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Protective Effect of Lemon Grass Oil and Citral on Amelioration of Cadmium-induced Nephrotoxicity and Hepatotoxicity

Sona Shaji[1], Suja Rani S.[1], Anoop Raj[2] and Sujith Samraj[1]

[1]Dept. of Veterinary Pharmacology and Toxicology, [2]Dept. of Veterinary Pathology, College of Veterinary and Animal Sciences, Mannuthy, Kerala (680 651), India

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Corresponding sujarani@kvasu.ac.in

0000-0002-8618-7798

ABSTRACT

The experiment was conducted during January to May, 2025 at Department of Veterinary Pharmacology and Toxicology, at College of Veterinary and Animal Sciences, Mannuthy, Kerala, India to study the potential nephro- and hepatoprotective effects of lemongrass oil (LGO) and its active constitutent, citral against cadmium (Cd) induced renal and hepato damage. Thirty-six adult male Sprague Dawley (SD) rats weighing 150–200 g were kept in well-ventilated polypropylene cages under standard laboratory conditions of 12 h/12 h light/dark cycle at 25°C±2°C with 30–70% relative humidity. The experimental rats were divided into six groups of six animals each. Group I received 0.1% Tween 80 and normal saline, and group II received both cadmium chloride (7 mg kg^{-1} b.wt.) and Tween 80, while groups III to VI received LGO and citral at 45 and 90 mg kg^{-1} body weight dose levels, respectively, as oral administration for 28 days, along with cadmium chloride treatment. Significantly elevated serum markers of renal and hepatic dysfunction, alongside the altered oxidative stress indicators, were restored in the present study with LGO and citral treatment. Histological examination further confirmed that LGO and citral at both dose levels attenuated Cd-induced structural damage in kidney and liver tissues. Thus, the results were indicative of significant nephroprotective and hepatoprotective potentials of citral and LGO on Cd-induced nephro- and hepatotoxicity, which might be attributed to its antioxidant activity.

KEYWORDS: Cadmium, lemongrass oil, citral, antioxidant

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Data Availability Statement: Legal restrictions are imposed on the public sharing of raw data. However, author have full right to transfer or share the data in raw form upon request subject to either meeting the conditions of the original consents and the original research study. Further, access of data needs to meet whether the user complies with the ethical and legal obligations as data controllers to allow for secondary use of the data outside of the original study.

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1. INTRODUCTION

In recent decades, growing concern has emerged over the impact of environmental chemical exposure on human health. Rapid industrialization and urbanization have led to the proliferation of synthetic and naturally occurring toxicants in the air, water, soil and food. Epidemiological studies increasingly demonstrate that prolonged, even low-level exposure to environmental chemicals can cause significant adverse health effects, including damage to vital organs. The kidneys, due to their central role in filtering and excreting xenobiotics and metabolic waste, and the liver, the primary organ encountering absorbed xenobiotics, are particularly vulnerable to such toxic insults. Among the countless environmental pollutants, heavy metals stand out due to their persistence in the ecosystem and cumulative toxicity. Cadmium (Cd), a non-essential and highly toxic heavy metal, has attained particular attention owing to its widespread industrial use, with human exposure occurring mainly through contaminated food and water, occupational inhalation and tobacco use (Tchounwou et al., 2012; Hecht et al., 2016). Despite the umpteen regulatory efforts, Cd contamination continues to rise, particularly in both industrialised and developing nations, as it is non-biodegradable and remains in the environment for centuries. The kidney serves as the main site for Cd accumulation and is the organ most significantly affected during prolonged exposure (Charkiewicz et al., 2023; Qu and Zheng, 2024). Given its critical role in filtration and detoxification, the kidney is particularly vulnerable to damage caused by Cd exposure (Smereczanski and Brzoska, 2023). Cadmium induces nephrotoxicity through multiple pathways, including the promotion of oxidative stress and inflammation, interference with cell adhesion, proliferation, and apoptosis, and alterations in epigenetic regulation (Dukic-Cosic et al., 2020; Hao et al., 2021; Wang et al., 2021). Over time, these mechanisms contribute to the deterioration of renal function, ultimately manifesting as chronic kidney disease (Genchi et al., 2021; Yan and Allen, 2021; Zhang et al., 2024). The liver, as the primary site of exposure, also interacts with a considerable amount of Cd during the initial phase. Damage to hepatocytes can arise from injury to endothelial cells, which triggers inflammation and eventually leads to oxidative stress driven by an imbalance in redox homeostasis (Arroyo et al., 2012; Renu et al., 2021; Kusak et al., 2024). The increasing prevalence of kidney and liver disorders highlights the need for effective protective strategies beyond symptom-based conventional treatments. Under these circumstances, herbal medicines have gained considerable attention due to their bioactive secondary metabolites, antioxidant and anti-inflammatory properties, and favourable safety profiles, which collectively mitigate oxidative stress and inflammation underlying renal and hepatic toxicity (Banik et al., 2020; Sujana et al., 2021; Ganta et al., 2023; Tienda-Vazquez et al., 2022). Essential oils are highly concentrated plant extracts composed of volatile constituents that provide distinct fragrance and therapeutic activity (Dhifi et al., 2016). They are known for their robust antioxidant, anti-inflammatory, antimicrobial, and various other beneficial activities (Ramsey et al., 2020). These effects are largely linked to their diverse chemical constituents, including terpenes, hydrocarbons, alcohols, aldehydes, ketones, and esters (de Sousa et al., 2023). Their lipophilic nature and low molecular weight facilitate membrane penetration, modulate membrane dynamics, and exert beneficial physiological effects, thereby alleviating oxidative stress and inflammatory responses and potential anticancer effects at both cellular and systemic levels (Osaili et al., 2023). Among them, lemon grass oil (LGO) and its primary component, citral, are known to inhibit the production of reactive oxygen species and pro-inflammatory cytokines, indicating its strong antioxidant and anti-inflammatory properties respectively (Wifek et al., 2016; Han and Parker, 2017; Kusuma et al., 2024). The limited exploration of LGO and citral in mitigating metal-induced damage highlighted the need for continued research into their renal and hepatoprotective effects. Accordingly, the present study was assessed the ameliorative potential of LGO and citral against Cd-induced nephro and hepatic toxicity in rats.

