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Jamun (*Syzygium cumini*) seed and orange (*Citrus sinensis*) peel extracts ameliorates toxic effects of lead on kidney biomarkers in rats

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ABSTRACT. Wistar rats were treated as Group A: Control; Group B: Lead (50 mg kg^{-1} b wt.); Group C: Lead (50 mg kg^{-1} b wt.) and jamun seed extract (JSE) (200 mg kg^{-1} b wt.); Group D: Lead (50 mg kg^{-1} b wt.) and orange peel extract (OPE) (200 mg kg^{-1} b wt.); Group E: OPE (200 mg kg^{-1} b wt.) and Group F: JSE (200 mg kg^{-1} b wt.). Serum urea, creatinine and serum uric acid levels were analyzed on days 7 and 14. Rats from Group B showed increased serum creatinine from days 7 to 14. Creatinine level decreased in group C and group D at days 7 and 14 as compared to group B. Increased serum urea was recorded in group B rats from 7 days. Rat from group C or group D showed decreased serum urea after days 7 day and 14 as compared to Group B. Lead exposure to rats provoked increased serum uric acid on days 7 and 14. Uric acid decreased in group C and group D on days 7 and 14 as compared to rats of group B. No alteration in creatinine, urea and uric acid level was seen in OPE and JSE treated rats at days 7 and 14.

Keywords: heavy metals; uric acid; creatinine; urea; nephrotoxic; phytochemicals.

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Introduction

Lead (Pb) is an environmental pollutant and well-known heavy metal which is highly poisonous and non-biodegradable trace element (Eruotor, Asiwe, & Eruotor, 2023; Elgazar, Shalaby, & Ibrahem, 2023). The main source of lead is gasoline, paints, lead-acid battery, eye cosmetics and printing of books (Ashour, Yassin, Aasi, & Ali, 2007; Yadav, Kushwaha, & Srivastav, 2023). It enters into the organisms' body through the contaminated foods, respiratory, dermal contact, electric wastes, vehicle exhausts and mucous membranes (Ashour et al., 2007; Owumi, Arunsi, Oyewumi, & Altayyar, 2022). Lead poisoning can induce various physiological and morphological impairments including the reproductive system, central nervous system, hematopoietic system, liver and kidneys in human and animal (Azzaz, El-Kholy, & Ramadan, 2022; Inayat et al., 2022; Eivani, Zareian, Ghahari, Dadpay, & Shojaee, 2023). Lead exposure can induce abnormal increase of serum uric acid and cause the Hyperuricemia as well as dysfunction of renal calculi, metabolic syndrome and cardiovascular system (Dai et al., 2015). Pb can induce increased formation of free radicals and alter the morphology of glomerular histoarchitecture and renal tubules and provoked kidney failure (Eruotor et al., 2023). Lead toxicity induce metabolic abnormalities and alter human and animal kidney functions as well as impairments in kidney bio-markers levels in blood such as urea, creatinine and uric acid (Mohammed, Sedky, & Elsawy, 2017; Abdulshaheed, Al-Kurdy, & Abbas, 2021). Lead is bio-accumulated in mammal's cells because it is not consumed during metabolism and affects cortical interstitial cells, renal tubules and renal parenchyma of kidney (Thuong, Lan, Van, Thanh, & Ke, 2023). Due to toxicity of lead, many countries now have strict controls on the use of lead paints and leaded gasoline (Ritchie, 2022; SunderRaj, & Ananthapadmanaban, 2024).

Syzygium cumini (family Myrtaceae) is commonly known as jamun, black plum and Indian blackberry (Srivastava et al., 2021a, b; Qamar et al., 2022). Jamun seed, fruit pulp and bark contain oleic, lauric, sterculic, myristic, vernolic acid, palmitic, stearic, linoleic, malvalic, phytosterols, corilagin, ellagitannins, ellagic acid, and gallic acid etc. It is used as antioxidant, anti-inflammatory, anti-microbial, anti-bacterial for the treatment of abnormalities such as diabetes mellitus, hepatoxicity and nephrotoxicity (Swami, Thakor, Patil, & Haldankar, 2012; Abbas et al., 2016; Kumar & Thakur, 2018).

Orange (*Citrus sinensis*) belongs to family Rutaceae. Orange peel contains numerous micronutrients such as rutin, cellulose, flavanone glycosides hesperidin, neohesperidin, naringin, hemi-cellulose, pectin substances, chlorophyll pigments, and other small molecules like limonene (Srivastva et al., 2021b). Orange peel extract improve the levels of kidney parameters such as, serum uric acid and serum urea,serum creatinine (Alfarajat, Mostafa, Abdel-Mogib, El-Gayar, & El-Khawaga, 2023). Orange peel extract contains specific antioxidant which protect against nephrotoxicity and improve kidney damage (Srivastva et al., 2021b).

