glycolysis and glycogenogenesis. Coriander reduces the activity of glucose-6-phosphatase and glycogen phosphorylase which leads to a decrease in gluconeogenesis and glycogenolysis **(Chithra and Leelamma, 2000) .** Coriander also improves insulin sensitivity, reduces α-glucosidase and α-amylase activity, inhibits glucose absorption, and increases glucose uptake in the peripheral tissues and liver **(Eidi *et al.*, 2009 and Aissaoui *et al.*, 2011).**

Aligita *et al.*, (2018) emphasized the previous results , they noted that ethanolic coriander leaf extract has anti diabetic effect when used at a concentration of 400 mg/kg body weight by regenerating and improving β pancreatic cells and reducing α-glucosidase enzyme activity . Also **Das *et al.*, (2019)** reported that coriander leaves have many therapeutic benefits , it can be used as antidiabetic agent and can be added to food to get great benefits.

These results are consistent with **Mishra *et al.*, (2021**) they reported that coriander seeds methanolic extract has the ability to fight oxidative stress which causes diabetes problems and complications. An in vivo study confirmed that treating diabetic rats with a portion of polyphenols from seeds of coriander can control serum blood glucose (**Mechchate *et al.*, 2021**).

Gazwi *et al.*, (2022) emphasized that fortification the diet of broiler chicks at six weeks of age with coriander extract led to a decrease in glucose level. This decrease may be due to the fact that coriander

stimulates insulin secretion and enhances muscle metabolism and glucose uptake.

Table (7) : Effect of coriander leaves and seeds ethanolic extract on oxidant and antioxidant markers of negative control and lead groups

Groups	GTF (mol/L) Mean ± SD	CAT (mol/L) Mean ± SD	MDA (mol/L) Mean ± SD
(2) Control (-)	530. 76^{a} ± 2.15	270.26^{a}± 1.90	15.03^{e} ± 1.95
(2) Control (+)	326.1^{f} ± 2.10	124.3^{f} ± 3.21	37.53^{a} ± 2.55
(3) Coriander leaves extract (100 mg / kg body weight)	453.86 ^{d}± 3.12	197.26^{d} ± 2.12	32.5^{b} ± 2. 19
(4) Coriander leaves extract (200 mg / kg body weight)	518.23^{b} ± 2.17	263.23^{b} ± 3.72	19.06^{d} ± 1.53
(5) Coriander seeds extract (100 mg / kg body weight)	383.4^{a} ± 3.34	129.43^{e} ± 2.47	36.83^{a} ± 1. 20
(6) Coriander seeds extract (200 mg / kg body weight)	492.73^{c} ± 2.18	233.3^{c}± 2.12	28.2^{c} ± 2.23
L.S.D	4.56	4.76	3.55

Values are mean ± SD. Values in the same column sharing the same superscript letters are not statistically significantly different (p≤ 0.05)

Data in table (7) show the effect of coriander leaves and seeds ethanolic extract on oxidant and antioxidant status of negative control and lead groups. The levels of glutathion transferase (GTF) and catalase (CAT) decreased after exposure to lead acetate while , malonaldhide (MDA) increased .The decrease in the level of GTF and CAT may be due to oxidative stress caused by exposure to lead acetate. GTF and CAT were increased by treating rats with coriander leaves and seeds ethanolic extract**.**The method of extracting the active substances from coriander affects the yield of flavonoids and phenols. It was found that water extraction is better than microwave and ultrasonic extraction **(Önder, 2018)**. The aqueous extract of coriander seeds, rich in flavonoids, showed antioxidant activity in animals suffering from lead toxicity in the kidneys and liver. Treatment with these extracts increased levels of CAT, GSH and SOD and reduced lipid peroxidation **(Samojlik *et al.*, 2010**) . Also , **Msaada *et al.*, (2017)** reported that the methanolic extract of coriander fruits can neutralize the harmful effect of free radicals, which confirms the

possibility of using coriander fruits as a natural source of antioxidants which can be exploited in food industries.

These results are in agreement with **Ergün , (2022)** who showed that different plant part of coriander contain high amount of phenolic components , he showed also that total flavonoid and phenolic content differed in stem , seed and leaf extracts, it was reported to be lower in the methanol extracts compared to hexane extracts

Histopathological examination of liver and brain

Brain :

Microscopic examination of brain of group 1 (control negative group) showing normal histological structure (**Photo 1).** Brain of group 2 (control positive group) showing neuronal cell vacuolar degeneration, pyknosis and necrosis with pericellular edema **(Photo 2) .** Brain of group 3 which treated with coriander leaves extract (100 mg / kg**)** showing mild necrobiotic changes of scattered neurons, neuronal cells pyknosis and neuronophagia of the necrotic neurons **(Photo 3).** Brain of group 4 which treated with coriander leaves extract (200 mg / kg) showing good protection of brain tissue with almost normal appearance of neurons and degenerated ones **(Photo 4).** Brain of group 5 treated with coriander seeds extract (100 mg / kg) showing scattered neuronal cells pyknosis and neurophagia of some necrotic neuron with mild edema around cells and blood vessels **(Photo 5**). Brain of group 6 which treated with coriander seeds extract (200 mg / kg) showing a moderate degree of neurodegeneration and necrosis with intermittent neurophagia with perivascular edema (**Photo 6**).

