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Research Article

Influence of Coriander Extract Supplement on Oxidative Stress in Rabbits Fed Heavy Metal-Contaminated Diets

[1]Ayman Abdel Mohsen Hassan, [1]Mohamed Samir Mahmoud Khalel, [1]Mohamed Helmey Yacout, [1]Amr Mohamed Shwerab, [1]Hassan Sayed Abbas, [1]Rehab Abd Elhay Mohamed, [1]Fatma Talaat Farag Abd El-Ghany, [1]Rada Ibrahem Mohamed Matari, [2]Ahmed M. Elokazy[2], [1]Marwa Abdelmonem Suliman and [1]Mohamed Basyony Mohamed Mahmoud

[1]Animal Production Research Institute, Agricultural Research Center, Giza 12619, Egypt
[2]Regional Center for Food and Feed, Agricultural Research Center, Giza 12619, Egypt

Abstract

Background and Objective: In rabbits given diets contaminated with heavy metals, coriander extract is thought to be a beneficial supplement for oxidative stress. This study aimed to investigate the potential effect of coriander extract supplement on heavy metal-induced oxidative stress in growing rabbit diets. **Materials and Methods:** In a completely randomised design, 84 developing male New Zealand White (NZW) rabbits, 6 weeks of age, weighing 674.86 g at birth, were randomly assigned to one of four groups consisting of 21 rabbits each. After acclimating for 7 days, the rabbits were fed the experimental diets for 70 days. The diets were formulated as follows: First group (CR0) served as a control, with 30% berseem hay (BH), while, the three other groups had partial substitution of (BH) with common reed (CR) (*Phragmites australis*) at 50% of (BH). The third and fourth groups were supplemented with coriander (*Coriandrum sativum* L.) extract at 250 and 500 mg/kg of diet, respectively. The final body weight, daily weight gain and nutrient digestibility of dry matter, crude protein, neutral detergent fiber and acid detergent fiber were measured. **Results:** The study found that including coriander extract in rabbit diets improved body weight, daily weight gain and nutrient digestibility. Nitrogen intake, urine nitrogen and nitrogen balance were higher in coriander extract groups. Levels of NH_3-N, total VFA and acetic acid were higher, while butyric acid was lower in coriander extract groups. Heavy metal accumulation in feces and urine was highest in coriander extract groups, but lowest in rabbit meat. Heavy metal-intoxicated rabbits showed adverse effects on cholesterol, triglycerides, liver and kidney function and disrupted antioxidant balance. **Conclusion:** Therefore, it can be concluded that the inclusion of coriander extract in rabbit feed affects oxidative stress caused by heavy metals in growing rabbits.

Key words: Heavy metals, coriander, rabbit, performance, residue, common reed, antioxidant

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Corresponding Author: Ayman Abdel Mohsen Hassan, Animal Production Research Institute, Agricultural Research Center, Giza 12619, Egypt

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

A serious threat to the health, production and biodiversity of aquatic and surrounding terrestrial ecosystems is posed by heavy metal contamination in aquatic ecosystems, which is a global problem. Large amounts of waste are generated in tailings at mining sites during metal extraction from ore processing. Due to chemical weathering, fine waste particles release potentially toxic metals into the ground and surface water. Aquatic macrophytes play a crucial role in absorbing and accumulating heavy metals, contributing to natural water purification. The presence of naturally growing plants on mine tailing ponds indicates their tolerance of heavy metal pollution and suggests their potential for phytoremediation. In a recent study, the concentrations of heavy metals (Fe, Mn, Ni, Zn, Pb, Cd, Co and Cu) in *Phragmites australis* plants growing spontaneously in shallow water were analyzed[1].

Heavy metal pollution is a growing issue in urban areas around the world[2]. These high-density elements occur naturally in the environment in a small amount[3], but mining manufacturing and the use of certain metals in fuels and coal can release toxic metals into the water and air. While some heavy metals like zinc and copper are beneficial in small quantities, others can accumulate in harmful levels and pose health risks[4]. Urbanization, industrialization and the use of agrochemicals and untreated wastewater for irrigation have led to the build-up of toxic heavy metals in soil, water and ultimately affecting food crops[5]. This has resulted in serious health hazards from the consumption of vegetables grown near industrial and peri-urban areas[6]. Furthermore, heavy metal contamination can decrease soil quality and affect plant products consumed by humans and animals, leading to a higher prevalence of heavy metal toxicity[7]. In developing countries, the use of untreated wastewater for irrigation is becoming more common due to shortages, further contributing to heavy metal contamination of agricultural soils[5].

Heavy metals can enter the bodies of humans and animal through various sources, with dietary intake of contaminated food being a major route of exposure[8]. Stable oxidative states of heavy metals can combine with different enzymes and proteins leading to their accumulation in the body and causing oxidative stress[9,10]. Heavy metals have a wide range of harmful effects on various organs in the body, including a decline in growth performance disturbances in liver and kidney functions and blood biochemical changes[11,12].

Traditional medicine systems around the world have used many plants for the treatment of kidney failure, with several herbs being prescribed to reduce renal damage and prevent kidney-related complications[13]. Studies on the different parts of *Coriandrum sativum* has revealed its potential as a medicinal plant with various pharmacological activities such as antibiotic anti-oxidant, anti-diabetic, anti-cholinesterase, anti-helminthic, sedative-hypnotic, anticonvulsant, cholesterol-lowering, anti-cancer and hepatoprotective effects[14-17]. Coriander belonging to the family Umbelliferae is widely distributed and mainly cultivated for its seeds which is used as a flavoring agent in food products, perfumes and cosmetics[18]. Research has shown that coriander extracts contain phenolic compounds and flavonoids, which contribute to its ant oxidative activity[19]. Coriander has also been found to suppress the deposition of lead by chelating the metal and promoting the excretion of heavy metals in the urine of patients as well as enhancing the efficacy of antibiotics[20,21].

