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Harsh Patel

Department of Veterinary,
Pharmacology and Toxicology,
College of Veterinary Science and
Animal Husbandry, Kamdhenu
University, Junagadh, Gujarat,
India

Urvesh Patel

Department of Veterinary,
Pharmacology and Toxicology,
College of Veterinary Science and
Animal Husbandry, Kamdhenu
University, Himmatnagar,
Gujarat, India

Maunik Prajapati

Department of Veterinary,
Pharmacology and Toxicology,
College of Veterinary Science and
Animal Husbandry, Kamdhenu
University, Junagadh, Gujarat,
India

Dhaval Fefar

Department of Veterinary,
Pathology, College of Veterinary
Science and Animal Husbandry,
Kamdhenu University, Anand,
Gujarat, India

Corresponding Author:

Harsh Patel

Department of Veterinary,
Pharmacology and Toxicology,
College of Veterinary Science and
Animal Husbandry, Kamdhenu
University, Junagadh, Gujarat,
India

Hematological and serum biochemical changes induced by individual and combined exposure to lithium carbonate and lead acetate in rats

Harsh Patel, Urvesh Patel, Maunik Prajapati and Dhaval Fefar

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Abstract

Heavy metal contamination in soil, water, and sediments is a global issue, drawing increasing attention due to its environmental and health effects. The accumulation of heavy metals like lithium and lead, particularly linked to the growing use of electric vehicles, poses serious threats to ecosystems, animals, and humans. To investigate the effects of individual and combined exposure to lithium carbonate (Li) and lead acetate (Pb) over 28 days in 24 adult male rats, the rats were divided into 4 groups. The rats of the control group were administered reverse osmosis water. The Li and Pb were administered orally for 28 days to rats of individual toxicity groups at a dose rate of 20 mg/kg body weight. The rats of the fourth group were administered with both compounds at a dose rate of 20 mg each/kg body weight orally for 28 days. Co-exposure to Li and Pb resulted in a reduction in platelet counts and an elevation in white blood cell levels, indicating interactive toxic effects. Serum biochemical analysis revealed increased alanine aminotransferase (ALT) and urea levels in the Li and Li + Pb groups, whereas alkaline phosphatase (ALP) and lactate dehydrogenase (LDH) activities were elevated across all treated groups. A significant rise in triglyceride levels was observed in the Li-treated group. Overall, the findings demonstrate that exposure to Li and Pb induces notable alterations in hematological and biochemical parameters, with both distinct and interactive toxicity profiles.

Keywords: Hepato-renal toxicity, lithium carbonate, lead acetate, hematological and biochemical parameters, rats

1. Introduction

Rapid industrialization and urbanization associated with mining, agriculture, waste management, and automobile industries have significantly increased heavy metal contamination in the environment. Heavy metals are persistent contaminants that bioaccumulate through the food chain and tend to concentrate in higher organisms, including humans and animals (Jarup, 2003) ^[16]. Their accumulation in soil and water occurs mainly through leaching processes, resulting in long-term exposure risks (Luoma and Rainbow, 2008) ^[22]. Due to their extended biological half-lives, heavy metals pose serious global public health concerns (Jaishankar *et al.* 2014) ^[15].

Among heavy metals, lithium (Li) and lead (Pb) are increasingly prevalent due to industrial expansion and rising demand for batteries, electric vehicles, and pharmaceuticals (Livingstone, 2003) ^[20]. Lithium is naturally present in soil and water, with reported concentrations of up to 200 µg/g in soil and 1-10 µg/ml in surface water, reaching as high as 5 mg/L in certain regions (Choubey *et al.* 2017) ^[8]. The earth's crust contains approximately 50-65 mg/kg of lithium, while soil concentrations range from 10-100 mg/kg in the United States and 10-50 mg/kg in Russia (Weiner, 1993; Léonard *et al.* 1995; Lagerkvist and Lindell, 2002) ^[41, 19, 18]. Elevated lithium levels have also been reported in drinking water, reaching 78 mg/L in parts of Texas (Trief *et al.* 1973) ^[37].

Lithium carbonate is widely used in the treatment of bipolar disorder; however, its narrow therapeutic index and slow excretion may result in accumulation and toxicity upon prolonged exposure (Grof, 2010; Warick, 1979; Yip & Yeung, 2007) ^[13, 40, 44]. Excess lithium exposure

induces oxidative stress, inflammation, and apoptosis, affecting multiple organ systems including the hematopoietic, renal, hepatic, and cardiovascular systems (Sahin *et al.* 2006; Chadha *et al.* 2008; Ostadhadi *et al.* 2018) [31, 7, 27]. Lithium-induced toxicity has been associated with altered antioxidant enzyme activities, increased lipid peroxidation, and disruption of mitochondrial function, leading to biochemical and hematological abnormalities (Kielczykowska *et al.* 2015) [17]. Lead is another highly toxic, non-biodegradable heavy metal with widespread environmental presence. It causes extensive physiological and biochemical dysfunctions across multiple organ systems, with the hematological system being particularly vulnerable due to lead's affinity for erythrocytes and hemoglobin (Goyer, 1991; Andjelkovic *et al.* 2019) [12, 3]. Despite declining blood lead levels globally, occupational workers, infants, and children remain at high risk (Godwin, 2001) [11]. Lead exposure contributes significantly to morbidity and mortality, especially in developing countries (Smith and Flegal, 1995) [35].