2. MATERIALS AND METHODS

The experiment was conducted from January to May, 2025 at the Department of Veterinary Pharmacology and Toxicology at the College of Veterinary and Animal Sciences, Mannuthy, Kerala, India.

2.1. Chemicals

Lemongrass (Cymbopogon spp.) essential oil (95010000064) was procured from Synthite Industries Pvt. Ltd., Kerala and citral (95 % C83007) was obtained from M/s Sigma Aldrich, India. Cadmium chloride (99% 35658-65-2) was purchased from M/s Sisco Research Laboratories Pvt. Ltd (SRL), Maharashtra, India. All the diagnostic kits were purchased from M/s Agappe Diagnostics Ltd., India.

2.2. Experimental animals

Thirty-six adult male Sprague Dawley (SD) rats, weighing 150-200 g, were procured from the Small Animal Breeding Station, Mannuthy, Kerala. All the animals were kept in well-ventilated polypropylene cages under standard laboratory conditions of 12 h/12 h light/dark cycle at 25°C±2°C with 30-70% relative humidity and were given an acclimatisation period of seven days before the experimentation. They were given standard rat feed (source: School of Animal Nutrition and Feed Technology, College of Veterinary and Animal

Sciences, Mannuthy) and drinking water ad libitum. The experimental protocol was approved by the Institutional Animal Ethics Committee of the College of Veterinary and Animal Sciences, Mannuthy (No. CVAS/MTY/IAEC/25/95), and the study was performed in accordance with the guidelines of the Committee for Control and Supervision of Experimentation on Animals (CPCSEA), Government of India.

2.3. Experimental design

Thirty-six adult male SD rats, weighing 150–200 g, were randomly allocated into six groups of six animals each. Group I served as a vehicle control and received vehicle (0.1% tween 80) along with normal saline, whereas group II, which served as a cadmium control, received both 0.1% tween 80 (vehicle) and cadmium chloride ($CdCl_2$) dissolved in saline at 7 mg kg^{-1}. Groups III and IV were administered LGO at 45 and 90 mg kg^{-1}, respectively, while groups V and VI received citral at the same respective doses, along with concurrent administration of $CdCl_2$ at 7 mg kg^{-1}. These animals were treated with vehicle/LGO/citral along with saline/$CdCl_2$ by oral gavage for 28 days.

The changes in body weight were recorded before and weekly during the course of the study. Hepatic and renal functions were assessed fortnightly through blood sample collection and by the estimation of serum biochemical parameters. The animals were humanely sacrificed on the 29th day of the experiment, and the organs, such as the liver and kidney, were collected, and their relative weights were recorded. The aliquots of liver and kidney were also collected immediately in vials containing ice cold Tris-HCl and phosphate buffer for the analysis of antioxidant parameters. Representative samples of both liver and kidney were collected in 10% neutral buffered formalin (NBF) for histopathological examination.

2.4. Body weight and relative organ weight

The body weight of animals was recorded before and at weekly intervals during the course of the experiment. The organ weights of liver and kidney were recorded, and the relative organ weights were calculated as organ weight relative to 100 g body weight (Freitag et al., 2015).

2.5. Serum biomarkers of renal and hepatic function

The serum biomarkers of renal function, such as creatinine and blood urea nitrogen (BUN), and hepatic function, viz., alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) were estimated in a semiautomatic analyser (M/s Hospitex, Italy) using ready-to-use diagnostic kits (M/s Agappe Diagnostic Ltd, India).

2.6. Antioxidant parameters

The level of lipid peroxides in kidney and liver tissue homogenate was assessed by determination of malondialdehyde (MDA) concentration in tissue homogenate by the method of Fraga et al. (1998), where thiobarbituric acid (TBA) reacts with MDA (an end product of fatty acid peroxidation) to form a red coloured pigment, which has maximum absorbance at 532 nm. The level of reduced glutathione (GSH) in both tissues was determined as per the method described by Ellman (1959). Reduced glutathione was measured by its reaction with 5,5' -dithiobis -2-nitrobenzoic acid (DTNB) to give a yellow-coloured complex with absorption maximum at 412 nm.

2.7. Histopathology

Representative samples of kidney and liver were collected in 10% NBF. The tissue samples were processed and embedded in paraffin for histopathological evaluation. The paraffin-embedded tissues were sectioned and stained with hematoxylin and eosin as per the technique followed by Suvarna et al. (2018) and were examined under the light microscope.

2.8. Statistical analysis

Data was analysed statistically using SPSS version 24.0. and expressed as Mean±SE. The statistical analysis of all data was done using one-way analysis of variance (ANOVA) followed by Duncan's multiple comparison method as a post hoc test. Statistical significance was set at $p<0.001$.

3. RESULTS AND DISCUSSION

Among various environmental pollutants, heavy metals pose a significant threat to human health, as even minimal exposure can result in considerable organ damage. Cadmium, in particular, has been implicated in numerous pathological conditions such as carcinogenesis, hepatotoxicity, skeletal disorders like osteomalacia, as well as osteoporosis and teratogenic effects. However, the kidneys remain the principal target of Cd accumulation and toxicity, making them highly susceptible to damage (Charkiewicz et al., 2023). Effective therapeutic approaches to mitigate the renal and hepatic toxicity remain limited despite the growing concern. Herbal medicines have gained popularity for their natural antioxidant properties, safety, and effectiveness in reducing oxidative stress. Being rich in bioactive phytochemicals such as flavonoids and polyphenols, plants serve as valuable sources for developing therapeutic agents. These secondary metabolites effectively scavenge reactive oxygen and nitrogen species, helping to mitigate cellular damage and restore physiological balance (Ganta et al., 2023).