Given these findings, it was important to evaluate the potential of *Coriandrum sativum* extract in improving rabbits' performance, its antioxidant activity and its hepato-protective effect against heavy metals-induced toxicity in rabbits.

MATERIALS AND METHODS

The research was conducted at the Rabbit Research Laboratory, Nubaria Experimental Station, Animal Production Research Institute, Agricultural Research Centre, Alexandria, Egypt. This study was took place during the Egyptian Autumn (September-November, 2023).

Extraction and preparation of *Coriandrum sativum* fractions: Coriander leaves were bought from the local market in Alexandria and ground into a fine powder. The aqueous extract of coriander was prepared according to the methods described by Kansal *et al.*[19]. As 125 g of coriander was mixed with 500 mL of distilled water. After 24 hrs of maceration at room temperature (37°C), the extract was heated for 30 min in a water bath at 65°C, filtered and concentrated by heating over the water bath (65°C) and dried using a rotary evaporator. The extract was then stored at 4°C and administrated to animals as needed at doses of 250 and 500 mg/kg diet/day, as described by Kumar *et al.*[21].

Study area and sampling: In April 2023, samples were gathered from areas where common reed (CR) (*Phragmites australis*) was naturally growing. Five 100 m^2 sampling sites were selected in Nubaria City, El-Bihara Government, Egypt. These sites were believed to be contaminated with heavy metals as a result of municipal waste and urban emissions. The collection of plant, irrigation water and sediment samples

Table 1: Ingredients and chemical composition of the control and experimental feed

	Experimental diet			
Ingredients	Control	T1	T2	T3
Alfalfa hay	30.00	15.00	15.00	15.00
Common reed	0.00	15.00	15.00	15.00
Barley grain	21.50	21.50	21.50	21.50
Yellow corn	11.00	11.00	11.00	11.00
Wheat bran	12.00	12.00	12.00	12.00
Soybean meal	20.00	20.00	20.00	20.00
Molasses	3.00	3.00	3.00	3.00
Dicalcium phosphate	1.00	1.00	1.00	1.00
Limestone	0.80	0.80	0.80	0.80
Sodium chloride salt	0.20	0.20	0.20	0.20
DL-Methionine	0.30	0.30	0.30	0.30
L-Lysine	0.10	0.10	0.10	0.10
Vit+Min premix[1]	0.10	0.10	0.10	0.10
Chemical composition of experimental basal diets (g/100g DM)				
Organic matter	93.64	91.16	91.32	91.29
Crude protein	16.74	16.31	16.23	16.28
Crude fiber	13.14	13.89	13.83	13.79
Ether extract	3.24	3.08	3.06	3.01
Neutral detergent fibre	35.76	39.36	39.22	39.39
Acid detergent fibre	17.86	21.51	21.42	21.55
Acid detergent lignin	4.76	6.11	6.15	6.14
Calculated and determined composition (g/100g DM)				
Lysine	0.63	0.58	0.58	0.58
Methionine	0.41	0.37	0.37	0.37
Calcium	0.83	0.89	0.89	0.89
Phosphorus	0.49	0.42	0.42	0.42

[1]Vit+Min premix. provides per kilogram of the diet: Vit. A, 12000 IU, Vit. E (dl-α-tocopheryl acetate) 20 mg, menadione 2.3 mg, Vit. D3, 2200 ICU, riboflavin 5.5 mg, calcium pantothenate 12 mg, nicotinic acid 50 mg, Choline 250 mg, Vit. B12 10 μg, Vit. B6 3 mg, thiamine 3 mg, folic acid 1 mg, d-biotin 0.05 mg. Trace mineral (mg/kg of diet): Mn 80 Zn 60, Fe 35, Cu 8 and Selenium 0.1 mg

followed the method outlined by Bonanno and Cirelli[22]. Three *Phragmites australis* plants were randomly collected from each sampling site and placed in plastic bags for transfer to the laboratory. Irrigation water (500 mL) was collected in three plastic bottles and three sediment samples (500 mL) were taken from each site. The sampling took place under climatic conditions; sunny, calm and without recent rain.

Animals, diets and experimental design: The study involved eighty four male New Zealand White (NZW) rabbits at six-weeks of age, with an initial body weight of 674.86±27.83 g. They were divided into four groups of 21 rabbits each, in a completely randomized design. Each group was further divided into seven replicates of three rabbits and their weight measured weekly. The rabbits were fed experimental diets for 70 days, after 7 days acclimatization periods. The diets included a control (CR0 with 30% (BH) and three other groups with partial substitution of (BH) with common reed (CR) by 50%, along with supplementation of coriander (*Coriandrum sativum* L.) at 250 and 500 mg/kg diet in the third and fourth groups, respectively. The chemical compositions of the diets were detailed in Table 1. The rabbits were housed wire batteries and maintained under standard environmental conditions with access to feed and water *ad libitum*. Weekly measurements of live body weight and feed intake were recorded and average daily gain (ADG) and feed conversion ratio (FCR) were calculated.

