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Ameliorative Effects of Jamun Seed and Orange Peel Extracts on Serum Calcium and Phosphate Levels of Cadmium Challenged Male Wistar Rats

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Abstract: The aim of the present study was to investigate the changes in the serum calcium and phosphorous induced by cadmium and to evaluate the protective role of jamun (*Syzygium cumini*) seed and orange (*Citrus sinensis*) peel extracts. Male wistar rats were divided into six groups and following treatments were given as – Group A: Control; Group B: Cadmium (Cd); Group C: Cadmium and jamun seed extract (Cd+ JSE); Group D: Cadmium + orange peel extract (Cd + OPE); Group E: Orange peel extract (OPE); Group F: Jamun seed extract (JSE). The Cadmium dose was 10 mg/kg b wt whereas orange peel and jamun seed extract dose was 200 mg/kg b wt/day. Blood samples were collected on day 7 and day 14 after these treatments and analyzed for serum calcium and phosphate.

Rats from Group B (cadmium challenged) showed decrease in serum calcium level after 7 day as compared to control (Group A). Serum calcium level decreased further after 14 day after cadmium treatment. There was a significant increase in serum calcium level in Group C at 7 days and 14 days as compared to Group B (Cd treated). In group D the serum calcium level exhibited an insignificant increase on day 7, however, the levels were significant after 14 days treatment as compared to group B. No significant change was noticed in serum calcium level when rats were treated with orange peel extract and jamun seed extract after 7 day and 14 day.

Rats from Group B showed progressive decrease from 7 day to 14 day in serum phosphate level as compared to control (Group A). There was no significant change in serum phosphate level of group C and D at 7 day treatment as compared to Group B (Cd treated), however, the phosphate levels were significantly increased on day 14 in group C and D as compared to group B. No significant change was noticed in serum phosphate level when rats were treated with orange peel extract and jamun seed extract after 7 day and 14 day.

Keywords: Cadmium, Phosphate, *Syzygium cumini*, *Citrus sinensis*, Antioxidant, Hypocalcemia, Hypophosphatemia

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Introduction

Heavy metals like cadmium (Cd) and arsenic are widespread environmental toxicants responsible for a number of adverse health effects in humans and other organisms (Guo *et al.*, 2016; Srivastava and Srivastav, 2017; Srivastava *et al.*, 2023). Cadmium is a major threat to human health around the world and associated with pollution and anthropogenic activity (Lordan and Zabetakis, 2022). Environmental and occupational cadmium exposure may be related to various types of cancer, including breast, lung, prostate, nasopharynx, pancreas and kidney carcinomas (Genchi Giuseppe *et al.*, 2020). Cadmium, a highly toxic environmental pollutant, is reported to induce toxicity and apoptosis of multiple organs and cells (Chen *et al.*, 2015). Exposure to cadmium is contributing to dysfunction of the internal organs and development of chronic diseases (Markiewicz-Górka *et al.*, 2019). Food contamination with cadmium may take place at various phases, such as agronomic conditions, food production, processing and consumer preparation for consumption. The presence of cadmium in food vary and is influenced by the geographic location, cadmium bioavailability from soil, crop genetics, and agronomic practices used and post harvest operations (Heather *et al.*, 2020). Cadmium is a non essential transition metal that has been introduced by various anthropogenic activities into the biosphere. In the past decades, environmental pollution of Cd had a significant health risk and there have been extensive studies on its toxicity (Sandbichler and Höckner, 2016). Environmental diseases related to exposure to cadmium develop mainly as result of industrial sewage pollution and/or contaminated food (Yamanobe *et al.*, 2015). As a normal cellular metabolic by-product, reactive oxygen species (ROS) are produced by living cells. Cells will accumulate a number of ROS when exposed to excessive stress, and the living beings are then gradually developing several response mechanisms in order to counteract to that exposure as well as use it for signal molecules. In the feedback mechanism, which involves a number of physiological processes such as apoptosis, necrosis and autophagocytosis, ROS molecules would be an inducer of oxidative stress (He *et al.*, 2017).

The most important prooxidants, whose excessive accumulation leads to oxidative stress and molecular damage, are reactive oxygen species (ROS) together with reactive nitrogen species (RNS). Their physiological functions are determined by the concentration of ROS. When present at low concentration and high concentration, ROS involved in signaling processes essential for normal cellular functions and leads to DNA, lipid, protein damage and apoptosis, respectively (Macvanin *et al.*, 2023).