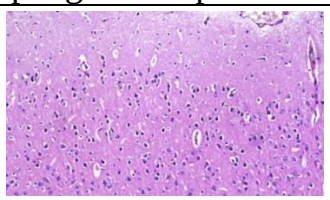	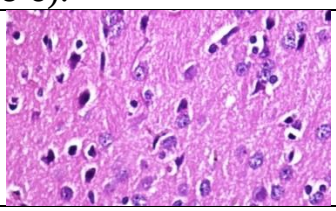
Photo (1): Brain of group 1 (control negative group) showing normal histological structure**.**	**Photo (2)** : Brain of group 2 (control positive group) showing neuronal cell vacuolar degeneration, pyknosis and necrosis with pericellular edema **(H&E, X400).**

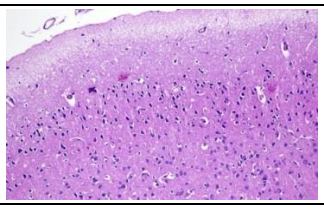	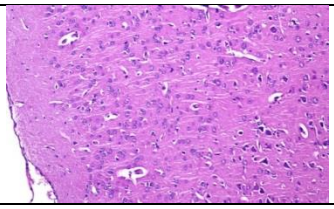
Photo (3) : Brain of group 3 which treated with coriander leaves extract (100 mg / kg**)** showing mild necrobiotic changes of scattered neurons, neuronal cells pyknosis and neuronophagia of the necrotic neurons **(H&E, X200).**	**Photo 4** : Brain of group 4 which treated with coriander leaves extract (200 mg / kg) showing good protection of brain tissue with almost normal appearance of neurons and degenerated ones **((H&E, X200).**
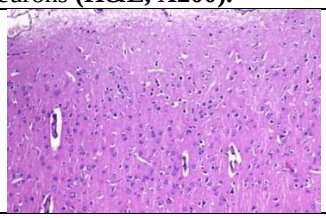	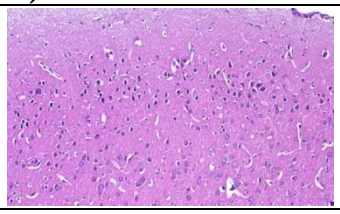
Photo (5) : Brain of group 5 treated with coriander seeds extract (100 mg / kg) showing scattered neuronal cells pyknosis and neurophagia of some necrotic neuron with mild edema around cells and blood vessels **(H&E, X200).**	**Photo (6):** Brain of group 6 which treated with coriander seeds extract (200 mg / kg) showing a moderate degree of neurodegeneration and necrosis with intermittent neurophagia with perivascular edema **(H&E, X200).**

Liver

Microscopic examination of liver of group 1 (control negative group) showing normal histological structure **(Photo 1)**. Liver of group 2 (control positive group) showing degenerative vacuolar neuron degeneration and necrosis with periclinal edema **(Photo 2).** Liver of group 3 that treated with coriander leaves extract (100 mg / kg**)** showing moderate degree of degeneration of the hepatic cells and scattered necrotic cells with good restoration of the hepatic cells **(Photo 3).**Liver of group 4 which treated with coriander leaves extract (200 mg / kg) showing good degree of protection of the hepatic parenchyma with only very few degenerated and rare necrotic cells as well as few dilated hepatic sinusoids **(Photo 4) .** Liver of group 5 which treated with coriander seeds extract (100 mg / kg**)** showing mild degree of hepatocellular degeneration and scattered necrotic cells **(Photo 5) .** Liver of groyp 6 treated with coriander seeds extract (200 mg / kg**)**showing mild degree of hepatocellular degeneration and scattered necrotic cells **(Photo 6).**