A digestibility trial was conducted to determine the nutritional digestibility coefficients of the experimental meals[23]. Seven rabbits from each treatment group were individually housed in metabolic cages and fed the experimental meals for seven days as a preparatory stage. Subsequently, feces were collected daily for five consecutive days before the morning feeding during the collection period. The collected feces were crushed, oven-dried at 70°C for 48 hrs and stored for further chemical analysis. The feed and dried feces were analyzed for dry matter (DM), crude protein (CP), crude fiber (CF), nitrogen-free extract (NFE), neutral detergent fiber (NDF) and acid detergent fiber (ADF)[24].

Carcass characteristics: At the conclusion of the study, seven rabbits from each group were chosen at random and subjected to a 12 hrs fast. They were then individually weighed and euthanized by cutting the jugular vein to assess carcass characteristics. Post-bleeding, rabbits were weighed again to calculate the dressing percentage (slaughter weight/body weight). The weights of the liver, kidneys, heart and testes were also recorded.

Chemical analysis: Samples of feed, feces and meat were finely ground through a 1-mm screen in a Cyclotec mill (Cyclotec 1093; Foss, Germany) and stored for analysis. Moisture content was determined by drying samples in an oven at 70°C. Crude protein (CP) content (N 6.25) was determined using Kjeldahl's method. Ether extract was determined using the Soxhlet extraction method with petroleum ether. Ash content was determined by incinerating samples in a muffle furnace at 550°C. Neutral detergent fiber (NDF), acid detergent fiber (ADF) and acid detergent lignin (ADL) contents were analyzed using a Tecator Fibertec System. Digestible energy (DE; Kcal/kg DM) was calculated as 2823-40.8×ADF-25.7ADL+47.4 CP[25]. Caecal fermentation analysis involved measuring pH values of samples with a digital pH meter. Caecal contents were centrifuged at 7,000×g for 10 min at 20°C and the resulting supernatant was split into two parts. One part was acidified with a 0.2 M hydrochloric acid solution (1 mL/mL sample) to determine Ammonia Nitrogen (NH_3-N) concentration using a spectrophotometer. The other part was treated with a solution of 5% orthophosphoric acid and 1% mercuric chloride to measure total Volatile Fatty Acids (VFAs) concentration and individual VFA proportions. Total VFAs were measured by steam distillation and acetic, propionic, butyric and valeric acids were analyzed using HPLC with a reversed-phase column and UV detector.

Metal concentration analysis: Samples (*Phragmites australis*, irrigation water, sediment, diets, urine, feces and meat) were dried at 75°C for 72 hrs, then homogenized or sieved. Heavy metals were analyzed using the wet digestion method by du Laing *et al.*[26]. Samples (0.5 g dry weight) were digested in 65% nitric acid in a microwave oven, filtered through 0.45 µm (Millipore) and measured using an atomic absorption spectrometer (Perkin-Elmer Model 5000 AAS, HGA-500, MHS-10) for Mn, Fe, Ni, Cu, Zn, Pb and Cd.

Blood biochemical and antioxidant capacity: After the experiment, blood samples were collected from seven rabbits in the group. The samples were allowed to clot for 1 hr at room temperature and then centrifuged at 5000 rpm for 10 min. The sera were carefully collected and stored at -20°C for subsequent biochemical analyses. The levels of serum total protein, albumin, globulin, total cholesterol, urea, creatinine, Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) were measured. Additionally, the activities of superoxide dismutase (SOD), glutathione peroxidase (GPx) and thiobarbituric acid reactive substances (TBARS) were determined using commercial kits from Biodiagnostic Company (Giza, Egypt) and a spectrophotometer (Optizen Pop, Mecasys, Korea).

Statistical analysis: The experimental design was completely randomized using the general linear means of SAS program. Measured parameters were analyzed using the following statistical model:

$$Y_{ij} = \mu + d_i + \varepsilon_{ij}$$

where, Y_{ij} is the measured value, µ is the overall mean effect, d_i is the i^{th} diet effect and ε_{ij} is the random error associated with the j^{th} rabbits assigned to the i^{th} diet. Differences among means were considered to be significant at the ($p<0.05$) level, as determined using Duncan's multiple range test[27].

RESULTS AND DISCUSSION

Growth performance, nutrient digestibility and nitrogen utilization: Data concerning growth performance, apparent nutrient digestibility and nitrogen utilization were presented in Table 2. The final body weight, daily weight gain and nutrient digestibility of DM, CP, NDF and ADF were significantly higher ($p<0.05$) for T3, T2 and control groups compared to the T1 group. There were no significant differences in daily feed intake among the rabbits groups ($p<0.05$). The feed conversion ratio was significantly improved ($p<0.05$) for T3, T2 and control groups compared to the T1 group. The nitrogen utilization of the diets is also presented in Table 2. The T3, T2 and control groups showed the highest ($p<0.05$) nitrogen intake (NI), urine nitrogen, nitrogen absorbed (NA) and nitrogen balance (NB) compared with T1 group. There were no significant differences in feces nitrogen of the rabbits in the different groups.