There is no report regarding JSE and OPE regarding the ameliorative effect of the toxic effects of lead on kidney biomarkers in rats. Hence, this study evaluated the changes in kidney biomarkers such as, serum urea, serum uric acid and serum creatinine levels of rats treated with lead and evaluated the protective role of Jamun (*Syzygium cumini*) seed extract and orange (*Citrus sinensis*) peel extract on the toxic effects of lead on these parameters.

Materials and methods

One hundred twenty Wistar rat (b wt. 50-60 g; 2 months age) were purchased from Asia Scientific Emporium, Varanasi, India and were acclimatized for 2 weeks under laboratory conditions (27- 30°C with a 12 hour dark light^{-1} cycle) in polypropylene cages. Standard diet and water *ad libitum* was provided to rats. The doses of lead, JSE and OPE given to the rats are based on the reports of the previous investigators- Lead (25,50 and 60 mg kg^{-1} b wt.– Bhattacharjee, Kulkarni, Chakraborty, Habbu, & Ray, 2021; 50 mg kg^{-1} b wt. – Eruotor et al., 2023; 40 mg kg^{-1} b wt. – Amriza, Rita, & Elmatris, 2022; 30 mg kg^{-1} b wt. – Kucukler et al., 2021); jamun peel extract (200 mg kg^{-1} b wt. – Srivastava et al., 2021a; 400 mg kg^{-1} b wt. – Kumar & Thakur, 2018; 400 mg kg^{-1} b wt. - Sarma, 2014; 250 mg kg^{-1} wt. – Sharma, Siddiqui, Kumar, Ram, & Chaudhary, 2013); orange peel extract (250 and 500 mg kg^{-1} b wt.—Ekhator et al., 2022; 200 mg kg^{-1} b wt. -Mohamed, Tohamy, Elgamal, & Moneim, 2014; Srivastava et al., 2021a).

Purified Lead Nitrate [Pb $(NO_3)_2$] was purchased from Qualigens Fine Chemicals, Mumbai, India and dissolved in distilled water to obtain the desired dose. Orange (*Citrus sinensis*) peel and jamun (*Syzygium cumini*) seed extracts were prepared according to Srivastava et al. (2021a, 2021b). This study was approved by the Research Degree Committee (RC/FSc/ZOO/2019-2020/07/22), D.D.U. Gorakhpur, Gorakhpur.

Experimental design

Acclimatized rats were grouped into A, B, C, D, E, and F groups (each with twenty rats) and treated daily (at 8 a.m.) as follow through gavages:

Group A: Control: Not treated;

Group B: (Lead): These rats were given lead (50 mg kg^{-1} b wt.);

Group C: Pb + JSE: These rats were given daily lead (50 mg kg^{-1} b wt.) and JSE (200 mg kg^{-1} b wt.) simultaneously;

Group D: Pb + OPE: These rats received daily lead (50 mg kg^{-1} b wt.) and OPE (200 mg kg^{-1} b wt.) simultaneously;

Group E: OPE: Rats were given OPE (200 mg kg^{-1} b wt.);

Group F: JSE: Rats were given JSE (200 mg kg^{-1} b wt.).

10 rats from each group were fasted overnight and killed under light ether anaesthesia on 7 day and 14 day. Sera were separated after collection of blood by centrifugation at 3000 rpm for 5 min. Sera was stored at -20℃.Analysis of serum urea, creatinine and uric acid was performed by using kits (Beacon Diagnostics Private Ltd, India). Each sample was analyzed in duplicate.

Statistical analysis

Results of analysis are expressed as multiple group comparisons were performed by using ANOVA (One way Analysis of Variance). Student's t test and Bonferroni post hoc test was used to determined the deference between control and treated groups. The significant levels were set at p-value < 0.05.

Results

In the present study, creatinine levels increased in rat of Group B (treated with lead 50 mg kg^{-1} b wt.) on 7 and 14 day as compared to control (group A) (Figure 1). Serum creatinine level significantly decreased after treatment with combination of lead and JSE (group C: Pb + JSE) and lead and OPE (group D: Pb + OPE) at 7 and 14 day as compared to Group B (only lead treated) (Figure 1). When only OPE or JSE was given to rat no significant changes were noticed in serum creatinine levels at 7 and 14 day (group E: 200 mg kg^{-1} b wt. and group F: 200 mg kg^{-1} b wt.). Results of ANOVA expressed that treatment is significant (7 days- $F = 4.815$, $p < 0.002$; 14 days- $F = 43.419$, $p < 0.0001$).

Serum urea levels increased significantly in rat treated with lead (group B: 50 mg kg^{-1} b wt.) from 7 to 14 day as compared to control (group A; Figure 2). Serum urea levels were decreased progressively from 7 day to 14 day after treatment with lead and jamun seed extract (group C: Pb + JSE) or lead and orange peel extract (group D: Pb + OPE) as compared to Group B (lead exposed). No significant changes were recorded in serum urea levels after treatment with OPE (group E: 200 mg kg-1 b wt.) or JSE (group F: 200 mg kg-1 b wt.) at 7 and 14 day (Figure 2). Results of ANOVA expressed that treatment is significant (7 days- $F = 29.475$, $p < 0.0001$; 14 days- $F = 55.954$, $p < 0.0001$).