Phytochemicals with antioxidant activity have been reported to be present in fruits, vegetables, spices and herbs, which scavenge free radicals (Mossa *et al.*, 2015; Srivastava *et al.*, 2018; Ahmed *et al.*, 2019; Bashandy *et al.*, 2019). Jamun (*Syzygium cumini*) belongs to family Myrtaceae. Antioxidant compound called flavonoids, phenols and anthocyanins are present in jamun fruits and seeds (Raza *et al.*, 2017; Srivastava *et al.*, 2018; Simon *et al.*, 2018). Antidiabetic, antimalarial, antibiotic, free radical scavenging , antiulcerogenic and antifertility properties are present in jamun seeds (Singh *et al.*, 2012; Kumari *et al.*, 2017; Chagas *et al.*, 2018; Srivastava *et al.*, 2018, 2021). Jagetia (2018) have reported reduction of free radicals and activation of different enzymes like catalase, glutathione peroxidase, glutathiones-transferase by jamun. It increases synthesis of glutathione and depletes lipid peroxidation.

Citrus (*Citrus sinensis*) is an important fruit variety that has a high yield of phytochemicals such as flavanones, polyphenols, anthocyanins and hydroxycinnamic acids, hespiridin , naringin . Abundant flavanones and polymethoxylated flavones are exclusively found in peel of citrus fruits. The antioxidative potential of the orange peel has been reported (Srivastava *et al.*, 2021). Hesperidin has been reported to increase the levels of superoxide dismutase (SOD), glutathione

S-transferase (GST), and total glutathione (GSH) in rats after chemical induction of oxidative stress (Jeon *et al.*, 2002). Arafa *et al.* (2009) reported that naringin in citrus peel increased superoxide dismutase, catalase (CAT) and vitamin E levels in New Zealand white rabbits with high cholesterol levels.

The aim of this study was to investigate alterations in serum calcium and inorganic phosphate levels induced by exposure of cadmium in male Wistar rats and to evaluate the protective role of jamun (*Syzygium cumini*) seed and orange (*Citrus sinensis*) peel extracts against the toxicological effects caused by exposure to cadmium.

Materials and Methods

Experimental design:

Male wistar rats were purchased from Asia Scientific Emporium, Varanasi, India and were acclimatized for 15 days in polypropylene cages. They were fed on standard food and water *ad libitum* during the experiment.

The acclimatized rats were divided into 6 groups (A-F) each group containing 10 rats. The rats were treated as follow at 8:00 am everyday throughout the experiment:

Group A: Control

Group B: Cadmium treatment (Cd)

Group C: Cadmium + Jamun seed extract (Cd+JSE)

Group D: Cadmium + Orange peel extract (CD+OPE)

Group E: Orange peel extract (OPE)

Group F: Jamun seed extract (JSE)

The cadmium dose was 10 mg/kg b wt/day whereas orange peel and jamun seed extract dose was 200 mg/kg b wt/day. Five rats from each group were sacrificed 24 h after the last dose on 7th and 14th day after the initiation of the experiment. Rats were fasted overnight before sacrifice. The experimental protocol and handling of the animals was approved by the Research Degree Committee of DDU Gorakhpur University, Gorakhpur, India.

Extract preparation:

The orange peels and jamun seeds were purchased locally. The orange peels and jamun seeds were washed with water and dried in hot air oven at 40°C. After drying they were crushed and powdered. Powdered orange peels and jamun peels were mixed with 90% ethanol in 1:20 ratio (w:v) and kept at orbital shaker for 48 h. Then the samples were filtered through Whatman no. 1 filter paper. The filtrates were dried in oven at 40°C and stored at −20°C. For use the dried residues of orange peel and jamun seed were dissolved with ethanol to provide required dose to be given to rats.

Blood analysis:

The rats were slightly anesthetized with ether and blood was taken by cardiac puncture using a 3 ml syringe equipped with 23 gauge needles. The blood samples were allowed to clot at room temperature for a period of 30 min. Sera were separated by centrifugation (at 3,000 rpm) and kept at -20°C. Analysis of serum calcium and serum inorganic phosphate was performed by using Beacon kit (Beacon Diagnostic Private Ltd). Each sample was analyzed in duplicate.

Statistical analysis:

Data are presented as the Mean±SE of five specimens. To determine the significance level a Student t - test was performed. In all studies all the treated groups are compared with the control group. Analysis of Variance (ANOVA) was used to establish the significant differences between different treatment groups.