There is a growing concern about the health risks of multi-heavy metal pollution from dietary feed exposed to heavy metals. Livestock is typically exposed to a mixture of toxic metals in the environment which can have multiple health hazards. Therefore, it is important to assess the toxic effects of combinations of different heavy metals. In this experiment, exposure to heavy metals significantly reduced the final body weight change in animals. These results were

Table 2: Effect of coriander leaves extract on growth performance, nutrient digestibility and nitrogen utilization on toxicity produced by heavy metals in rabbit diet

	Experimental diet					
Parameter	Control	T1	T2	T3	SEM	p-value
Initial body weight (g)	674.73	683.46	669.36	671.88	27.83	0.836
Final body weight (g)	2735.84[a]	2075.33[c]	2579.57[b]	2806.57[a]	36.07	0.001
Daily weight gain (g/day)	29.44[a]	19.88[c]	27.29[b]	30.50[a]	1.06	0.001
Daily feed intake (g/day)	107.64	89.64	101.75	104.64	21.95	0.746
Feed conversion ratio	3.66[a]	4.51[b]	3.73[a]	3.43[a]	0.28	0.016
Apparent nutrient digestibility (%)						
Dry matter	67.36[a]	59.63[b]	67.95[a]	68.44[a]	1.14	0.011
Crude protein	64.51[a]	56.75[b]	63.72[a]	65.27[a]	1.45	0.021
Crude fiber	47.88[a]	39.03[b]	48.04[a]	49.89[a]	2.06	0.014
Neutral detergent fibre	53.75[a]	45.28[b]	53.06[a]	54.55[a]	1.06	0.008
Acid detergent fibre	44.19[a]	37.61[b]	43.21[a]	45.32[a]	1.83	0.002
Nitrogen utilization (g/h/d)						
Nitrogen intake	2.60[a]	2.14[c]	2.42[b]	2.50[ab]	0.11	0.014
Urine nitrogen	0.60[b]	0.95[a]	0.48[c]	0.43[c]	0.05	0.001
Feces nitrogen	0.92	0.93	0.88	0.87	0.07	0.783
Nitrogen absorption	1.68[a]	1.22[b]	1.54[a]	1.63[a]	0.12	0.019
Nitrogen balance	1.08[a]	0.26[b]	1.05[a]	1.20[a]	0.11	0.009

[a,b,c]Means in the same row having different superscripts differ significantly ($p<0.05$) and SEM: Standard error of the mean

consistent with studies by Shehata[12] who found that rabbits exposed to 0.5% lead acetate in their diet have decreased final body weight, daily body gain and feed intake. Additionally, Falke and Zwennis[28] reported that female rabbits given lead at a dose of 0.8-1.20 µg/kg b.wt., three times a week experienced a decrease in body weight. The decrease in growth performance with high levels of lead acetate may be due to a wide variety of adverse effects including loss of appetite, depletion of essential minerals (such as Zn, Ca, Se, Cu and Mg) from the body, reduced digestion or absorption of nutrients in the diets and decrease in growth performance[29].

Exposure of growing rabbits to high levels of lead (50 or 70) resulted in decrease in growth performance; but this may not be a reliable indicator for monitoring led toxicity[30]. The present study found that exposure to lead acetate (T1-20 or T2-30) did not impact FI, DBWG and FCR in rabbits. Lead treatment did not affect the FCR, consistent with previous research by Shehata[12]. However, increasing lead dose led to a gradual decrease in BWG in animal[31]. The control groups increased body weight may be due to the higher fibre content of the diet which improves nutrient digestibility and absorption[3]. Additionally, the diet's crude protein content and palatability may have contributed to its acceptability and utilization. The presence of nutritional factors and reduced anti-nutritive factors (NFs) in the diets likely allowed for effective nutrient utilization and absorption, resulting in the highest mean weight gain in rabbits.

This could be due to a possible direct impact of lead on the digestive system leading to a decrease in digestion and absorption, ultimately reducing FI as a central effect of lead toxicity[32].

Some studies have found that exposure to lead has no impact on body weight in animals[33], while others, including our research, have shown that high levels of lead can reduce body weight[34].

The effect of heavy metals on nutrient digestibility depends on both the type of toxic elements and the composition of the feed. For example, nickel may decrease feed intake, leading to lower growth rates, but does not significantly affect nutrient digestibility in rabbits, even at high levels (e.g., 500 mg/kg). A decrease in the digestibility of crude fiber to approximately 20% is considered to be within normal physiological ranges[35]. Coriander seed components have been shown to promote intestinal health, enhancing the availability of essential nutrients for absorption and potentially improving animal growth performance[36]. Additionally, increased enzyme activity due to improved intestinal health can lead to better nutrient absorption[36]. The effectiveness of essential oils on digestibility may also depend on factors such as the composition of the basal diet, feed intake level and environmental conditions[37]. The supplementation of coriander has been found to increase digestibility coefficients, possibly due to its stimulatory effects on pancreatic secretions, leading to increased secretion of digestive enzymes and improved nutrient absorption from the digestive tract.

Carcass characteristics and chemical composition of meat: Table 3 shows that supplementation led to significant changes in organ weight (%). The T1 group had significantly lower dressing %, compared to the T2, T3 and control groups. The coriander supplementation and control groups significantly reduced the weight % of liver, kidneys and heart, compared to

Table 3: Effect of coriander leaves extract on carcass characteristics and chemical composition of meat on toxicity produced by heavy metals in rabbit diet

	Experimental diet					
Parameter	Control	T1	T2	T3	SEM	p-value
Carcass characteristics						
Live body weight (g)	2208.76	2042.52	2219.53	2264.42	156.84	0.625
Slaughter weight (g)	1465.36^{a}	1121.42^{b}	1486.31^{a}	1507.83^{a}	0.46	0.006
Dressing (%)	66.34^{a}	54.90^{b}	66.97^{a}	66.59^{a}	0.55	0.019
Carcass dressing (%)						
Edible giblets (%)						
Liver	2.86^{b}	3.95^{a}	2.95^{b}	2.99^{b}	0.08	0.014
Kidney	0.82^{b}	1.07^{a}	0.85^{b}	0.88^{b}	0.05	0.021
Heart	0.36^{b}	0.41^{a}	0.34^{b}	0.37^{b}	0.02	0.017
Testis	0.95^{a}	0.71^{b}	0.88^{a}	0.93^{a}	0.06	0.001
Chemical composition of meat (%)						
Moisture	71.86^{b}	74.22^{a}	71.65^{b}	71.73^{b}	0.22	0.011
Protein	20.74^{b}	18.87^{c}	21.05^{a}	21.44^{a}	0.95	0.009
Ether extract	5.25^{b}	7.43^{a}	4.97^{c}	4.84^{c}	0.41	0.022
Ash	3.76^{b}	4.45^{a}	3.82^{b}	3.79^{b}	0.07	0.014