Increased serum uric acid levels were recorded in the rat treated with lead (group B) as compared to Group A (control) at 7 and 14 day (Figure 3). After treatment with combined dose of lead and jamun seed extract (group C: Pb + JSE) or lead and orange peel extract (group D: Pb + OPE) significant decrease in serum uric acid levels were recorded as compared to Group B (lead treated rat) at 7 and 14 day (Figure 3). The rat treated with OPE (group E: 200 mg kg^{-1} b wt.) or JSE (group F: 200 mg kg^{-1} b wt.), no significant changes were observed at 7 day and 14 day (Figure 3). Results of ANOVA expressed that treatment is significant (7 days- $F = 11.014$, $p < 0.0001$; 14 days- $F = 32.610$, $p < 0.0001$).

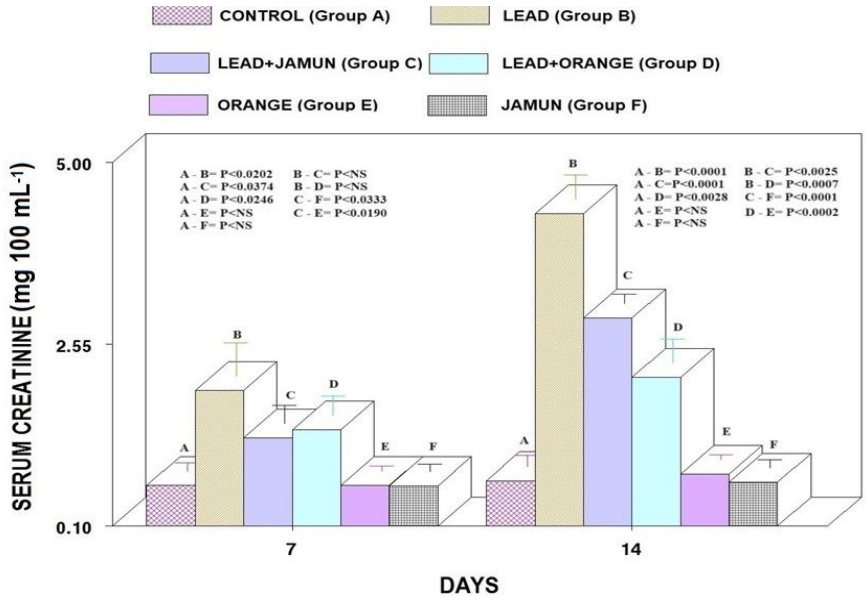

Figure 1. Serum creatinine levels (mg 100 mL^{-1}) of Wistar rat treated either with lead, lead+jamun seed extract, lead+orange peel extract, orange peel extract or jamun seed extract. All values indicate mean ± SE of six specimens.

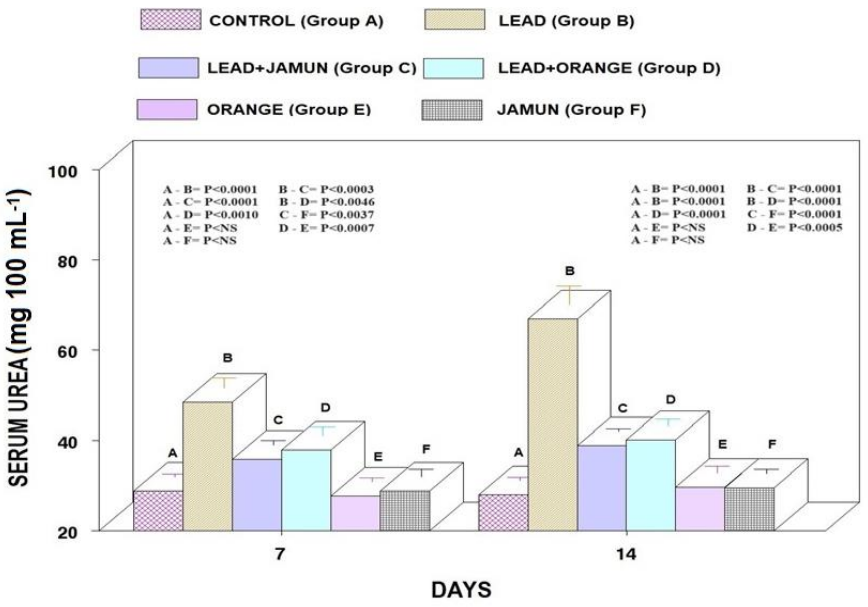

Figure 2. Serum urea levels (mg 100 mL^{-1}) of Wistar rat treated either with lead, lead+jamun seed extract, lead+orange peel extract, orange peel extract or jamun seed extract. All values indicate mean ± SE of six specimens.