Major sources of lead contamination include paints, batteries, cosmetics, medicines, fuel, and industrial effluents. Lead concentrations exceeding permissible limits have been reported in Indian water bodies, including Gujarat lakes, where values far exceeded WHO and Indian standards (Moore, 1988; Smith and Smith, 2004; Vediya and Patel, 2011; Patel and Vediya, 2012) [25, 34, 29, 38]. After ingestion, lead is absorbed via the gastrointestinal tract and distributed through the bloodstream to vital organs, causing hematological disturbances, oxidative stress, and biochemical alterations (Barbosa *et al.* 2005; Flora *et al.* 2012) [4, 10]. Lead interferes with antioxidant enzymes, binds to functional protein groups, disrupts calcium-dependent cellular processes, and accumulates in renal tissues, thereby altering serum biochemical parameters (Mabrouk *et al.* 2016; Samarghandian *et al.* 2017) [23, 32].

Recent studies indicate that combined exposure to heavy metals may result in synergistic toxicity. Luo *et al.* (2023) [21] demonstrated enhanced toxicity of lithium and lead combinations in mouse brain stem cells, while Cunha *et al.* (2023) [9] reported amplified stress responses following combined exposure in *Mytilus galloprovincialis*. These findings suggest that simultaneous exposure to lithium and lead may exert greater toxicological effects than individual exposures.

However, limited information is available regarding the combined haematological and serum-biochemical effects of lithium and lead exposure in mammalian systems. Therefore, the present study was designed to evaluate the toxicological interaction of lithium carbonate and lead acetate, administered individually and in combination, on haematological and serum-biochemical parameters in rats following daily oral exposure for 28 days.

2. Materials and Methods

2.1 Test compounds

Lithium carbonate ($\geq 99.5\%$ purity, CAS No. 554-13-2) and lead acetate ($\geq 97.0\%$ purity, CAS No. 6080-56-4) were procured from Himedia, India. Stock solutions were prepared by dissolving 400 mg of each compound separately in 50 mL of Milli-Q water. The powders were accurately weighed using a calibrated analytical balance (Model: MS 204S/A01, Mettler Toledo, US). The prepared stock solutions were further diluted as required to obtain the desired concentrations for administration to rats.

2.2 Experimental animals

The study was conducted using 24 male Wistar rats aged 7-8 weeks, obtained from the Zydus Research Centre, Ahmedabad, Gujarat. Experimental procedures were approved by the Institutional Animal Ethics Committee (IAEC) under Protocol No. KU-JVC-IAEC-SA-123-23 and were carried out in compliance with the Committee for Control and Supervision of Experiments on Animals (CCSEA, 2003) guidelines. Animals were housed in polypropylene cages equipped with stainless steel grills and provided with corn cob bedding, which was changed twice weekly. Standard laboratory conditions were maintained, including a 12 h light/dark cycle, ambient temperature ranging from 23.19 ± 0.13 °C to 25.76 ± 0.13 °C, and relative humidity between $48 \pm 0.53\%$ and $65 \pm 0.74\%$. Rats were allowed *ad libitum* access to standard pellet feed (VRK Nutritional Solutions, Maharashtra) and filtered reverse osmosis drinking water supplied in 300 mL polypropylene bottles. Prior to treatment, animals were acclimatized for 7 days, during which they were individually identified by tail marking using a black marker. The experiment followed a Completely Randomized Design (CRD), with animals randomly allocated into four treatment groups ($n = 12$ per group) based on body weight, ensuring a variation within $\pm 5\%$.

2.3 Exposure

Rats in the control group (C) received reverse osmosis (R.O.) water in volumes ranging from 0.75 to 1.12 mL, adjusted according to individual body weights. Lithium carbonate and lead acetate were administered separately at 20 mg/kg body weight (BW) daily for 28 consecutive days to the Li and Pb groups, respectively. The Li + Pb group received both lithium carbonate and lead acetate at the same dose rate of 20 mg/kg BW each, administered daily for 28 days. The selected dose levels were chosen based on earlier studies reporting clear toxicological effects without inducing overt mortality, thereby making them appropriate for sub-chronic exposure assessments (Sahin *et al.* 2006; Toghyani *et al.* 2012; Ben Saad *et al.* 2017; Saad *et al.* 2017) [31, 36, 5, 30].

2.4 Haematology and Serum biochemical analysis

On the 29th day, blood samples (3-4 mL) were collected from the retro-orbital plexus under light anesthesia. Samples intended for hematological analysis were collected in sterile K₃EDTA tubes, while those for serum biochemistry were collected in anticoagulant-free vials, allowed to clot at room temperature, and centrifuged at 10,000 g for 10 min (Eppendorf 5430 R, Germany). The separated serum was stored at -80 °C and analyzed within 2 days. Hematological parameters, including hemoglobin (Hb), total erythrocyte count (TEC), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platelet count (PLT), total leukocyte count (TLC), and differential leukocyte count (DLC), were measured using an automated hematology analyzer (Abacus Junior Vet 5, Diatek, Hungary). Biochemical parameters, namely alanine aminotransferase (ALT), aspartate aminotransferase (AST), total protein (TP), albumin (ALB), globulin, albumin/globulin ratio, alkaline phosphatase (ALP), lactate dehydrogenase (LDH), serum creatinine (CK), urea, and triglycerides, were determined using standard diagnostic kits on an automated biochemistry analyzer (LANDWIND C100, Diatek, China).

2.5 Statistical analysis

Statistical analyses of all data were carried out using GraphPad Prism 9.0. The Kolmogorov-Smirnov test was used to evaluate the normality of data, along with Bartlett's test to confirm the equal variance. Data with normal distribution and homogeneous variance were analyzed by parametric one-way analysis of variance (ANOVA) followed by Tukey's HSD test. The data that didn't have either a normal distribution or equal variances were analyzed by the Kruskal-Wallis test followed by Dunn's test. The value of $p < 0.05$ was considered statistically significant.