^{a,b,c}Means in the same row having different superscripts differ significantly (p<0.05) and SEM: Standard error of the mean

the T1 group. However, the T1 group had a significantly lower testis %, compared to the T2, T3 and control groups. The T1 group also had significantly higher moisture, ether extract and ash in the chemical composition of meat, percentage, compared to the T2, T3 and control groups. However, the T1 group had a significantly lower protein in the chemical composition of meat, percentage, compared to the T2, T3 and control groups.

Goat kidneys had the highest increase in Cd concentration, followed by the liver, which had the highest level of Cd exposure and finally the hair. Hair reflects external Cd emissions in the living area as it is replaced annually. Kidneys are a good indicator of the body's Cd levels. The liver, hair and the rest of the body have 30%, 17% and significantly lower potential to store Cd, respectively, compared to the kidneys' Cd concentration[38]. The kidney, hair and eventually feces can detect the availability and load of cadmium[39]. A healthy reproductive system, including the hypothalamus, pituitary gland, ovaries and is essential for successful reproduction.

Continuous exposure to lead (Pb) can have an impact on the development and production of sperm cells in males[40]. In both male and female rats, exposure to lead may also lower serum levels of sex steroids[41]. Unbound cadmium (Cd) to metallothionein can cause testicular necrosis and negatively impact follicular growth in ovarian tissue, ultimately resulting in ovarian atrophy[42]. Vascular disruptions are the main cause of the seminiferous epithelium's degeneration and other alterations in the testes following exposure to mercury. The ovaries, placenta and uterus can also experience effects such localised edema, haemorrhage and vascular thrombosis in the testes[40].

Caecal fermentation: There were no significant differences in pH values and propionic acid levels among the rabbits in the different groups. However, the concentrations of NH_3-N and total VFA in rabbit cecal varied significantly (p<0.05) among the treatments (Table 4). Specifically, the concentrations of NH_3-N and total VFA, as well as acetic acid, were significantly (p<0.05) increased in the T3, T2 and control groups compared with the T1 group. Conversely, the concentration of butyric acid was significantly (p<0.05) decreased in the T3, T2 and control groups compared with the T1 group. The production of NH_3-N results from the protein digestion process by fermenting microorganisms in the cecum. Insufficient NH_3-N levels in fermentation can hinder microbial growth and activity during feed degradation. The NH_3-N is crucial for microbial protein synthesis in the rumen[43]. Low NH_3-N levels, combined with 3% Pb in the diet, may be due to Pb's toxic effects on bacteria involved in feed degradation. The Pb, along with As, Cd and Hg, can inhibit gas formation and enzyme activity in the rumen[44], disrupting fermentation and affecting pH, ammonia, VFA levels and microbial populations[45]. The Pb exposure can also hinder rumen metabolism by forming organometallic lipid components that inhibit microbial growth and respiration[46].

Concentrations of heavy metals in the sediment, water and *Phragmites australis*: Table 5 presented the concentrations of heavy metals, in sediments, water and *Phragmites australis*. The highest amounts of Fe, Mn, Zn, Ni, Cu, Pb amounts and Cd were found in all three mediums. *Phragmites australis* is a widely distributed species that thrives in various wetland environments. It is highly adaptable and can grow in contaminated areas such as mine tailing ponds. The sediments

Table 4: Effect of coriander leaves extract on caecal fermentation on toxicity produced by heavy metals in rabbit diet

	Experimental diet					
Parameter	Control	T1	T2	T3	SEM	p-value
pH	6.45	6.38	6.41	6.49	0.11	0.745
NH_3-N (mmol/L)	12.75^{a}	10.88^{c}	11.96^{b}	12.56^{ab}	58.97	0.001
Total VFA (mmol/L)	65.47^{a}	61.33^{c}	63.29^{b}	65.89^{a}	0.89	0.001
Acetic acid (mole %)	62.21^{a}	57.52^{c}	60.35^{b}	62.08^{a}	0.76	0.001
Propionic acid (mole %)	21.63	20.91	21.17	21.36	0.83	0.815
Butyric acid (mole %)	8.14^{b}	8.87^{a}	8.31^{b}	8.11^{b}	0.16	0.004

^{a,b,c}Means in the same row having different superscripts differ significantly (p<0.05) and SEM: Standard error of the mean

Table 5: Concentrations of heavy metals in the sediment, water and *Phragmites australis* rabbit (µg/g) (n = 5)

	Concentrations of heavy metals		
Item	Sediment	Water	*Phragmites australis*
Mn	688.91	0.83	154.74
Fe	3854.33	1.97	321.33
Ni	85.85	0.33	20.52
Cu	54.88	0.26	11.06
Zn	382.1	0.53	268.16
Cd	4.75	0.11	2.34
Pb	32.2	0.18	19.07

showed notably high levels of Fe, Zn, Pb and Cu, close to phytotoxic levels. The mobility of Pb in soil and its translocation to plant organs make it difficult to assess its toxicity to plants, but threshold values range from 2 to 200 mg/kg. Metal accumulation in aquatic plants depends on various factors, such as metal concentration, substrate availability, water and sediment properties, species-specific uptake and plant growth conditions. The detected amounts of Fe in *Phragmites australis* were higher than in plants from shallow lakes and soils affected by mining activities, but lower than in plants on acidic mine drainage[47].