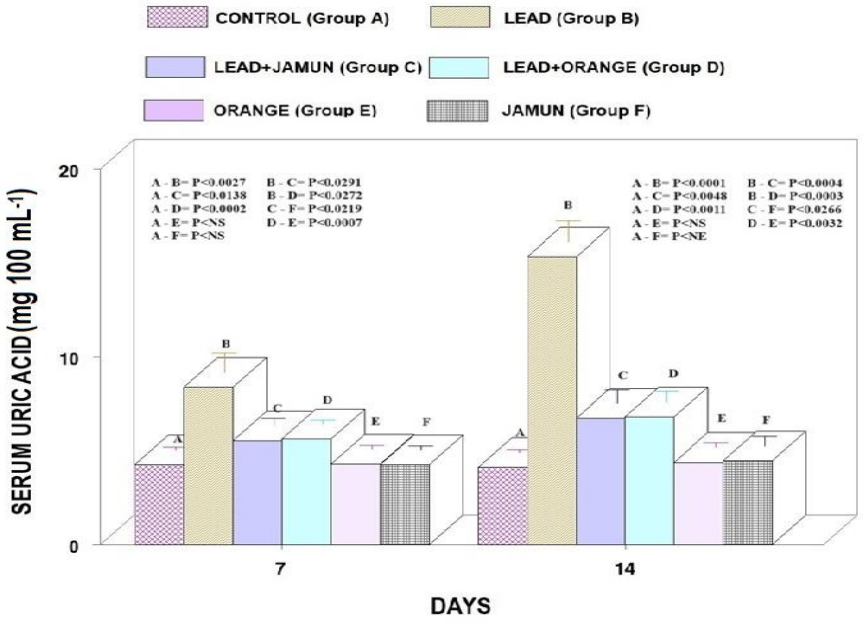

Figure 3. Serum uric acid levels (mg 100 mL^{-1}) of Wistar rat treated either with lead, lead+jamun seed extract, lead+orange peel extract, orange peel extract or jamun seed extract. All values indicate mean ± SE of six specimens.

The above results clearly indicate that JSE and OPE are effective in ameliorating the effect of lead on kidney bio-markers.

Discussion

Lead exposure to rats caused alternations in the kidney bio-markers which is evident by increased urea, creatinine and uric acid levels. Previous researchers have also reported similar results in toxicants exposed rats-Acrylamide (Uthra et al., 2022), Deltamethrin (Mostafa, Atef, & el Din, 2022), Cadmium (Ilesanmi & Adeogun, 2022), Paraoxon (Sobolev, Sokolova, Jenkins, & Goncharov, 2021), Methotrexate (Alum et al., 2023), Oxazaphosphorine (Lukasz et al., 2017), Tartrazine (El-Desoky, Wabaidur, AlOthman, & Habila, 2022), Chlorpyrifos (Aung et al., 2020) and Gentamicin (Akhitha, Raghavendra, & Kumar, 2019). Few investigators have also reported alterations in kidney biomarkers after exposure to various toxicants in – (i) fishes-Bisphenol A (Srivastava & Reddy, 2020), Diazinon (Banaee et al., 2023), Imidacloprid (Qadir, Latif, Ali, & Iqbal, 2014) and Deltamethrin (Hamed, 2016); and (ii) Amphibian- Cadmium (Medina, González, Klyver, & Odstrcil, 2016) and Oxyfluorfen (El-Rahman, Ahmed, Khalil, & Abd-Elhakim, 2019). In the present study, we have observed a significant decrease in the levels of serum creatinine, serum urea, serum uric acid in the blood of rat after treatment with JSE and OPE which evident preventive effect of JSE and OPE against lead nephrotoxicity.

This study noticed an increased levels of serum creatinine in rats after lead exposure which is in agreement with observations of Eivani et al. (2023) who have also reported lead-induced increase in serum creatinine levels of rat. In group C (Pb+ JSE) and group D (Pb+ OPE), the creatinine levels decreased on 7 and 14 day in comparison to Group B (lead treated rat) this indicates that OPE and JSE are effective in protecting kidney and improved the serum creatinine levels which was increased after treatment with lead. There was no change observed in creatinine levels after treatment with orange peel extract or jamun seed extract to rat. In past, no study exists regarding the effects of JSE and OPE on creatinine levels of lead exposed rats.