3. Results

3.1 Haematology and serum biochemical analysis

A significant reduction in platelets and an increase in WBCs were observed in the Li + Pb-treated groups compared to the control group. Platelet levels were significantly lower in the Li + Pb-treated group than in the Li-treated group, possibly due to the specific effects of Pb exposure. In contrast, a significantly increased WBC was observed in the Li + Pb-treated group compared to the Pb-treated group, which might be associated with the Li exposure. Other haematological parameters in all toxicity groups were not significantly different. The effects of daily oral administration of Li, Pb, and Li + Pb for 28 days on hematological parameters in rats are shown in Tables 1 and illustrated in Figures 1 & 2.

A significant increase in ALT and urea was observed in the Li and Li + Pb-treated groups compared to the control group. The AST level in the Pb-treated group was significantly lower than that of the Li-treated group. A significant increase in ALP and LDH was observed in all toxicity groups compared to the control group. A significant increase in triglyceride was observed in the Li-treated group compared to the control group; whereas AST, TP, albumin, globulin, A/G Ratio, and creatinine were not significantly altered by all treatments compared to the control group. The LDH and the triglyceride levels in the Pb and Li + Pb-treated groups were significantly lower than those of the Li-treated group, which shows the interaction of both metals. The effects of daily oral administration of Li, Pb, and Li + Pb for 28 days on serum-biochemical parameters in rats are shown in Tables 2 and illustrated in Figures 3 & 4.

4. Discussion

The present study investigated the toxicological effects of lithium carbonate (Li), lead acetate (Pb), and their combined exposure in adult Wistar rats following 28 days of oral administration. Control rats were unexposed, while treatment groups received Li, Pb, or Li + Pb (20 mg/kg BW each). A comprehensive evaluation was performed to assess hematological and biochemical parameters in male rats.

Combined Li and Pb exposure significantly reduced platelet counts and elevated WBC levels compared to controls, indicating distinct toxicant interactions. The more pronounced thrombocytopenia in the Li + Pb group than in Li alone appears largely Pb-driven, consistent with reports of dose-dependent lead-induced hematological toxicity (Andjelkovic *et al.* 2019; Abubakar *et al.* 2019; Oyem *et al.* 2021; Bidanchi *et al.* 2022) [3, 1, 28, 6]. The elevated WBC counts in Li + Pb rats, greater than in Pb alone, suggest lithium's modulatory influence. Previous studies show variable hematological effects of lithium ranging from leukocytosis with reduced monocytes (Malhotra & Dhawan, 2008) [24], to no changes (Kielczykowska *et al.* 2014) [17], or reductions in MCV, MCH, and platelets with concurrent WBC increases (Ben Saad *et al.*

2017; Alamri & Alfaifi, 2024) [5, 2]. Such discrepancies likely reflect dose, duration, and experimental differences. Lithium's effects on blood cells are linked to altered RBC membrane dynamics and stimulation of leukopoiesis, leading to leukocytosis (Malhotra & Dhawan, 2008) [24], while Pb induces leukocytosis via toxic injury to lymphoid organs and inflammatory stimulation of germinal centers (Yagminas *et al.* 1990) [42]. Lithium has also been reported to enhance phagocytic activity, increasing WBC counts with reduced monocytes (Yildirim *et al.* 2018) [43]. Collectively, these findings suggest that Pb predominantly drives thrombocytopenia, while Li modulates leukopoietic and immune responses. Their combined exposure produces distinct hematological alterations decreased platelet counts and increased WBC levels reflecting both toxic and adaptive immunomodulatory effects.

Lithium and lead exposures produced distinct and interactive effects on liver and kidney function markers. Lithium significantly increased ALT and urea, indicating hepatocellular stress and impaired renal clearance, consistent with lithium-induced hepatotoxicity and nephrotoxicity (Vijaimohan *et al.* 2010; Mwaheb *et al.* 2016) [39, 26]. Elevated urea likely reflects lithium accumulation in proximal tubules causing nephron damage and reduced filtration (Zhang *et al.* 2022) [45], while increased ALT, LDH, and triglycerides indicate oxidative stress-mediated hepatocellular injury and disrupted lipid metabolism. Lead exposure similarly elevated ALP and LDH, supporting its role in hepatocellular necrosis and oxidative stress (Ibrahim *et al.* 2012; Bidanchi *et al.* 2022) [14, 6]. Raised ALP reflects impaired detoxification and membrane integrity, LDH indicates widespread cellular injury (Seddik *et al.* 2010) [33], and elevated urea confirms renal impairment. Combined Li + Pb exposure showed unique interactions: ALT and urea elevations mirrored lithium's effect, but LDH and triglycerides were lower than in Li alone, suggesting Pb modulates lithium's impact on lipid metabolism. Lead-induced oxidative stress and enzymatic inhibition may suppress triglyceride synthesis or enhance breakdown, counteracting lithium's hypertriglyceridemic effect. Overall, lithium primarily impairs hepatic and renal function through oxidative stress and membrane disruption, whereas lead exerts broader enzymatic and renal effects; their co-exposure modifies these outcomes, particularly in lipid metabolism, indicating toxicodynamic interactions.