Residue heavy metals concentration of feed intake, urine, feces and meat: The feed intake of rabbits in the T1, T2 and T3 groups showed a statistically significant (p<0.05) increase in heavy metal content compared to the control group (Table 6). The rabbits fed with T2 and T3 groups had the highest levels of Mn, Fe and Ni. The Cu, Zn, Cd and Pb in their feces and urine compared to the control group (p<0.05). However, the rabbits' meat fed with control, T2 and T3 groups had the lowest levels of heavy metal accumulation compared to the T1 group (p<0.05). The study found differences in heavy metal content in the urine, faces and muscles depending on the feed additive. The essential metal contents in the faces and meat of rabbits fed with *Coriandrum sativum* extract were in the following descending order: Fe>Zn>Mn> Pb>Ni>Cu>Cd.

Minerals play a crucial role in unlocking the genetic potential of highly productive rabbit genotypes. Zinc, copper and manganese are essential components of many enzyme systems. They are required for the growth, development and reproduction of animals. The bioavailability of trace elements depends on their forms and sources of entry into the animal body as well as their physiological state[48]. In studies on the contamination of food of animal origin, it was found that cadmium and lead are more harmful among toxic metals, considering both the number of exceedances in the permissible content and the associated risks[49]. The liver and, to a lesser extent, muscles, accumulate heavy metals, such as lead and cadmium, in addition to micronutrients[50].

Active components such as monoterpenes, limonene, α-pinene, p-cymene, γ-terpinene, citronellol, borneol, camphor, coriandrin, geraniol, dihydrocoriandrin, flavonoids coriandrons A-E and essential oils, cilantro offers both therapeutic and nutritional benefits. It has shown various pharmacological effects like digestive stimulation, antihyperlipidemia, antihyperglycemic, antioxidant, hypotensive and antiproliferative activities. Coriander is also included in detox diets[51]. It can be easily grown in kitchen gardens, flower pots or commercially. It is affordable and has the potential to eliminate harmful metal ions like lead, copper and mercury[52]. A substance called HMD (heavy metal detox) has been found to be effective in mobilizing these metal ions[53].

Blood serum biochemical and antioxidant capacity: The results of plasma biochemical components showed that the concentrations of total protein, albumin and globulin in the T2, T3 and control groups were significantly higher (p<0.05) compared to the T1 group (Table 7). Additionally, heavy metal-intoxicated rabbits had significantly increased levels of total

Table 6: Residue heavy metals concentration of feed intake, urine, feces and meat rabbit (µg/g)

	Experimental diet					
Parameter	Control	T1	T2	T3	SEM	p-value
Mn						
Intake	1.42^{b}	24.76^{a}	24.68^{a}	24.79^{a}	1.68	0.001
Urine	0.005^{c}	1.06^{b}	1.23^{a}	1.28^{a}	0.07	<0.001
Feces	0.94^{c}	14.65^{b}	16.65^{a}	17.47^{a}	0.96	<0.001
Meat	0.38^{c}	7.46^{a}	5.88^{b}	5.68^{b}	0.22	<0.001
Fe						
Intake	21.76^{b}	60.62^{a}	60.71^{a}	60.68^{a}	2.27	0.001
Urine	1.57^{c}	1.95^{b}	2.45^{a}	2.49^{a}	0.09	<0.001
Feces	14.14^{c}	35.75^{b}	40.64^{a}	40.96^{a}	0.33	<0.001
Meat	5.78^{c}	21.67^{a}	17.11^{b}	17.02^{b}	0.16	<0.001
Ni						
Intake	0.004^{b}	3.15^{a}	2.99^{a}	3.07^{a}	0.14	0.001
Urine	ND	0.004^{b}	0.017^{a}	0.017^{a}	0.05	0.0001
Feces	0.002^{c}	1.65^{b}	1.84^{a}	1.92^{a}	0.09	0.001
Meat	ND	1.37^{a}	1.12^{b}	1.13^{b}	0.03	0.001
Cu						
Intake	0.011^{b}	1.75^{a}	1.71^{a}	1.69^{a}	0.07	0.001
Urine	0.001^{c}	0.013^{b}	0.019^{a}	0.021^{a}	0.002	<0.0001
Feces	0.005^{c}	0.91^{b}	1.12^{a}	1.14^{a}	0.03	<0.001
Meat	0.004^{c}	0.72^{a}	0.57^{b}	0.53^{b}	0.11	<0.001
Zn						
Intake	25.64^{b}	65.87^{a}	63.46^{a}	64.99^{a}	2.77	0.001
Urine	1.32^{c}	2.87^{b}	3.94^{a}	4.09^{a}	0.14	<0.001
Feces	19.57^{c}	41.18^{b}	46.66^{a}	47.25^{a}	1.07	<0.001
Meat	4.33^{c}	17.85^{a}	11.07^{b}	11.99^{b}	1.01	<0.001
Cd						
Intake	0.008^{b}	0.31^{a}	0.29^{a}	0.30^{a}	0.03	0.001
Urine	ND	0.004^{b}	0.007^{a}	0.008^{a}	0.001	<0.0001
Feces	0.003^{c}	0.16^{b}	0.21^{a}	0.22^{a}	0.01	<0.001
Meat	ND	0.12^{a}	0.072^{b}	0.071^{b}	0.04	0.001
Pb						
Intake	0.33^{b}	4.11^{a}	4.06^{a}	4.08^{a}	0.10	0.001
Urine	0.012^{c}	0.14^{b}	0.21^{a}	0.23^{a}	0.04	0.001
Feces	0.29^{c}	2.32^{b}	2.76^{a}	2.81^{a}	0.15	<0.001
Meat	0.021^{c}	1.24^{a}	1.02^{b}	1.01^{b}	0.02	<0.001