In the present study, increased serum urea levels were recorded in lead treated rats at 7 and 14 day. Previous investigators have also observed increased serum urea levels in toxicants exposed rats - Tartrazine (Rahayu, Wahyuni, Fitriani, & Agung, 2022); Bisphenol A (Kobroob, Peerapanyasut, Chattipakorn, & Wongmekiat, 2018); Cypermethrin and chlorpyrifos (Ajobola et al., 2019) and Acetaminophen (Roy et al., 2015). Serum urea levels were significantly decreased after treatment with combination of lead and JSE or OPE as compared to Group B (only lead treated rat). There was no significant change observed in serum urea levels in rat which was treated with OPE and JSE. The effect of JSE and OPE on lead induced changes in serum urea of rat has not been investigated earlier.

Administration of lead provoked a significant increase in serum uric acid levels of Group B (lead treated rat) in comparison to control (group A) from 7 to 14 day. The current study derives support from studies of Ashour et al. (2007) who have also reported increased serum uric acid levels in rat after treatment with lead. In the present study, the combined dose of lead with JSE or OPE was given to the rat significantly reduced levels of serum uric acid. This clearly indicate that JSE and OPE were effective in recovering uric acid levels to nearly control values.

In the present study the recovery in lead induced kidney biomarkers e.g. creatinine, urea and uric acid by treatment with jamun seed and orange peel extracts can be attributed to the presence of phytochemicals present in the extracts. In past, few studies have reported the pharmacological properties of jamun seed, such as (i) its antidiabetic potential including the ability to prevent complications associated with diabetes e.g. nephropathy, neuropathy, gastropathy, diabetic cataract, and peptic ulceration; (ii) cardioprotective, (iii) gastroprotective, (iv) hepatoprotective, and (v) neuropsychopharmacology effects (Kumar et al., 2022). In past, dietary supplementation of orange peel powder has been reported to attenuate the toxic effect of bisphenol A-induced hepatic and splenic dysfunction, which has been attributed to its phenol and flavonoid content (AbdEl-Gwaad, El-Wahab, Mohamed, Sharaf, & Osman, 2020).

Conclusion

In conclusion, lead exposure to rat alters serum urea, serum creatinine serum uric acid levels. The jamun seed extract and orange peel extract administration showed preventive effect against renal toxicity induced by lead exposure in rat. JSE and OPE administration showed restoration of serum urea, creatinine, serum uric acid levels to near the control value. Therefore, it is advisable that the organisms exposed to heavy metals specially lead should be given dietary supplement of these botanical extracts which would ease the several toxic symptoms.

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References

Abbas, T., Ahmad, K. R., Asmatullah, Lone, K. P., Kanwal, M. A., & Suleman, S. (2016). Reno-hepatic protective effects of Jambul against chromium induced anomalies in mice. *Punjab University Journal of Zoology, 31*(1), 59-67.

AbdEl-Gwaad, H. M. S., El-Wahab, H. M. F. A., Mohamed, E. A. K., Sharaf, E. H. A. A., & Osman, A. A. H. M. (2020). Modulatory effect of dry orange (*citrus sinensis*) peel powder on bisphenol A-induced hepatic and splenic toxicity in rats. *The Journal of Basic and Applied Zoology, 81*(49). DOI: https://doi.org/10.1186/s41936-020-00183-x

Abdulshaheed, H. G., Al-Kurdy, M. J. J., & Abbas, G. A. (2021). Effects of lead toxicity on renal biochemical indices before and after treatment with *Pimpinella anisum* aqueous extract. *Annals of the Romanian Society for Cell Biology, 25*(4), 4943-4949.

Ajobola, I. O., Adenike, S. F., Afolabi, S. A., Toba, A. A., Olayinka, A. J., Jamiu, A. M., ... Stephen, A. O. (2019). Cypermethrin and chlorpyrifos raises serum urea level and causes abnormal sperm morphology in Wistar rats. *Biointerface Research in Applied Chemistry, 9*(3), 3969-3973. DOI: https://doi.org/10.33263/BRIAC93.969973

Akhitha, N., Raghavendra, M., & Kumar, M. V. K. (2019). Protective effect of *Bauhinia Tomentosa* L. extract against gentamicin induced nephrotoxicity in Wistar male albino rats. *International Journal of Pharmaceutical Sciences and Research, 10*(3), 1412-1419. DOI: https://doi.org/10.13040/IJPSR.0975-8232.10(3).1412-19

Alfarajat, S. M. F., Mostafa, M. E., Abdel-Mogib, M., El-Gayar, H. A., & El-Khawaga, O. Y. (2023). Reno-protective effect of *Citrus sinensis* by regulating antioxidant capability and gene expression in adenine-induced chronic kidney in rats. *Biointerface Research in Applied Chemistry, 13*(4), 349. DOI: https://doi.org/10.33263/BRIAC134.349

Alum, E. U., Famurewa, A. C., Orji, O. U., Aja, P. M., Nwite, F., Ohuche, S. E., ... Chima, S. F. (2023). Nephroprotective effects of *Datura stramonium* leaves against methotrexate nephrotoxicity via attenuation of oxidative stress-mediated inflammation and apoptosis in rats. *Avicenna Journal of Phytomedicine, 13*(4), 377-387. DOI: https://doi.org/10.22038/AJP.2023.21903