Table 1: Haematological parameters in male rats exposed to lithium carbonate and lead acetate

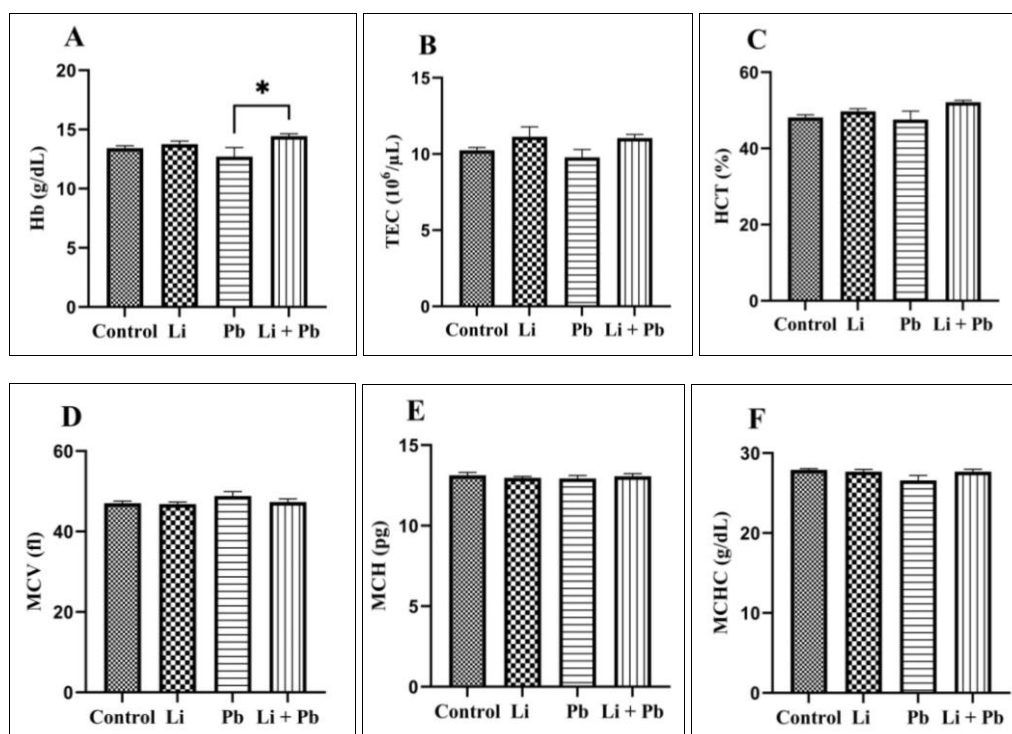
Parameters	Treatment groups (Mean $\pm$ SE; $n = 6$)			
	Control	Li	Pb	Li + Pb
Hb (g/dL)	13.4 $\pm$ 0.19 ^{ab}	13.8 $\pm$ 0.28 ^{ab}	12.7 $\pm$ 0.77 ^a	14.4 $\pm$ 0.22 ^b
TEC (10 ⁶ /μL)	10.2 $\pm$ 0.18	11.1 $\pm$ 0.65	9.78 $\pm$ 0.52	11 $\pm$ 0.24
HCT (%)	48.1 $\pm$ 0.69	49.7 $\pm$ 0.73	47.6 $\pm$ 2.22	52.1 $\pm$ 0.49
MCV (fl)	47.0 $\pm$ 0.58	46.8 $\pm$ 0.48	48.8 $\pm$ 1.08	47.3 $\pm$ 0.80
MCH (pg)	13.1 $\pm$ 0.17	13 $\pm$ 0.08	12.9 $\pm$ 0.19	13.1 $\pm$ 0.16
MCHC (g/dL)	27.9 $\pm$ 0.15	27.7 $\pm$ 0.28	26.6 $\pm$ 0.61	27.7 $\pm$ 0.31
Platelets (10 ³ /μL)	693 $\pm$ 23.2 ^a	676 $\pm$ 41.8 ^a	566 $\pm$ 36.4 ^{ab}	509 $\pm$ 47 ^b
WBCs (10 ³ /μL)	6.4 $\pm$ 1.16 ^b	7.03 $\pm$ 0.57 ^{ab}	5.63 $\pm$ 1.03 ^b	10 $\pm$ 0.31 ^a
Neutrophils (%)	22.1 $\pm$ 3.80	17.9 $\pm$ 1.80	29.1 $\pm$ 8.77	11.8 $\pm$ 0.86
Lymphocyte (%)	69.4 $\pm$ 5.60	73.9 $\pm$ 1.83	64.3 $\pm$ 9.52	80.9 $\pm$ 2.45
Monocytes (%)	8.57 $\pm$ 1.96	8.22 $\pm$ 0.84	6.58 $\pm$ 1.77	7.38 $\pm$ 1.75

Note: Values with different superscripts in a row were significantly different ($p < 0.05$)

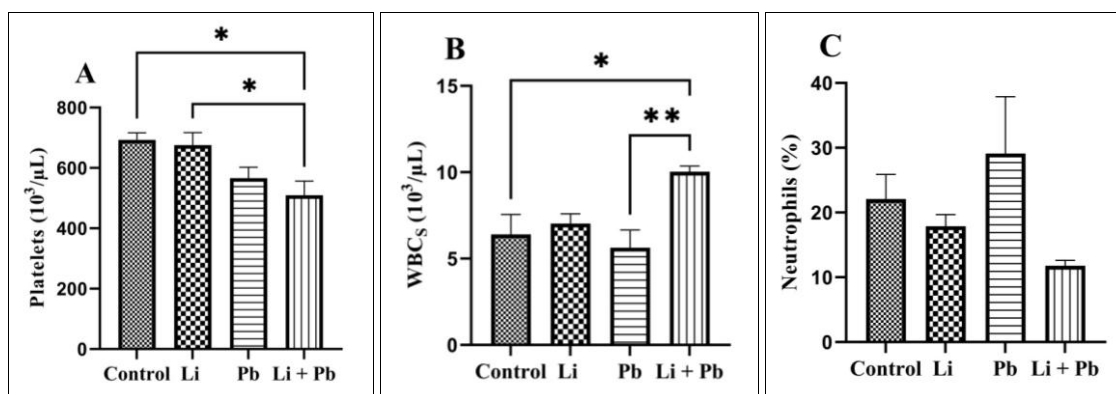
Table 2: Serum-biochemical parameters in male rats exposed to lithium carbonate and lead acetate