3.1. Body weight and relative organ weight

In the present study, there was no significant change in body weights and weight gain among various treatment groups at weekly intervals during the experimental period. However, a slight decrease in body weight and weight gain was observed

on the 28th day of the experiment in the Cd control group as compared to other groups, although nonsignificant (Table 1). Mahaffey and Fowler (1977) reported a reduction in weight gain in animals exposed to Cd and arsenic, either individually or in combination, suggesting that Cd exposure may slightly impair normal growth. Also, the inapparent body weight and weight gain changes observed in the LGO and citral treated rats was in corroboration with study by Li et al. (2018), wherein LGO and citral treatment exerted no significant changes in body weight gain in acetaminophen-induced hepatotoxic animals suggesting, they exerted either neutral or potentially beneficial effects on body weight, supporting their safety profile in terms of growth regulation. The relative organ weights of the kidney and liver did not vary significantly between the treatment groups (Table 1). However, the present findings were in alignment with previous studies by Asagba (2010) and Haouem and Hani (2013), in which no significant changes in the relative organ weights of kidney and liver were reported in Cd exposed rats against the normal treated groups, indicating that Cd induced toxicity might not be represented through the changes in organ weights at all the times.

3.2. Serum biomarkers of renal function

Serum creatinine and BUN are routine biomarkers for evaluating renal function, and their levels vary inversely with glomerular filtration rate (Baum et al., 1975). The Cd control group showed a significant increase in serum creatinine and BUN levels as compared to the normal control group on days 14 and 28 of the experiment. However, citral and LGO at both 45 and 90 mg kg^{-1} dose levels significantly (p<0.001) reduced serum creatinine and BUN levels in Cd-treated animals after 14 and 28 days of treatment (Table 2). The increase in renal biomarkers reflects potential nephrotoxic effects of Cd exposure and was consistent with previous reports that have documented similar elevations in serum renal markers following Cd administration (Renugadevi and Prabu, 2009; Dkhil et al., 2014; Ansari et al., 2021; Iserhienrhien and Okolie, 2022). A complete restoration of serum creatinine was observed in both doses of citral on the 14th and 28th day of the experiment, suggesting its pronounced effect compared to the LGO. These findings can be corroborated by the study conducted by Tabari et al. (2024), wherein the serum creatinine and BUN levels were attenuated by LGO and citral in diclofenac-induced nephrotoxicity in mice.

3.3. Serum biomarkers of hepatic function

Levels of hepatic marker enzymes such as AST and ALP were significantly (p<0.001) elevated in the Cd control group on both the 14th and 28th day of the experiment, as compared to the normal control, while a slight elevation was observed in the serum ALT after the treatment with Cd. However, the treatment with LGO and citral at 45 and 90 mg kg^{-1} dose levels significantly reduced the hepatic serum markers and was comparable to the normal control group, and a prominent effect was observed in the citral-treated group (Table 3). The significantly increased biomarkers are indicative of the potential liver injury induced by Cd and various Cd-induced hepatorenal studies substantiating the present results (Kandemir et al., 2021; Omar et al., 2024; Ijaz et al., 2023). Serum ALT, a highly sensitive and relatively

Table 1: Effect of LGO and citral on body weights and relative organ weights

Parameters	Normal control	Cadmium control	LGO 45	LGO 90	Citral 45	Citral 90
Body weight (g)						
Day 0	172.83±3.83	171.83±3.91	173.33±6.13	169.83±1.77	171.66±6.42	168. 83±6.57
Day 7	186.50±2.84	187.83±6.08	188.00±7.17	187.50±5.51	188.00±5.39	185.83±8.23
Day 14	196.16±2.91	195.83±8.34	200.00±9.42	195.00±7.27	200.50±4.65	193.00±8.84
Day 21	209.00±3.64	202.50±9.89	205.16±10.92	200.50±7.82	208.00±6.73	199.83±10.90
Day 28	214.83±4.62	207.00±9.87	213.50±11.64	210.00±8.42	213.16±8.41	211.50±10.30
Weight gain (g)						
Day 7	13.66±2.41	16.00±4.32	14.66±2.74	17.66±4.97	16.33±3.14	17.00±5.17
Day 14	23.33±4.47	24.00±7.84	26.66±4.07	25.16±6.45	28.83±5.61	24.16±4.95
Day 21	36.16±5.96	30.66±8.26	31.83±6.53	30.66±6.89	36.33±5.51	31.00±5.36
Day 28	42.00±7.22	35.16±8.51	40.16±6.52	40.16±7.56	41.50±5.36	42.66±6.30
Relative organ weight (g 100^{-1})						
Kidney	0.74±0.02	0.79±0.02	0.77±0.02	0.75±0.02	0.78±0.01	0.80±0.02
Liver	3.51±0.10	3.89±0.08	3.99±0.11	3.87±0.08	3.95±0.08	3.90±0.15

Values are expressed as Mean±SEM, n=6

Table 2: Effect of LGO and citral on renal serum biomarkers

	Normal control	Cadmium control	LGO 45	LGO 90	Citral 45	Citral 90
Creatinine (mg dl^{-1})						
Day 0	0.63±0.02	0.64±0.02	0.62±0.02	0.61±0.01	0.64±0.02	0.64±0.03
Day 14	0.68±0.02^{a}	1.48±0.06^{b}	0.76±0.03^{a}	0.76±0.06^{a}	0.76±0.04^{a}	0.62±0.04^{a}
Day 28	0.81±0.06^{a}	1.47±0.13^{c}	1.25±0.08^{bc}	1.15±0.10^{b}	0.87±0.03^{a}	0.65±0.04^{a}
Blood urea nitrogen (mg dl^{-1})						
Day 0	10.00±0.14	9.91±0.13	10.12±0.15	9.87±0.21	9.79±0.14	10.06±0.06
Day 14	9.70±0.26^{a}	12.53±0.44^{b}	10.59 ±0.23^{a}	10.24±0.36^{a}	10.26±0.20^{a}	10.17±0.32^{a}
Day 28	9.65±0.14^{a}	13.94±0.10^{c}	10.79±0.32^{b}	10.37±0.16^{b}	10.22±0.17^{b}	10.50±0.19^{b}