Amriza, M. Z., Rita, R. S., & Elmatris, S. (2022). Java Plum (*Syzygium cumini* (L.) Skeels) leaf extract lowers serum urea levels in lead-acetate-induced rats. *PHARMACY: Jurnal Farmasi Indonesia Pharmaceutical Journal of Indonesia, 19*(2), 274-281. DOI: https://doi.org/10.30595/pharmacy.v19i2.13611

Ashour, A. E. R. A., Yassin, M. M., Aasi, N. M. A., & Ali, R. M. (2007). Blood, serum glucose and renal parameters in lead-loaded albino rats and treatment with some chelating agents and natural oils. *Turkish Journal of Biology, 31*(1), 25-34.

Aung, S., Talib, N. A., Abdullah, N. Z., Zainone, Z. M., Harun, N., Noor, N. M., & Razak, T. A. (2020). The effects of chronic low dose exposure of chlorpyrifos on the rat kidney. *IIUM Medical Journal Malaysia, 19*(1), 43-51.

Azzaz, N., El-Kholy, S. E. E., & Ramadan, O. I. (2022). Protective effects of *Nigella sativa* and *Propolis* against cadmium or lead induced nephrotoxicity: An experimental histological and biochemical study. *International Journal of Medical Arts, 4*(3), 2235-2242. DOI: https://doi.org/10.21608/ijma.2022.113892.1423

Banaee, M., Impellitteri, F., Multisanti, C. R., Sureda, A., Arfuso, F., Piccione, G., & Faggio, C. (2023). Evaluating silymarin extract as a potent antioxidant supplement in diazinon-exposed rainbow trout: oxidative stress and biochemical parameter analysis. *Toxics, 11*(9), 737. DOI: https://doi.org/10.3390/toxics11090737

Bhattacharjee, A., Kulkarni, V. H., Chakraborty, M., Habbu, P. V., & Ray, A. (2021). Ellagic acid restored lead-induced nephrotoxicity by anti-inflammatory, anti-apoptotic and free radical scavenging activities. *Heliyon, 7*(1), e05921. DOI: https://doi.org/10.1016/j.heliyon.2021.e05921

Dai, H., Huang, Z., Deng, Q., Li, Y., Xiao, T., Ning, X., ... Yuan, H. (2015). The effects of lead exposure on serum uric acid and hyperuricemia in chinese adults: a cross-sectional study. *International Journal of Environmental Research and Public Health, 12*(8), 9672-9682. DOI: https://doi.org/10.3390/ijerph120809672

Eivani, M., Zareian, P., Ghahari, L., Dadpay, M., & Shojaee, S. (2023). The effect of *Melissa officinalis* hydro alcoholic extract on liver enzymes, markers of kidney function and testosterone in lead poisoned rats. *Journal of Kerman University of Medical Sciences, 30*(1), 40-45. DOI: https://doi.org/10.34172/jkmu.2023.06

Ekhator, O. C., Osarumwense, E. P., Akowe, A. B., Egbe, U. J., Aghedo, N. O., Omozuwa, O. P., & Ekhator, C. M. (2022). Antioxidant and chelating effects of *Citrus sinensis* peel extract on wistar rats administered with lead and cadmium. *Bio-Research, 20*(3), 1638-1648. DOI: https://doi.org/10.4314/br.v20i3.1

El-Desoky, G. E., Wabaidur, S. M., AlOthman, Z. A., & Habila, M. A. (2022). Evaluation of Nano-curcumin effects against Tartrazine-induced abnormalities in liver and kidney histology and other biochemical parameters. *Food Science & Nutrition, 10*(5), 1344-1356. DOI: https://doi.org/10.1002/fsn3.2790

Elgazar, A. F., Shalaby, M. A., & Ibrahem, E. S. (2023). Potential effectiveness of flesh-red dragon fruit juice in the improvement of consequence injury from lead acetate-induced neurotoxicity in rats. *Journal of Pharmaceutical Negative Results, 14*(3), 894-906. DOI: https://doi.org/10.47750/pnr.2023.14.03.116

El-Rahman, G. I. A., Ahmed, S. A. A., Khalil, A. A., & Abd-Elhakim, Y. M. (2019). Assessment of hematological, hepato-renal, antioxidant, and hormonal responses of *Clarias gariepinus* exposed to sub-lethal concentrations of oxyfluorfen. *Aquatic Toxicology, 217*, 105329. DOI: https://doi.org/10.1016/j.aquatox.2019.105329

Eruotor, H. O., Asiwe, J. N., & Eruotor, T. M. (2023). *Cymbopogon citratus* protect against lead-induced suppression of haematological and tubuloglomerular functions as well as disruption of hepatocellular membranes in male Wistar rats. *Journal of Trace Elements and Minerals, 3*, 100045. DOI: https://doi.org/10.1016/j.jtemin.2022.100045

Hamed, H. (2016). Ameliorative effects of *Spirulina platensis* on deltamethrin-induced biochemical alterations and oxidative stress in the african catfish; *Clarias gariepinus*. *Open Journal of Marine Science, 6*(1), 1-10. DOI: https://doi.org/10.4236/ojms.2016.61001

Ilesanmi, O. B., & Adeogun, E. O. (2022). Nephroprotective effect of *Ipomoea cairica* leaf extract against cadmium-induced renal damage. *Nigerian Journal of Biochemistry and Molecular Biology, 37*(4), 282-288.