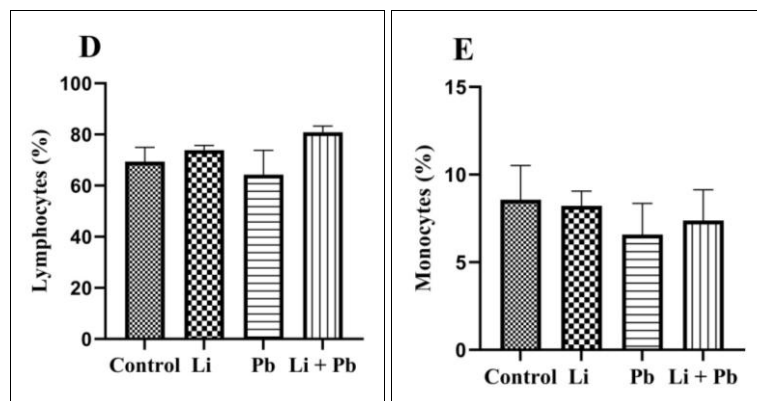
Parameters	Treatment groups (Mean $\pm$ SE; $n = 6$)			
	Control	Li	Pb	Li + Pb
ALT (IU/L)	37.06 $\pm$ 1.93 ^b	44.80 $\pm$ 1.82 ^a	41.63 $\pm$ 1.49 ^{ab}	45.62 $\pm$ 1.70 ^a
AST (IU/L)	98.81 $\pm$ 5.71 ^{ab}	118.94 $\pm$ 6.39 ^a	90.00 $\pm$ 10.65 ^b	95.29 $\pm$ 5.00 ^{ab}
Total protein (g/dL)	6.63 $\pm$ 0.21	5.99 $\pm$ 1.22	6.46 $\pm$ 0.18	6.74 $\pm$ 0.17
Albumin (g/dL)	3.85 $\pm$ 0.11	3.57 $\pm$ 0.71	3.71 $\pm$ 0.08	3.90 $\pm$ 0.05
Globulin (g/dL)	2.79 $\pm$ 0.12	2.43 $\pm$ 0.52	2.76 $\pm$ 0.10	2.85 $\pm$ 0.13
A/G Ratio	1.39 $\pm$ 0.04	1.42 $\pm$ 0.12	1.35 $\pm$ 0.04	1.38 $\pm$ 0.05
ALP (IU/L)	44.99 $\pm$ 1.70 ^b	70.87 $\pm$ 5.62 ^a	72.44 $\pm$ 2.90 ^a	74.67 $\pm$ 4.94 ^a
LDH (IU/L)	707.92 $\pm$ 18.03 ^d	1610.08 $\pm$ 14.75 ^a	1344.42 $\pm$ 20.98 ^b	958.20 $\pm$ 26.71 ^c
Creatinine (mg/dL)	0.385 $\pm$ 0.020	0.425 $\pm$ 0.018	0.398 $\pm$ 0.027	0.408 $\pm$ 0.020
Urea (mg/dL)	33.15 $\pm$ 1.08 ^b	39.62 $\pm$ 1.60 ^a	35.43 $\pm$ 0.57 ^{ab}	39.32 $\pm$ 2.13 ^a
Triglyceride (mg/dL)	109.5 $\pm$ 9.77 ^b	166 $\pm$ 11.49 ^a	111.5 $\pm$ 6.88 ^b	113.81 $\pm$ 19.57 ^b

Note: Values with different superscripts in a row were significantly different ($p < 0.05$)



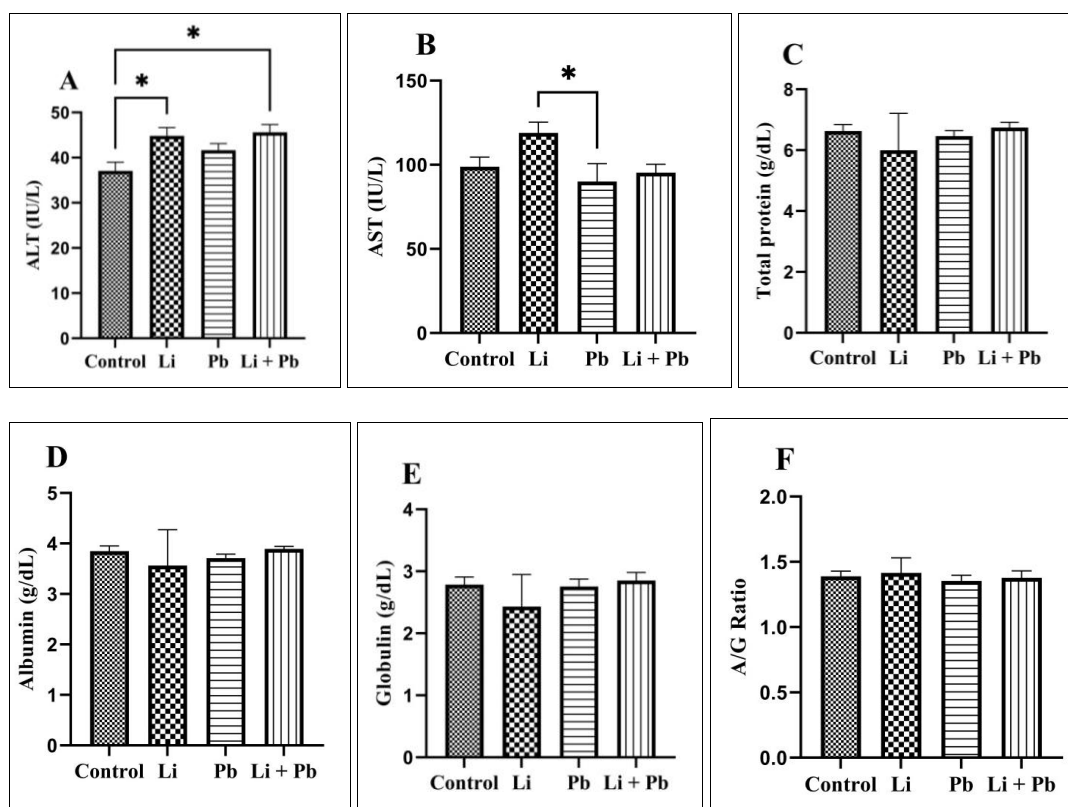
(A, B, C, F): Data were analyzed using the Kruskal-Wallis test followed by the Dunn's test. (D, E): Data were analyzed using one-way analysis of variance (ANOVA) followed by Tukey's HSD test. Where * indicates $p < 0.05$