^{a,b,c}Means in the same row having different superscripts differ significantly (p<0.05) and SEM: Standard error of the mean

cholesterol, triglycerides, liver function enzymes (AST and ALT) and kidney function tests (serum creatinine and urea) compared to the control and coriander extract supplemented groups. The heavy metal-intoxicated rabbits also showed a disturbance in serum oxidant-antioxidant balance, with reduced levels of serum-reduced SOD, CAT and GPx and elevated serum TBARS compared to the normal control and coriander extract supplemented groups. However, supplementation with coriander extracts at the tested doses resulted in an increase in serum SOD, CAT and GPx levels as well as antioxidant enzyme activity and a decrease in serum TBARS levels heavy metals-intoxicated rabbits supplemented with coriander extracts at the tested doses compared to the heavy metals group.

Albumin, the main protein component of plasma, plays a crucial role in the body's immune system by producing antibodies. The liver is essential for detoxifying harmful compounds like heavy metals, such as lead. The study by Shehata[12] found that exposure to high levels of lead had a significant negative impact on total protein (TP) and albumin (AL) levels. Elevated liver enzymes, indicative of liver injury, were observed in individuals exposed to high levels of lead, leading to damage to liver cells and an increase in apoptotic hepatocytes[12,34]. Additionally, increased levels of urea and creatinine, markers of renal health, were associated with elevated lead levels. This study highlights the detrimental effects of lead exposure on liver and kidney function.

According to Alagawany *et al.*[11] proposed the serum TP levels in laying Japanese quails exposed to lead were lower compared to the control group. Additionally[54], found that lead acetate exposure led to malnutrition and protein synthesis issues in the liver resulting in decreased TP levels in quails. In

Table 7: Effect of coriander leaves extract on some blood serum biochemical parameters and antioxidant capacity in toxicity produced by heavy metals in rabbit diet

	Experimental diet					
Parameter	Control	T1	T2	T3	SEM	p-value
Blood serum biochemical parameters						
Total protein	6.64[a]	5.75[b]	6.33[a]	6.71[a]	0.37	0.018
Albumin	3.36[a]	2.98[b]	3.21[a]	3.37[a]	0.14	0.022
Globulin	3.28[a]	2.77[b]	3.12[a]	3.34[a]	0.20	0.019
A/G ratio	1.02	1.08	1.03	1.01	0.03	0.652
Total cholesterol (mg/dL)	145.79[b]	218.86[a]	155.46[b]	141.75[b]	9.46	0.004
Triglycerides (mg/dL)	97.57[b]	125.97[a]	99.75[b]	96.57[b]	2.77	0.008
Urea (mg/dL)	16.87[b]	32.85[a]	20.42[b]	18.05[b]	3.07	0.011
Creatinine (mg/dL)	0.75[b]	1.35[a]	0.82[b]	0.78[b]	0.05	0.009
Aspartate Aminotransferase (AST) (U/L)	21.55[b]	28.69[a]	22.64[b]	21.31[b]	1.26	0.012
Alanine Aminotransferase (ALT) (U/L)	29.75[b]	37.88[a]	29.97[b]	28.55[b]	1.32	0.014
Serum antioxidant capacity						
Superoxide dismutase, SOD (mg/dL)	216.86[a]	108.76[b]	199.86[a]	221.75[a]	19.65	0.021
Catalase, CAT (mg/dL)	2.46[a]	1.07[b]	2.15[a]	2.48[a]	0.24	0.006
Glutathione -S- peroxidase, GPx (mg/dL)	38.79[a]	22.75[b]	37.86[a]	38.96[a]	1.23	0.002
Thiobarbituric Acid Reactive Substances, TBARS (mmol/L)	23.19[b]	34.57[a]	24.66[b]	23.05[b]	1.04	0.011

[a,b]Means in the same row having different superscripts differ significantly (p<0.05) and SEM: Standard error of the mean

our study, the feed containing heavy metals induced nephrotoxicity (p<0.05), as evidenced by elevated serum concentrations of Mn, Fe, Ni, Cu, Zn, Cd and Pb along with inhibited serum kidney activity. Velaga *et al.*[55] noted that serum Delta Aminolevulinic Acid Dehydratase (δ ALAD) activity is an indicator enzyme of lead toxicity and its activity is inhibited when lead binds to its active center. Lead toxicity also increases the excretion of accumulated δ ALAD into the urine, where it may auto-oxidize to - form reactive oxygen species and induce lipid peroxidation[56].

The accumulation of lead in kidney tissues is attributed to the fact that the kidney may be a major target organ for lead toxicity with the epithelial cells of proximal convoluted tubules and Bowman's capsule being particularly sensitive to lead-induced nephrotoxicity. The proximal convoluted tubules are the primary sites of reabsorption and active transport leading to a higher concentration of lead in the epithelial lining of these tubules[57]. Lead accumulation in the kidney causes damage to renal tubules, leading to a decrease in the number of functional nephrons weakened reabsorption processes and generation of reactive oxygen species that damage cells and lead to apoptosis. These adverse effects on renal function result in elevated levels of nitrogen containing compounds such as urea, creatinine and uric acid in the blood, proteinuria and reduction in creatinine clearance[58].