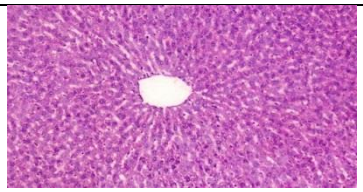	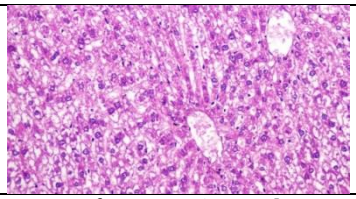
Photo (1): Liver of group 1 (control negative group) showing normal histological structure.	**Photo 2 :** Liver of group 2 (control positive group) showing degenerative vacuolar neuron degeneration and necrosis with periclinal edema **(H&E, X400).**
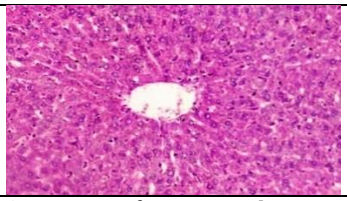	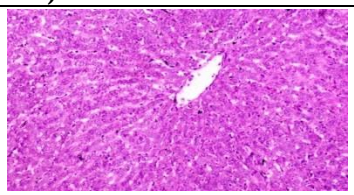
Photo (3) : Liver of group 3 that treated with coriander leaves extract (100 mg / kg**)** showing moderate degree of degeneration of the hepatic cells and scattered necrotic cells with good restoration of the hepatic cells **(H&E, X200).**	**Photo (4)** : Liver of group 4 which treated with coriander leaves extract (200 mg / kg) showing good degree of protection of the hepatic parenchyma with only very few degenerated and rare necrotic cells as well as few dilated hepatic sinusoids **(H&E, X 200) .**
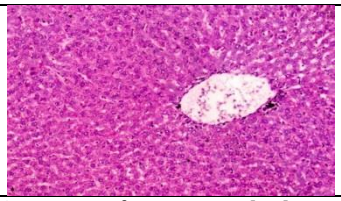	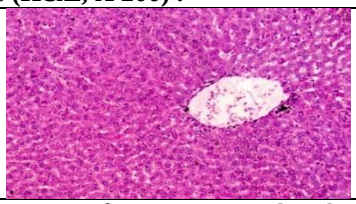
Photo (5) : Liver of group 5 which treated with coriander seeds extract (100 mg / kg**)** showing mild degree of hepatocellular degeneration and scattered necrotic cells **(H&E, X200).**	**Photo 6** : Liver of groyp 6 treated with coriander seeds extract (200 mg / kg**)**showing mild degree of hepatocellular degeneration and scattered necrotic cells **(H&E, X200).**

Finally, histopathological investigation results were in line with that observed for the biochemical analysis

Conclusion:

From this study, it was found that both the leaves and seeds of coriander have effective activity against lead toxicity. Therefore, this study recommends the necessity of using coriander leaves and seeds by adding them to food to reduce the harmful effects caused by lead in the body.

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دراسة التأثير الوقائي المحتمل للمستخلص الإيثانولي لأوراق وبذور الكزبرة ضد سمية الرصاص في الفئران

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المستخلص

المركبات النشطة بيولوجيًا الموجودة في المصادر الطبيعية لديها القدرة على العمل كمنظفات للأكسجين الحر أو خالبات للمعادن ، مما يتيح استخدامها كمضاد طبيعي لسمية المعادن الثقيلة ، لذلك في هذا البحث تم تقييم المستخلص الإيثانولي لأوراق وبذور الكزبرة لمعرفة تأثيره المحتمل في خفض التأثير الضار للرصاص . تم تقسيم ثلاثين فأر عشوائياً إلى ست مجموعات ، المجموعة الأولى مجموعة ضابطة سالبة ، المجموعة الثانية تلقت جرعة يومية من أسيتات الرصاص (40 مجم / كجم من وزن الجسم عن طريق الفم) لمدة 7 أيام للحث على احداث الإجهاد التأكسدي ثم تم إعادة تصنيفها إلى 5 مجموعات حيث تركت المجموعة الثانية كمجموعة ضابطة موجبة ، تلقت المجموعة الثالثة والرابعة جرعة فموية من مستخلص أوراق الكزبرة (100 و 200 مجم / كجم) على التوالي ، بينما تناولت المجموعة الخامسة والسادسة جرعة فموية من مستخلص بذور الكزبرة (100 و 200 مجم / كجم) على التوالي .تم تقدير محتوى مستخلص أوراق وبذور الكزبرة من المواد الفينولية والفلافونيدية كذلك تم تقييم تأثير هذه العلاجات على تركيز الرصاص في مصل الدم والكبد والدماغ وعلامات وظائف الكلى والكبد وصورة الدهون والاجهاد التأكسدى ومستويات الجلوكوز والتغيرات النسيجية المرضية في الكبد والدماغ. وأظهرت النتائج زيادة في مؤشرات وظائف الكبد والكلى ، ومستوى الدهون ومستوى الجلوكوز وعلامات الإجهاد التأكسدي في الفئران المعالجة بخلات الرصاص ، بينما تم تخفيف التأثيرعن طريق مستخلص أوراق الكزبرة وبذورها ، كما أدى المستخلص إلى تحسين بنية أنسجة الكبد والدماغ ، وكان تأثير أوراق الكزبرة أكثر وضوحًا من تأثير البذور ، وقد تبين من النتائج السابقة أن الكزبرة تمتلك نشاط مضاد للأكسدة وبالتالي يمكن استخدامها كمخلب طبيعي لسمية الرصاص .

الكلمات المفتاحية : الاجهاد التأكسدى - السمية الكبدية - خالبات المعادن – خلات الرصاص