Fig 1: Haematological parameters in male rats exposed to lithium carbonate and lead acetate



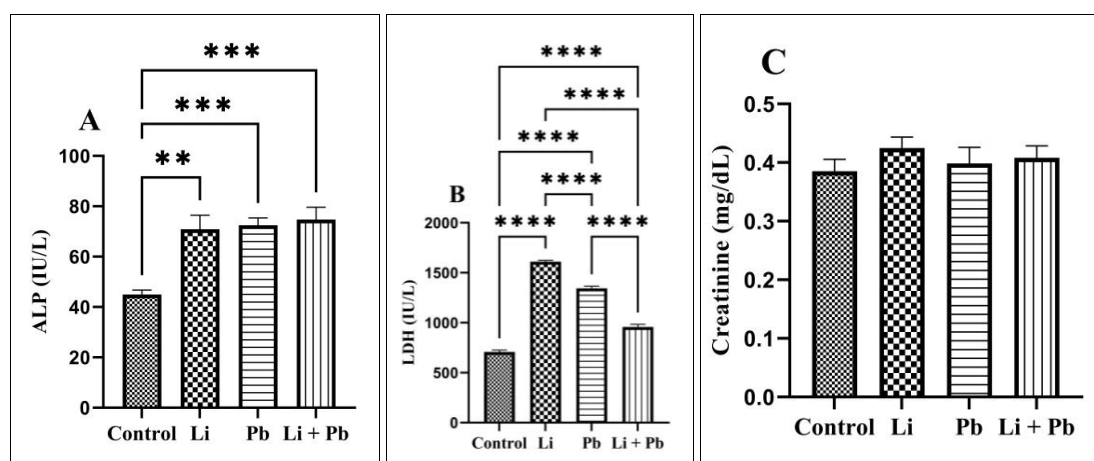
(A, B, C, D, E): Data were analyzed using the Kruskal-Wallis test followed by the Dunn's test. Where * indicates $p < 0.05$, ** indicates $p < 0.01$

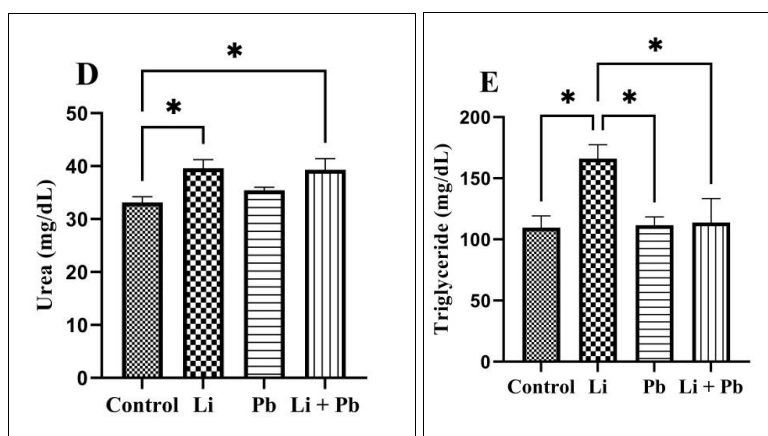
Fig 2: Haematological parameters in male rats exposed to lithium carbonate and lead acetate



(A, F): Data were analyzed using one-way analysis of variance (ANOVA) followed by Tukey's HSD test. (B, C, D, E): Data were analyzed using the Kruskal-Wallis test followed by the Dunn's test. Where * indicates $p < 0.05$

Fig 3: Serum biochemical parameters in male rats exposed to lithium carbonate and lead acetate





(A): Data were analyzed using the Kruskal-Wallis test followed by the Dunn's test. (B, C, D, E): Data were analyzed using one-way analysis of variance (ANOVA) followed by Tukey's HSD test. Where * indicates $p < 0.05$, ** indicates $p < 0.01$, *** indicates $p < 0.005$, **** indicates $p < 0.001$

Fig 4: Serum biochemical parameters in male rats exposed to lithium carbonate and lead acetate

5. Conclusion

Hematological analysis showed thrombocytopenia and leukocytosis in the Li + Pb group, with Pb primarily affecting platelets and Li influencing white blood cells. Liver and kidney function markers (*e.g.*, ALT, ALP, LDH, BUN) were significantly altered, especially in the combined exposure group, indicating hepato-renal toxicity. Overall, the study confirmed that while both Li and Pb are toxic individually, co-exposure leads to more severe hematological and biochemical underlining the need to consider combined exposures in toxicological risk assessments.