Values are expressed as Mean±SEM, n=6; Values bearing different superscripts vary significantly at p<0.001 in the row

Table 3: Effect of LGO and citral on hepatic biomarkers

	Normal control	Cadmium control	LGO 45	LGO 90	Citral 45	Citral 90
AST (IU l^{-1})						
Day 0	96.05±1.17	98.08±1.01	94.92±1.89	98.93±1.95	99.33±1.15	93.96±1.88
Day 14	91.22±0.43^{a}	124.43±1.64^{d}	111.74±0.87^{c}	114.10±1.37^{c}	111.83±1.34^{c}	104.22±1.40^{b}
Day 28	94.02±1.16^{a}	149.52±1.76^{d}	117.33±0.84^{c}	114.66±1.35^{c}	102.62±2.19^{b}	99.41±1.38^{b}
ALT (IU l^{-1})						
Day 0	59.39±2.88	60.01±1.85	58.25±2.80	59.36±1.21	58.60±2.15	57.69±1.72
Day 14	63.11±0.47	63.20±1.86	60.37±2.37	62.21±2.83	61.91±3.20	60.00±3.04
Day 28	63.84±0.61	72.45±5.56	65.72±3.33	62.50±1.27	60.67±2.64	59.21±2.05
ALP (IU l^{-1})						
Day 0	70.11±1.19	75.94±2.56	72.07±1.81	71.03±1.06	72.19±1.88	70.44±1.67
Day 14	73.85±3.45^{a}	154.12±3.21^{b}	78.47±5.74^{a}	76.86±4.67^{a}	73.76±6.08^{a}	74.38±3.01^{a}
Day 28	74.74±2.01^{a}	247.28±3.32^{c}	114.48±3.02^{b}	115.09±2.34^{b}	117.24±1.92^{b}	109.76±1.49^{b}

Values are expressed as Mean±SEM, n=6; Values bearing different superscripts vary significantly at p<0.001 in the row

specific biomarker for hepatocellular injury, is routinely employed in both preclinical and clinical assessments of hepatotoxicity, whereas AST, commonly evaluated alongside ALT, is less specific to hepatic tissue due to its broader distribution in other organs such as skeletal and cardiac muscles. Likewise, ALP is a marker enzyme associated with hepatobiliary dysfunction and altered bone metabolism. Furthermore, elevation of ALP is more frequently associated with skeletal abnormalities such as reduced bone mineral density or an increased risk of osteoporosis (Ozer et al., 2008; Cheng and Zhao, 2023). Hence, a slight increase in the liver-specific enzyme ALT, together with marked elevation of non-specific hepatic markers such as AST and ALP, as observed in the Cd control group, might be indicative of broader systemic toxicity rather than isolated hepatocellular damage by Cd exposure. Previous scientific reports have already demonstrated oxidative stress and structural damage in multiple organs upon Cd exposure, including bone abnormalities, and hence provide substantial validation to the present findings (Winiarska-Mieczan, 2014; Duranova et al., 2014; Kong et al., 2023). Also, the study by Uchida et al. (2017) has reported the hepatoprotective effect of citral on acetaminophen-induced liver injury by attenuation of hepatic serum levels, restoring the hepatic function, similar to the present study.

3.4. Antioxidant parameters

The current study evaluated antioxidant markers such as lipid peroxides (LPO) and GSH in the kidney as well as liver tissues. The Cd control group demonstrated a significant (p<0.001) elevation in the liver and kidney LPO levels as compared to the normal control group, whereas the treatment with LGO and citral at both doses significantly (p<0.001) reduced the lipid peroxide levels in both liver and kidneys (Table 4). Besides, a restoration to normal condition was observed in both doses of citral in the

Table 4: Effect of LGO and citral on antioxidant parameters

	Normal control	Cadmium control	LGO 45	LGO 90	Citral 45	Citral 90
LPO (nM MDA g^{-1})						
Kidney	81.65±1.28^{a}	105.94±0.85^{c}	89.58±0.77^{b}	90.23±1.89^{b}	82.58±1.55^{a}	83.59±3.58^{a}
Liver	41.81±0.76^{a}	73.40±3.50^{c}	48.95±1.88^{b}	46.33±1.39^{ab}	46.53±0.75^{ab}	49.49±0.84^{b}
GSH (µg mg^{-1})						
Kidney	2.19±0.09^{a}	3.22±0.07^{b}	2.50±0.13^{a}	2.42±0.16^{a}	2.57±0.18^{a}	2.60±0.11^{a}
Liver	4.42±0.21^{a}	8.30±0.29^{c}	5.89±0.29^{b}	5.44±0.24^{b}	5.33±0.17^{b}	5.37±0.15^{b}