Inayat, I., Ahmad, S. N., Suleman, S., Siddique, S., Ali, R., Shameem, S., ... Ahmad, K. R. (2022). Study of histo-curative potential of jambul (*Syzygium cumini*) fruit pulp extract in mice kidney under chromic lead (Pb) exposure. *Pakistan Journal of Scientific and Industrial Research Series B: Biological Sciences, 65B*(3), 222-227.

Kobroob, A., Peerapanyasut, W., Chattipakorn, N., & Wongmekiat, O. (2018). Damaging effects of Bisphenol A on the kidney and the protection by melatonin: Emerging evidences from in vivo and in vitro studies. *Oxidative Medicine and Cellular Longevity, 2018*, 3082438. DOI: https://doi.org/10.1155/2018/3082438

Kucukler, S., Benzer, F., Yildirim, S., Gur, C., Kandemir, F. M., Bengu, A. S., ... Dortbudak, M. B. (2021). Protective effects of chrysin against oxidative stress and inflammation induced by lead acetate in rat kidneys: a biochemical and histopathological approach. *Biological Trace Element Research, 199*(4), 1501-1514. DOI: https://doi.org/10.1007/s12011-020-02268-8

Kumar, M., & Thakur, R. (2018). *Syzygium cumini* seed extract ameliorates arsenic-induced blood cell genotoxicity and hepatotoxicity in Wistar albino rats. *Reports of Biochemistry and Molecular Biology, 7*(1), 110-118.

Kumar, M., Zhang, B., Nishad, J., Verma, A., Sheri, V., Dhumal, S., ... Lorenzo, J. M. (2022) Jamun (*Syzygium cumini* (L.) Skeels) seed: A review on nutritional profile, functional food properties, health-promoting applications, and safety aspects. *Processes, 10*(11), 2169. DOI: https://doi.org/10.3390/pr10112169

Lukasz, D., Skowron, B., Baranowska, A., Płoszaj, K., Bądziul, D., & Thor, P. (2017). The influence of oxazaphosphorine agents on kidney function in rats. *Medicina, 53*(3), 179-189. DOI: https://doi.org/10.1016/j.medici.2017.05.004

Medina, M. F., González, M. E., Klyver, S. M. R., & Odstrcil, I. M. A. (2016). Histopathological and biochemical changes in the liver, kidney, and blood of amphibians intoxicated with cadmium. *Turkish Journal of Biology, 40*(1), 229-238. DOI: https://doi.org/10.3906/biy-1505-72

Mohamed, N. A. E., Tohamy, A. A., Elgamal, B., & Moneim, A. E. A. (2014). Ameliorative effect of citrus peel extract on castration-induced oxidative stress in liver and kidney of rats. *Journal of Applied Pharmaceutical Science, 4*(7), 064-068. DOI: https://doi.org/10.7324/JAPS.2014.40711

Mohammed, G. M., Sedky, A., & Elsawy, H. (2017). A study of the modulating action of quercetin on biochemical and histological alterations induced by lead exposure in the liver and kidney of rats. *Chinese Journal of Physiology, 60*(3), 183-190. DOI: https://doi.org/10.4077/CJP.2017.BAF439

Mostafa, T., Atef, K., & el Din, M. (2022). Protective effects of royal jelly against hepatorenal toxicity induced by deltamethrin in male albino rats: biochemical and histopathological studies. *SVU-International Journal of Veterinary Sciences, 5*(3), 18-27. DOI: https://doi.org/10.21608/svu.2022.120519.1178

Owumi, S. E., Arunsi, U. O., Oyewumi, O. M., & Altayyar, A. (2022). Accidental lead in contaminated pipe-borne water and dietary furan intake perturbs rats' hepatorenal function altering oxidative, inflammatory, and apoptotic balance. *BMC Pharmacology Toxicology, 23*(1), 76. DOI: https://doi.org/10.1186/s40360-022-00615-0

Qadir, S., Latif, A., Ali, M., & Iqbal, F. (2014). Effects of Imidacloprid on the Hematological and Serum Biochemical Profile of Labeo rohita. *Pakistan Journal of Zoology, 46*(4), 1085-1090.