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Availability of data and materials: All data are available in the manuscript and supplementary file.

Competing interests: The authors declare that they don't have competing interests.

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Authors' contributions

Harsh R. Patel: Investigation, validation, formal analysis, writing - original draft.

Urvesh D. Patel: Conceptualization, writing - review and editing, supervision.

Maunik D. Prajapati: Investigation, validation, formal analysis.

Dhaval T. Fefar: Writing - review and editing

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References

1. Abubakar K, Mailafiya MM, Danmaigoro A, Chiroma SM, Rahim EBA, Zakaria MZAB. Curcumin attenuates

lead-induced cerebellar toxicity in rats via chelating activity and inhibition of oxidative stress. *Biomolecules*. 2019;9(9):453-479. DOI:10.3390/biom9090453.

2. Alamri ZZ, Alfaifi SM. Biochanin A has protective and therapeutic effects against Li_2CO_3 -induced nephrotoxicity in rat model. *Indones Biomed J*. 2024;16(3):208-217. DOI:10.18585/inabj.v16i3.3077.

3. Andjelkovic M, Buha Djordjevic A, Antonijevic E, Antonijevic B, Stanic M, Kotur-Stevuljevic J, *et al*. Toxic effect of acute cadmium and lead exposure in rat blood, liver, and kidney. *Int J Environ Res Public Health*. 2019;16(2):274-294. DOI:10.3390/ijerph16020274.

4. Barbosa F Jr, Tanus-Santos JE, Gerlach RF, Parsons PJ. A critical review of biomarkers used for monitoring human exposure to lead: advantages, limitations, and future needs. *Environ Health Perspect*. 2005;113(12):1669-1674. DOI:10.1289/ehp.7917.

5. Ben Saad A, Dalel B, Rjeibi I, Smida A, Ncib S, Zouari N, *et al*. Phytochemical, antioxidant and protective effect of cactus cladodes extract against lithium-induced liver injury in rats. *Pharm Biol*. 2017;55(1):516-525. DOI:10.1080/13880209.2016.1255976.

6. Bidanchi RM, Lalrindika L, Khushboo M, Bhanushree B, Dinata R, Das M, *et al*. Antioxidative, anti-inflammatory and anti-apoptotic action of ellagic acid against lead acetate induced testicular and hepato-renal oxidative damages in male rats. *Environ Pollut*. 2022;302:119048. DOI:10.1016/j.envpol.2022.119048.

7. Chadha VD, Bhalla P, Dhawan DK. Zinc modulates lithium-induced hepatotoxicity in rats. *Liver Int*. 2008;28(4):558-565. DOI:10.1111/j.1478-3231.2008.01674.

8. Choubey PK, Chung KS, Kim MS, Lee JC, Srivastava RR. Advanced review on the exploitation of lithium: Part II from seawater and spent lithium-ion batteries. *Miner Eng*. 2017;110:104-121. DOI:10.1016/j.mineng.2017.04.008.

9. Cunha M, Cruz I, Pinto J, Benito D, Ruiz P, Soares AM, *et al*. Influence of temperature on effects of lead and lithium in *Mytilus galloprovincialis*. *Sci Total Environ*. 2023;902:165786. DOI:10.1016/j.scitotenv.2023.165786.

10. Flora G, Gupta D, Tiwari A. Toxicity of lead: a review with recent updates. *Interdiscip Toxicol*. 2012;5(2):47-58. DOI:10.2478/v10102-012-0009-2.

11. Godwin HA. The biological chemistry of lead. *Curr Opin Chem Biol*. 2001;5(2):223-227. DOI:10.1016/S1367-5931(00)00194-0.