Values are expressed as Mean±SEM, n=6; Values bearing different superscripts vary significantly at $p<0.001$ in the row

kidney, demonstrating its high potential in scavenging free radicals. These results align with earlier studies, showing a significant rise in MDA levels in the Cd control group due to enhanced lipid peroxidation, along with disruptions in antioxidant defenses and associated tissue damage (Ghonim et al., 2017; Iserheinrhien and Okolie, 2022). Interestingly, in contrast to the typical decline in GSH levels observed under oxidative stress, the present study recorded ($p<0.001$) elevated GSH concentrations in the Cd-treated group as compared to the normal control. This unexpected increase may reflect a compensatory cellular response aimed at counteracting Cd-induced oxidative stress. However, treatment with LGO and citral at both doses brought the GSH levels comparable to those of normal control groups (Table 4). This normalisation suggests a possible alleviation of oxidative burden and restoration of redox homeostasis by citral and LGO treatment. The elevated GSH levels in the Cd control group might have resulted from enhanced GSH biosynthesis, driven by increased activity of γ-glutamyl cysteine synthetase (GCL), the key enzyme regulating GSH production. This process relies on ATP and precursor amino acids such as glutamate, cysteine and glycine, which might initially get stimulated as part of a protective response (Dukic-Cosic et al., 2020). Ogasawara et al. (2014) investigated the role of GSH in Cd exposure using Jurkat T cells. They found that low Cd levels rapidly elevated GSH via the Nrf2 transcription factor, suggesting a detoxification response. Because silencing Nrf2 expression can increase Cd toxicity, which further supports the present findings and proposed hypothesis of increased GSH production for countering the Cd-induced oxidative stress in kidney and liver tissues.

3.5. Histopathology of the kidney

Normal histological features with intact glomeruli and tubules were observed in the normal control group, whereas Cd control group revealed severe tubular degeneration and tubular vacuolation. In addition, minimal bifocal interstitial perivascular infiltration of predominantly mononuclear inflammatory cells was also noted. The treatment with LGO 45 and 90 mg kg^{-1} dose levels reduced the severity of lesions and showed moderate tubular degeneration and tubular vacuolation as compared to the Cd control group. Meanwhile, citral treated group at the 45 mg kg^{-1} dose level exhibited only a mild degenerative change in the tubules, alongside a restoration to near-normal architecture in renal tissues by citral at 90 mg kg^{-1} (Plate 1). Numerous other studies also have revealed the nephrotoxic effects of Cd as evidenced by the congestion of renal corpuscles, atrophied glomeruli, degenerated convoluted tubules, perivascular edema and others (Ansari et al., 2021; Badawy et al., 2023; Omar et al., 2024). In a study conducted by Hagagg (2015), lemon grass (*Cymbopogon citratus*) extract exhibited nephroprotective effects in cisplatin-induced kidney injury as evident from reduced severity of tubular degeneration, focal sub-acute interstitial nephritis, and tubular necrosis, which corroborates the possible nephroprotective effects as presented in this study.

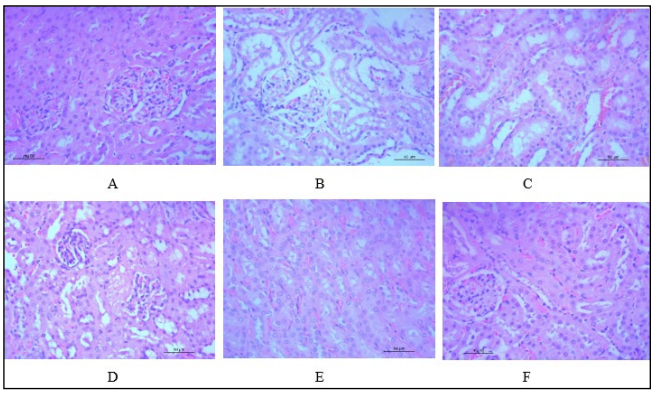

Plate 1: Kidney sections (H&E) at 40X magnification. A) Normal control B) Cadmium control C) LGO 45 mg D) LGO 90 mg E) Citral 45 mg F) Citral 90 mg

3.6. Histopathology of liver

On histological examination, the normal control group preserved the architecture, as evidenced by the well-defined hepatic lobules. On the contrary, the Cd control group showed moderate vacuolar degeneration, showing macrovesicular steatosis within hepatocytes. However,

LGO and citral treatment at both dose levels reduced the degree of Cd-induced degenerative changes, with LGO groups showing mild microvesicular degeneration, and citral at 45 mg kg^{-1} depicting only a minimal microvesicular degeneration. Further, the liver sections of animals treated with citral at a 90 mg kg^{-1} dose level revealed restoration of normal architecture of hepatocytes even after Cd exposure, indicating higher therapeutic efficacy (Plate 2). Similar findings were observed in a study by Rahim et al. (2014), wherein well-arranged hepatocytes with non-vacuolated cytoplasm were exhibited by the Cymbopogon spp. administered group in hydrogen peroxide-induced liver injury and validated the potential antioxidant properties of LGO and its major constituent, citral. Furthermore, the study conducted by Uchida et al. (2017) also revealed that LGO treatment effectively improved the degenerative changes, central vein congestion, infiltration of inflammatory cells, and vacuolization of hepatocytes induced by the acetaminophen treatment.

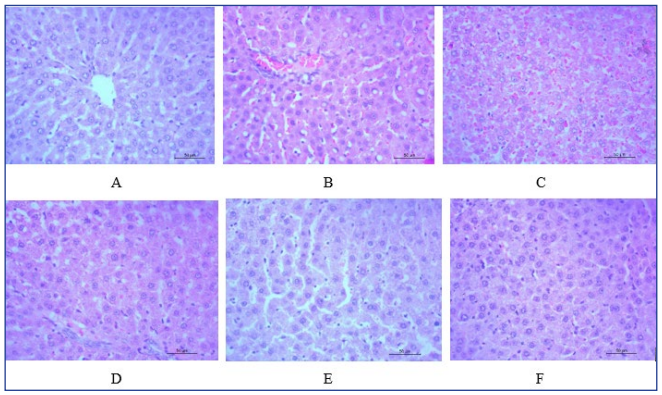

Plate 2: Liver sections (H&E) at 40X magnification. A) Normal control B) Cadmium control C) LGO 45 mg D) LGO 90 mg E) Citral 45 mg F) Citral 90 mg

4. CONCLUSION

Chronic exposure to Cd was associated with oxidative stress, inflammation, and progressive dysfunction of the kidney and liver. Due to limited effective therapeutic strategies for Cd-induced toxicity, the present study evaluated lemongrass oil and its major component, citral. Both LGO and citral effectively mitigated Cd-induced nephrotoxicity and hepatotoxicity, and demonstrated strong antioxidant potential. Hence, LGO and citral might be recommended for advanced efficacy and safety studies as promising therapeutic agents for the effective management of Cd toxicity in both humans and animals.