Lead-intoxicated rats showed an elevated level of blood urea and creatinine, indicating impaired kidney function and reduced excretion of these products in urine[59]. The increase in uric acid concentrations may be caused by the breakdown of purines by an increase in uric acid production or by a decrease in its. Uric acid is the end product of the breakdown of tissue nucleic acid, which includes purine and pyrimidine bases. The increase in total urinary protein excretion is due to a decrease in the reabsorption of low molecular weight proteins by injured tubules[60]. Nephrotoxicity is a significant complication that causes functional changes such as inhibited protein synthesis, reduced glutathione levels, lipid peroxidation and mitochondrial damage. Oxidative damage is considered a key factor in most chronic kidney diseases[61].

Exposure to heavy metals like lead, mercury, arsenic and cadmium can cause kidney damage[62]. Lead is particularly harmful to the liver and kidneys, as it settles in the proximal tubule of the nephron, leading to nephrotoxicity[21,63]. Lead cause oxidative damage in tissues by increasing the generation of reactive oxygen species (ROS) and depleting antioxidant reserves[64,65]. Coriander extracts contain active components such as flavonoids, polyphenols and carotenoids which have antioxidant, anti-inflammatory and free radical scavenging properties[66]. Quercetin can decrease arginine consumption in urea synthesis by inhibiting hepatic arginase making arginine more available for protein synthesis. This can enhance renal regenerating capabilities, reduce tubular reabsorption of electrolytes and improve renal blood flow and glomerular filtration rate[67].

The current results showed a significant decline in AST and ALT values, which may be due to the liver-protective properties of the biological ingredients in coriander leaves like sterol, carotenoids, tocopherol and phospholipids ALT and AST are liver enzymes that indicate liver function and their levels increase in the blood during liver damage 'hepatocellular degeneration[17]. Additionally, significant decrease in SOD, CAT and GPX activities, as well as an increase in TBARS levels, was observed in rabbits exposed to heavy metals. These findings were consistent with those of Reddy *et al.*[68]. Heavy metal exposure can lead to a depletion of important antioxidants in the body, such as glutathione and protein bound sulfhydryl groups. This can result in an increase in reactive oxygen species, leading to lipid peroxidation. The changes in enzymatic antioxidant activity may be due to the generation of reactive oxygen species by heavy metals, or by reducing the body's antioxidant defense system. Additionally, heavy metals can interfere with essential trace elements needed for proper antioxidant enzyme function, making them potential targets for toxicity[69,70].

In a study by Shaheen *et al.*[71] and Rabeh and Aboraya[72], it was found that administering coriander extracts to rabbits exposed to heavy metals led to a significant increase in serum antioxidant enzyme activity (SOD, CAT and GPX), and a decrease in TBARS levels. This effect is attributed to the presence of quercetin in coriander extracts, which has strong antioxidant properties and can protect against oxidative damage in the serum and kidneys[73]. Fennel aqueous extract contains flavonoids and phenolic compounds that can scavenge free radicals through various mechanisms, such as scavenging or quenching free radicals, chelating metal ions, or inhibiting enzymatic systems that generate free radicals[74]. Fennel plants also contain significant concentrations of essential trace elements such as iron, selenium, manganese and zinc which are involved in antioxidant enzyme systems. For example, iron is a cofactor of catalase, an enzyme that plays a role in antioxidant defense systems by breaking down hydrogen peroxide[75]. Ora and Naidoo[76] identified these elements as principal constituents of fennel plants. Coriander contains important trace elements such as selenium, copper and zinc which are essential for antioxidant enzyme function. These elements help maintain glutathione levels and support the body defense against oxidative stress.

Coriander has been traditionally used as a remedy for diabetes and lowering cholesterol due to its hypoglycaemic and hypolipidaemic effect in animals[77]. The proposed mechanism of the hypoglycaemic effect of coriander involves normalizing blood sugar levels and reducing elevated levels of insulin, low density lipoproteins, cholesterol and triglycerides in obese, hyperglycaemic and hyperlipidaemic animal models[77].

CONCLUSION

The study findings showed that the growth performance, nitrogen balance and cecum activity of rabbits were enhanced when their diet included a partial substitution of berseem hay with common reed by 50%, along with supplementation of coriander (*Coriandrum sativum* L.) at 250 and 500 mg/kg diet. Additionally, the inclusion of coriander (*Coriandrum sativum* L.) at 250 and 500 mg/kg diet in rabbits' diet containing common reed and berseem hay helped reduce heavy metal accumulation in rabbit meat. Moreover, it improved antioxidant balance, resulting in increased levels of serum-SOD, CAT and GPx and decreased levels of serum TBARS compared to rabbits fed a diet with berseem hay and common reed by 50% without coriander (*Coriandrum sativum* L.) supplementation. Adding coriander extract to rabbit feed can help reduce oxidative stress caused by heavy metals in growing rabbits.

SIGNIFICANCE STATEMENT

The study investigated the impact of coriander extract supplementation on heavy metal-induced oxidative stress in rabbit diets. Eighty-four male New Zealand White (NZW) rabbits were divided into four groups, each fed a different diet for 70 days. The third and fourth groups were supplemented with coriander extract at 250 and 500 mg/kg, respectively. Results showed that the inclusion of coriander extract increased the final body weight, daily weight gain and nutrient digestibility of the rabbits. It also increased nitrogen intake, urine nitrogen, nitrogen absorbed and nitrogen balance. The levels of heavy metals were highest in the rabbits' feces and urine, but the metals showed the lowest accumulation in the meat. Heavy metal-intoxicated rabbits had increased total cholesterol, triglycerides, liver function and kidney function tests.

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