12. Goyer R. Toxic effects of metals. In: Amdur MO, Doull J, Klaassen CD, editors. Casarett and Doull's toxicology. 4th ed. New York: Pergamon Press; c1991. p. 623-680.
13. Grof P. Sixty years of lithium responders. *Neuropsychobiology*. 2010;62(1):8-16. DOI:10.1159/000314305.
14. Ibrahim NM, Eweis EA, El-Beltagi HS, Abdel-Mobdy YE. Effect of lead acetate toxicity on experimental male albino rat. *Asian Pac J Trop Biomed*. 2012;2(1):41-46. DOI:10.1016/S2221-1691(11)60187-1.
15. Jaishankar M, Tseten T, Anbalagan N, Mathew BB, Beeregowda KN. Toxicity, mechanism and health effects of some heavy metals. *Interdiscip Toxicol*. 2014;7(2):60-72. DOI:10.2478/intox-2014-0009.
16. Järup L. Hazards of heavy metal contamination. *Br Med Bull*. 2003;68(1):167-182. DOI:10.1093/bmb/ldg032.
17. Kielczykowska M, Kocot J, Kurzepa J, Lewandowska A, Żelazowska R, Musik I. Selenium administration alleviates lithium-induced blood disturbances in rats. *Biol Trace Elem Res*. 2014;158:359-364. DOI:10.1007/s12011-014-9952-4.
18. Lagerkvist BJ, Lindell B. Lithium and lithium compounds. Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals; 2002. Available from: <http://hdl.handle.net/2077/4277>
19. Léonard A, Hantson P, Gerber GB. Mutagenicity, carcinogenicity and teratogenicity of lithium compounds. *Mutat Res*. 1995;339(3):131-137. DOI:10.1016/0165-1110(95)90007-1.
20. Livingstone DR. Oxidative stress in aquatic organisms in relation to pollution and aquaculture. *Rev Med Vet (Toulouse)*. 2003;154(6):427-430.
21. Luo H, Li J, Song B, Zhang B, Li Y, Zhou Z, *et al*. Binary combined toxicity of lithium, lead and manganese on murine neural stem cells. *Environ Sci Pollut Res*. 2023;30(2):5047-5058. DOI:10.1007/s11356-022-22433.
22. Luoma SN, Rainbow PS. Metal contamination in aquatic environments. *J Fish Biol*. 2008;7:129s-141.
23. Mabrouk A, Bel Hadj Salah I, Chaieb W, Ben Cheikh H. Protective effect of thymoquinone against lead-induced hepatic toxicity in rats. *Environ Sci Pollut Res*. 2016;23:12206-12215. DOI:10.1007/s11356-016-6419-5.
24. Malhotra A, Dhawan DK. Zinc improves antioxidative enzymes and hematology in lithium-treated rats. *Nutr Res*. 2008;28(1):43-50. DOI:10.1016/j.nutres.2007.11.002.
25. Moore MR. Haematological effects of lead. *Sci Total Environ*. 1988;71(3):419-431. DOI:10.1016/0048-9697(88)90214-8.
26. Mwaheb MA, Sayed O, Mohamed S. Protective effect of rosemary extract on lithium-induced renal and testis toxicity in rats. *J Drug Metab Toxicol*. 2016;7(4):1-7. DOI:10.4172/2157-7609.1000216.
27. Ostadhadi S, Norouzi-Javidan A, Nikoui V, Zolfaghari S, Moradi A, Dehpour AR. Nitric oxide involvement in additive antidepressant-like effect of agmatine and lithium in mice. *Psychiatry Res*. 2018;266:262-268. DOI:10.1016/j.psychres.2018.03.010.
28. Oyem JC, Chris-Ozoko LE, Enaohwo MT, Otabor FO, Okudayo VA, Udi OA. Antioxidative properties of *Ocimum gratissimum* on lead-induced oxidative damage in rats. *Toxicol Rep*. 2021;8:215-222. DOI:10.1016/j.toxrep.2021.01.003.
29. Patel SS, Vediya SD. Study of toxic metals in Sarkhej Lake water, Gujarat, India. *Int J Pharm Life Sci*. 2012;3(9):1985-1986.
30. Saad AB, Rjeibi I, Alimi H, Ncib S, Smida A, Zouari N, *et al*. Lithium-induced oxidative stress and protective effects of *Malva sylvestris*. *Biomed Pharmacother*. 2017;86:127-135. DOI:10.1016/j.biopha.2016.12.105.
31. Sahin O, Sulak O, Yavuz Y, Uz E, Eren I, Yilmaz HR, *et al*. Lithium-induced lung toxicity in rats: effect of caffeic acid phenethyl ester. *Pathology*. 2006;38(1):58-62. DOI:10.1080/00313020500464904.
32. Samarghandian S, Azimi-Nezhad M, Farkhondeh T, Samini F. Anti-oxidative effects of curcumin on immobilization-induced oxidative stress in rats. *Biomed Pharmacother*. 2017;87:223-229. DOI:10.1016/j.biopha.2016.12.105.
33. Seddik L, Bah TM, Aoues A, Brnderdour M, Silmani M. Dried leaf extract protects against lead-induced neurotoxicity in rats. *Eur J Sci Res*. 2010;42(1):139-151.
34. Smith AJ, Smith K. Guidelines for humane education: alternatives to animal use. *Altern Lab Anim*. 2004;32(1):29-39. DOI:10.1177/026119290403201s07.
35. Smith DR, Flegal AR. Lead in the biosphere: recent trends. *Ambio*. 1995;24(1):21-23.
36. Toghiani T, Gholami M, Zendedel A, Assadollahi V. Effects of low-dose lithium carbonate on spermatogenesis in rats. *J Life Sci*. 2012;9(4):4360-4367.
37. Trieff NM, Frey SM, Rao MS, Bunce HI, Herman B. Analysis for lithium in Texas drinking waters; 1973.
38. Vediya SD, Patel SS. Toxic metal contamination of Vastral Lake, Gujarat, India. *Int J Pharm Life Sci*. 2011;2(10):1174-1176.
39. Vijaimohan K, Devi CS, Mallika J. Chemoprotective effect of sobatum against lithium-induced oxidative damage in rats. *J Young Pharm*. 2010;2(1):68-73. DOI:10.4103/0975-1483.62217.
40. Warick LH. Lithium poisoning: Report of a case with neurologic, cardiac and hepatic sequelae. *West J Med*. 1979;130(3):259-263.
41. Weiner ML. The human dose response to lithium from trace to toxic levels. In: *Lithium in medicine and biology*. Carnforth: Marius Press; c1993. p. 15-25.
42. Yagminas AP, Franklin CA, Villeneuve DC, Gilman AP, Little PB, Valli VEO. Subchronic oral toxicity of triethyl lead in male rats. *Toxicol Sci*. 1990;15(3):580-596. DOI:10.1016/0272-0590(90)90043-J.
43. Yildirim S, Celikezen FC, Oto G, Sengul E, Bulduk M, Tasdemir M, *et al*. Protective effects of lithium borate in cadmium-induced toxicity in rats. *Biol Trace Elem Res*. 2018;182(2):287-294. DOI:10.1007/s12011-017-1089-9.
44. Yip KK, Yeung WT. Lithium overdose causing non-convulsive status epilepticus. *Hong Kong Med J*. 2007;13(6):471-474.
45. Zhang P, Gandhi H, Kassis N. Lithium-induced nephropathy: A case report. *BMC Nephrol*. 2022;23(1):309-313. DOI:10.1186/s12882-022-02934-0.

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