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6. REFERENCE

Ansari, M.N., Rehman, N.U., Karim, A., Imam, F., Hamad, A.M., 2021. Protective effect of *Thymus serrulatus* essential oil on cadmium-induced nephrotoxicity in rats, through suppression of oxidative stress and downregulation of NF-κB, iNOS expression. Molecules 26, 1252–1267. https://doi.org/10.3390/molecules26051252.

Arroyo, V.S., Flores, K.M., Ortiz, L.B., Gómez-Quiroz, L.E., Gutiérrez-Ruiz, M.C., 2012. Liver and cadmium toxicity. Journal of Drug Metabolism and Toxicology 5, 1–8. DOI: 10.4172/2157-7609.S5-001.

Asagba, S.O., 2010. Comparative effect of water and food-chain mediated cadmium exposure in rats. Biometals 23, 961–971. https://doi.org/10.1007/s10534-010-9313-5.

Badawy, S., Abd-Elraouf, M., Gab-Allah, M.S., El-Mashad, A.B.I., Tantawy, A.A., Amin, A.A., 2023. Nephroprotective properties of palm dates and olive leaves extracts on cadmium-induced acute renal toxicity in albino rats. Journal of Advanced Veterinary Research 13, 1497–1506. Available from: https://www.advetresearch.com/index.php/AVR/article/view/1461.

Banik, B., Das, S., Das, M.K., 2020. Medicinal plants with potent anti-inflammatory and anti-arthritic properties found in eastern parts of the Himalaya: an ethnomedicinal review. Pharmacognosy Reviews 14(28). https://dx.doi.org/10.5530/phrev.2020.14.16.

Baum, N., Dichoso, C.C., Carlton Jr, C.E., 1975. Blood urea nitrogen and serum creatinine: Physiology and interpretations. Urology 5, 583–588. https://doi.org/10.1016/0090-4295(75)90105-3.

Charkiewicz, A.E., Omeljaniuk, W.J., Nowak, K., Garley, M., Niklinski, J., 2023. Cadmium toxicity and health effects a brief summary. Molecules 28, 6620–6628. https://doi.org/10.3390/molecules28186620.

Cheng, X., Zhao, C., 2023. The correlation between serum levels of alkaline phosphatase and bone mineral density in adults aged 20 to 59 years. Medicine 102, e34755. https://doi.org/10.1097/md.0000000000034755.

de Sousa, D.P., Damasceno, R.O.S., Amorati, R., Elshabrawy, H.A., de Castro, R.D., Bezerra, D.P., Nunes, V.R.V., Gomes, R.C., Lima, T.C., 2023. Essential oils: Chemistry and pharmacological activities. Biomolecules 13, 1144. https://doi.org/10.3390/biom13071144.

Dkhil, M.A., Al-Quraishy, S., Diab, M.M., Othman, M.S., Aref, A.M., Moneim, A.E.A., 2014. The potential protective role of *Physalis peruviana* L. fruit in cadmium-induced hepatotoxicity and nephrotoxicity. Food and Chemical Toxicology 74, 98106. https://doi.org/10.1016/j.fct.2014.09.013.

Dhifi, W., Bellili, S., Jazi, S., Bahloul, N., Mnif, W., 2016. Essential oils' chemical characterization and investigation of some biological activities: A critical review. Medicines 3, 25–27. https://doi.org/10.3390/medicines3040025.

Dukic-Cosic, D., Baralic, K., Javorac, D., Djordjevic, A.B., Bulat, Z., 2020. An overview of molecular mechanisms in cadmium toxicity. Current Opinion in Toxicology 19, 56–62. Available from: https://ui.adsabs.harvard.edu/link_gateway/2020COTox.19...56D/doi: 10.1016/j.cotox.2019.12.002.

Duranova, H., Martiniakova, M., Omelka, R., Grosskopf, B., Bobonova, I., Toman, R., 2014. Changes in compact bone microstructure of rats subchronically exposed to cadmium. Acta Veterinaria Scandinavica 56, 1–8. Available from: https://pubmed.ncbi.nlm.nih.gov/25279860/.

Ellman, G.L., 1959. Tissue sulfhydryl groups. Archives of Biochemistry and Biophysics 82, 70–77. https://doi.org/10.1016/0003-9861(59)90090-6.

Fraga, C.G., Leibovitz, B.E., Tappel, A.L., 1988. Lipid peroxidation measured as thiobarbituric acid-reactive substances in tissue slices: characterization and comparison with homogenates and microsomes. Free Radical Biology and Medicine 4, 155–161. https://doi.org/10.1016/0891-5849(88)90023-8.

Freitag, A.R., Thayer, L.R., Leonetti, C., Stapleton, H.M., Hamlin, H.J., 2015. Effects of elevated nitrate on endocrine function in Atlantic salmon, Salmo salar. Aquaculture 436, 8–12. https://doi.org/10.1016/j.aquaculture.2014.10.041.

Ganta, S., Amuru, S.R., Anchapakula, S.L., Subramanyam, S.S.K., Begum, S.F., Buddareddy, H., Nelaballe, V.K., Pallampalli, S., Depuru, B., 2023. Hepato and nephroprotective effects of six important medicinal plants against toxic oxidative stress. Medicinal Plants-International Journal of Phytomedicines and Related Industries 15, 13–25. https://doi.org/10.5958/0975-6892.2023.00004.7.

Genchi, G., Sinicropi, M.S., Lauria, G., Carocci, A., Catalano, A., 2020. The effects of cadmium toxicity. International Journal of Environment Research and Public Health 17, 3782–3806. https://doi.org/10.3390/ijerph17113782.