Qamar, M., Akhtar, S., Ismail, T., Wahid, M., Abbas, M. W., Mubarak, M. S., ... Esatbeyoglu, T. (2022). Phytochemical profile, biological properties, and food applications of the medicinal plant *Syzygium cumini*. *Foods, 11*(3), 378. DOI: https://doi.org/10.3390/foods11030378

Rahayu, M. S., Wahyuni, S., Fitriani, I., & Agung, H. B. (2022). Effect of tartrazine on blood urea nitrogen, creatinine levels, and renal tubular necrosis in adult male Wistar rats (*Rattus norvegicus*): an experimental study. *Bali Medical Journal, 11*(3), 1755-1759. DOI: https://doi.org/10.15562/bmj.v11i3.3663

Ritchie, H. (2022). Many countries have eliminated lead from paint. How do we achieve the same everywhere? *Our World in Data*. Retrieved from https://ourworldindata.org/lead-paint

Roy, S., Pradhan, S., Das, K., Mandal, A., Mandal, S., Patra, A., ... Nandi, D. K. (2015). Acetaminophen induced kidney failure in rats: A dose response study. *Journal of Biological Sciences, 15*(4), 187-193. DOI: https://doi.org/10.3923/jbs.2015.187.193

Sarma, S. (2014). Role of *Syzygium cumini* seed-extract on streptozotocin-nicotinamide-induced type-2 diabetes of Albino Rat. *International Journal of Pure & Applied Bioscience, 2*(4), 125-131.

Sharma, B., Siddiqui, S., Kumar, S. S., Ram, G., & Chaudhary, M. (2013). Liver protective effects of aqueous extract of *Syzygium cumini* in Swiss albino mice on alloxan induced diabetes mellitus. *Journal of Pharmacy Research, 6*(8), 853-858. DOI: https://doi.org/10.1016/j.jopr.2013.07.020

Sobolev, V. E., Sokolova, M. O., Jenkins, R. O., & Goncharov, N. V. (2021). Nephrotoxic effects of paraoxon in three rat models of acute intoxication. *International Journal of Molecular Sciences, 22*(24), 13625. DOI: https://doi.org/10.3390/ijms222413625

Srivastava, B. D., Srivastava, M., Srivastav, S. K., Urata, M., Suzuki, N., & Srivastav, A. K. (2021a). Cypermethrin-induced alterations in serum calcium and phosphate of rats: protective role of jamun seed and orange peel extracts. *Jordan Journal of Biological Sciences, 14*(3), 417-422. DOI: https://doi.org/10.54319/jjbs/140306

Srivastava, B. D., Srivastava, M., Srivastav, S. K., Urata, M., Suzuki, N., & Srivastav, A. K. (2021b). Protective effects of jamun (*Syzygium cumini*) seed and orange (*Citrus sinensis*) peel extracts against cypermethrin-induced nephrotoxicity in rats. *Egyptian Journal of Basic and Clinical Pharmacology, 11*, 101492. DOI: https://doi.org/10.32527/2021/101492

Srivastava, B., & Reddy, P. B. (2020). Haematological and serum biomarker responses in *Heteropneustes fossilis* exposed to Bisphenol A. *Nature Environment and Pollution Technology, 19*(4), 1577-1584. DOI: https://doi.org/10.46488/NEPT.2020.v19i04.024

SunderRaj, A. J., & Ananthapadmanaban, D. (2024) Environmental aspects of lead free soldering and study of legislations banning lead based solders in different countries. *Environmental Science Archives, III*(1), 87-94. DOI: https://doi.org/10.5281/zenodo.10717758

Swami, S. B., Thakor, N. S. J., Patil, M. M., & Haldankar, P. M. (2012). Jamun (*Syzygium cumini* (L.)): a review of its food and medicinal uses. *Food and Nutrition Sciences, 3*(8), 1100-1117. DOI: https://doi.org/10.4236/fns.2012.38146

Thuong, H. N. T., Lan, C. T. N., Van, T. T., Thanh, H. N. T., & Ke, Q. T. (2023). Effect of lead on hematological parameters and histopathology of the liver, kidney and spleen of female albino mice. *Asian Journal of Health Sciences, 9*(1), ID52. DOI: https://doi.org/https://doi.org/10.15419/ajhs.v9i1.523

Uthra, C., Reshi, M. S., Jaswal, A., Yadav, D., Shrivastava, S., Sinha, N., & Shukla, S. (2022). Protective efficacy of rutin against acrylamide-induced oxidative stress, biochemical alterations and histopathological lesions in rats. *Toxicology Research, 11*(1), 215-225. DOI: https://doi.org/10.1093/toxres/tfab125

Yadav, R. P., Kushwaha, V. B., & Srivastav, S. K. (2023). Toxicity of cadmium and lead in mammal: a brief review. *International Journal of Zoological Investigations, 9*(2), 722-729. DOI: https://doi.org/10.33745/ijzi.2023.v09i02.081