Ghonim, A., Abdeen, A., El-Shawarby, R., Abdel-Aleem, N., El-Shewy, E., Abdo, M., Abdelhiee, E., 2017. Protective effect of cinnamon against cadmium-induced hepatorenal oxidative damage in rats. International Journal of Pharmacology and Toxicology 5, 17–22. https://doi.org/10.14419/ijpt.v5i1.7119.

Haggag, M., 2015. Protective effect of lemon grass (*Cymbopogon citratus*) water extract against nephrotoxicity induced by cisplatin in male rats. Egyptian Journal of Nutrition and Health 10, 1–12. Available from: https://web.archive.org/web/20180614133243id_/http://ejnh.journals.ekb.eg:80/article_4824_aea526b2bf64a1f5b52519501a25e753.pdf.

Han, X., Parker, T.L., 2017. Lemongrass (*Cymbopogon flexuosus*) essential oil demonstrated an anti-inflammatory effect in pre-inflamed human dermal fibroblasts. Biochimie Open 4, 107–111. https://doi.org/10.1016/j.biopen.2017.03.004.

Hao, R., Song, X., Sun-Waterhouse, D., Tan, X., Li, F., Li, D., 2021. MiR-34a/Sirt1/p53 signaling pathway contributes to cadmium-induced nephrotoxicity: A preclinical study in mice. Environmental Pollution 282, 117029–117036. https://doi.org/10.1016/j.envpol.2021.117029.

Haouem, S., El Hani, A., 2013. Effect of cadmium on lipid peroxidation and on some antioxidants in the liver, kidneys and testes of rats given a diet containing cadmium-polluted radish bulbs. Journal of Toxicologic Pathology 26, 359–364. https://doi.org/10.1293/tox.2013-0025.

Hecht, E.M., Arheart, K., Lee, D.J., Hennekens, C.H., Hlaing, W.M., 2016. A cross-sectional survey of cadmium biomarkers and cigarette smoking. Biomarkers 21, 429–435. https://doi.org/10.3109/1354750X.2016.1153717.

Ijaz, M.U., Aziz, S., Hamza, A., Batool, M., Alkahtani, S., Riaz, M.N., Ashraf, A., 2023. Curative effects of kaempferide on cadmium-instigated hepatotoxicity in male albino rats. Journal of King Saud University-Science 35, 102885–102891. https://doi.org/10.1016/j.jksus.2023.102885.

Iserhienrhien, L.O., Okolie, N.P., 2022. Protective effect of *Geophila obvallata* (Shumach) Didr leaf extract and its fractions against cadmium-induced nephrotoxicity in male Wistar rats. Toxicology Reports 9, 87–93. https://doi.org/10.1016/j.toxrep.2021.12.008.

Kandemir, F.M., Caglayan, C., Darendelioglu, E., Kucukler, S., Izol, E., Kandemir, O., 2021. Modulatory effects of carvacrol against cadmium-induced hepatotoxicity and nephrotoxicity by molecular targeting regulation. Life Sciences 277, 119610. https://doi.org/10.1016/j.lfs.2021.119610.

Kong, Z., Liu, C., Olatunji, O.J., 2023. Asperuloside attenuates cadmium-induced toxicity by inhibiting

oxidative stress, inflammation, fibrosis, and apoptosis in rats. Scientific Reports 13, 5698. https://doi.org/10.1038/s41598-023-29504-0.

Kusak, R., Nasiadek, M., Stragierowicz, J., Hanke, W., Kilanowicz, A., 2024. Changes in endogenous essential metal homeostasis in the liver and kidneys during a six-month follow-up period after Subchronic Cadmium Exposure. International Journal of Molecular Sciences 25, 3829. https://doi.org/10.3390/ijms25073829.

Kusuma, I.Y., Perdana, M.I., Vágvölgyi, C., Csupor, D., Tako, M., 2024. Exploring the clinical applications of lemongrass essential oil: A scoping review. Pharmaceuticals 17, 159. https://doi.org/10.3390/ph17020159.

Li, C.C., Yu, H.F., Chang, C.H., Liu, Y.T., Yao, H.T., 2018. Effects of lemongrass oil and citral on hepatic drug-metabolizing enzymes, oxidative stress, and acetaminophen toxicity in rats. Journal of Food and Drug Analysis 26, 432–438. https://doi.org/10.1016/j.jfda.2017.01.008.

Mahaffey, K.R., Fowler, B.A., 1977. Effects of concurrent administration of lead, cadmium, and arsenic in the rat. Environmental Health Perspectives 19, 165–171. https://doi.org/10.1289/ehp.7719165.

Ogasawara, Y., Takeda, Y., Takayama, H., Nishimoto, S., Ichikawa, K., Ueki, M., Suzuki, T., Ishii, K., 2014. Significance of the rapid increase in GSH levels in the protective response to cadmium exposure through phosphorylated Nrf2 signaling in Jurkat T-cells. Free Radical Biology and Medicine 69, 58–66. https://doi.org/10.1016/j.freeradbiomed.2014.01.005.

Omar, E.M., El-Sayed, N.S., Elnozahy, F.Y., Hassan, E., Amr, A., Augustyniak, M., El-Samad, L.M., El Wakil, A., 2024. Reversal effects of royal jelly and propolis against cadmium-induced hepatorenal toxicity in rats. Biological Trace Element Research 202, 1612–1627. https://doi.org/10.1007/s12011-023-03775-0.

Osaili, T.M., Dhanasekaran, D.K., Zeb, F., Faris, M.E., Naja, F., Radwan, H., Ismail, L.C., Hasan, H., Hashim, M., Obaid, R.S., 2023. A status review on health-promoting properties and global regulation of essential oils. Molecules 28, 1809–1828. https://doi.org/10.3390/molecules28041809.

Ozer, J., Ratner, M., Shaw, M., Bailey, W., Schomaker, S., 2008. The current state of serum biomarkers of hepatotoxicity. Toxicology 245, 194–205. https://doi.org/10.1016/j.tox.2007.11.021.

Qu, F., Zheng, W., 2024. Cadmium exposure: mechanisms and pathways of toxicity and implications for human health. Toxics 12, 388. https://doi.org/10.3390/toxics12060388.

Rahim, S.M., Taha, E.M., Al-janabi, M.S., Al-douri, B.I., Simon, K.D., Mazlan, A.G., 2014. Hepatoprotective effect of *Cymbopogon citratus* aqueous extract against hydrogen peroxide-induced liver injury in male rats. African Journal of Traditional, Complementary and Alternative Medicines 11, 447–451. https://doi.org/10.4314/ajtcam.v11i2.31.

Ramsey, J.T., Shropshire, B.C., Nagy, T.R., Chambers, K.D., Li, Y., Korach, K.S., 2020. Essential oils and health. The Yale Journal of Biology and Medicine 93, 291. https://pmc.ncbi.nlm.nih.gov/articles/PMC7309671/.

Renu, K., Chakraborty, R., Myakala, H., Koti, R., Famurewa, A.C., Madhyastha, H., Vellingiri, B., George, A., Gopalakrishnan, A.V., 2021. Molecular mechanism of heavy metals (Lead, Chromium, Arsenic, Mercury, Nickel and Cadmium)-induced hepatotoxicity–A review. Chemosphere 271, 129735. https://doi.org/10.1016/j.chemosphere.2021.129735.

Renugadevi, J., Prabu, S.M., 2009. Naringenin protects against cadmium-induced oxidative renal dysfunction in rats. Toxicology 256, 128–134. https://doi.org/10.1016/j.tox.2008.11.012.

Smereczanski, N.M., Brzoska, M.M., 2023. Current levels of environmental exposure to cadmium in industrialized countries as a risk factor for kidney damage in the general population: A comprehensive review of available data. International Journal of Molecular Sciences 24, 8413–8442. https://doi.org/10.3390/ijms24098413.

Sujana, D., Saptarini, N.M., Sumiwi, S.A., Levita, J., 2021. Nephroprotective activity of medicinal plants: A review on in silico-, *in vitro*, and *in vivo*-based studies. Journal of Applied Pharmaceutical Science 11, 113–127. https://dx.doi.org/10.7324/JAPS.2021.1101016.

Suvarna, S.K., Layton, C., Bancroft, J.D., 2018. Bancroft's Theory and Practice of Histologic Techniques. (8th Ed.). Churchill Livingstone, Elsevier, Philadelphia. p. 557. Available from: https://knustmeltsa.wordpress.com/wp-content/uploads/2020/08/bancrofts-theory-and-practice-of-histological-techniques-7th-edition-0702042269autosaved1.pdf.

Tabari, M.A., Houshyar, M., Araghi, A., Mirzakhani, N., Crescenzo, G., Cardone, R., Zizzadoro, C., 2024. Nephroprotective and hepatoprotective effects of lemongrass essential oil and citral on diclofenac-induced toxicity in mice. Biomedicine & Pharmacotherapy 180, 117541–117549. https://doi.org/10.1016/j.biopha.2024.117541.

Tchounwou, P.B., Yedjou, C.G., Patlolla, A.K., Sutton, D.J., 2012. Heavy metal toxicity and the environment. In: Luch, A. (Ed.), Molecular, clinical and environmental toxicology. Volume 3: Environmental Toxicology.

Springer, Basel. p. 164. https://doi.org/10.1007/978-3-7643-8340-4_6.

Tienda-Vázquez, M.A., Morreeuw, Z.P., Sosa-Hernández, J.E., Cardador-Martínez, A., Sabath, E., Melchor-Martínez, E.M., Iqbal, H.M., Parra-Saldívar, R., 2022. Nephroprotective plants: a review on the use in pre-renal and post-renal diseases. Plants 11, 818. https://doi.org/10.3390/plants11060818.

Uchida, N.S., Silva-Filho, S.E., Cardia, G.F.E., Cremer, E., Silva-Comar, F.M.D.S., Silva, E.L., Bersani-Amado, C.A., Cuman, R.K.N., 2017. Hepatoprotective effect of citral on acetaminophen-induced liver toxicity in mice. Evidence-Based Complementary and Alternative Medicine 2017, 1796209. https://doi.org/10.1155/2017/1796209.

Wang, M., Chen, Z., Song, W., Hong, D., Huang, L., Li, Y., 2021. A review of cadmium exposure in the population and intervention strategies against cadmium toxicity. Bulletin of Environmental Contamination and Toxicology 106, 65–74. https://doi.org/10.1007/s00128-020-03088-1.

Wifek, M., Saeed, A., Rehman, R., Nisar, S., 2016. Lemongrass: a review on its botany, properties, applications and active components. International Journal of Chemical and Biochemical Sciences 9, 79–84. Available from: https://www.researchgate.net/publication/336134806_Lemongrass_a_review_on_its_botany_properties_applications_and_active_components.

Winiarska-Mieczan, A., 2014. Cumulative rate and distribution of Cd and Pb in the organs of adult male Wistar rats during oral exposure. Environmental Toxicology and Pharmacology 38, 751–760. https://doi.org/10.1016/j.etap.2014.08.016.

Yan, L.J., Allen, D.C., 2021. Cadmium-induced kidney injury: Oxidative damage as a unifying mechanism. Biomolecules 11, 1575–1592. https://doi.org/10.3390/biom11111575.

Zhang, K., Long, M., Dong, W., Li, J., Wang, X., Liu, W., Huang, Q., Ping, Y., Zou, H., Song, R., Liu, G., 2024. Cadmium induces kidney iron deficiency and chronic kidney injury by interfering with the iron metabolism in rats. International Journal of Molecular Sciences 25, 763–765. https://doi.org/10.3390/ijms25020763.