Results

The serum calcium level of rat treated with cadmium (Group B) exhibited a decrease after 7 day ($P < 0.0001$) and day 14 ($P < 0.0001$) as compared with control (Group A)(Fig. 1). In cadmium and jamun seed extract treated rats (Group C), the serum calcium increased on 7 day ($P < 0.0197$) and on 14 day ($P < 0.0001$) as

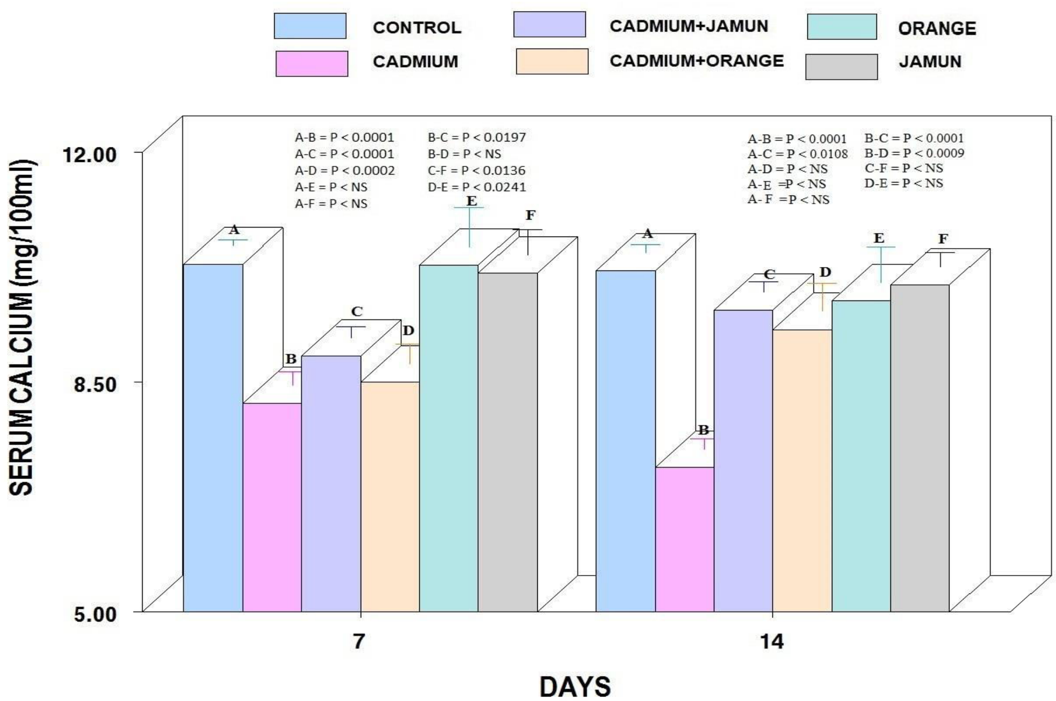

Fig. 1: Serum calcium levels (mg/100 ml) of Wistar rat: control (group A); cadmium (group B), cadmium + jamun seed extract (group C), cadmium + orange peel extract (group D), orange peel extract (group E) and jamun seed extract (group F) extract. All values indicate mean + S.E. of five specimens.

compared to Group B. In cadmium and orange peel extract treated rats (Group D), the serum calcium level insignificantly increased on 7 day as compared to Group B. However, on day 14 the calcium level showed a significant increase (P< 0.0009) as compared to Group B (Fig. 1). This indicates that orange peel and jamun seed are effective in recovering the calcium levels which was decreased by treatment with cadmium. In orange peel extract (Group E) and Jamun seed extract (Group F) there was no change in serum calcium level on 7 and 14 day. Analysis of Variance (ANOVA) indicated that the treatment was significant (7 day - F = 8.346, P<0.0001; 14 day - F = 12.294, P < 0.0001).

In cadmium (Group B) exposed rat the serum phosphate levels gradually decreased from 7 day (P < 0.0006) to 14 day (P< 0.0001) as compared to control (Group A) (Fig. 2). In cadmium and jamun seed extract (Group C), the serum phosphate level exhibited insignificant increase at day 7, however, on 14 day there was a significant increase (P< 0.0467) as compared to the level of Group B. In Group D serum phosphate levels insignificantly increased on day 7, whereas the levels were noticed significantly increased (P< 0.0146) on 14 day as compared to Group B. In orange peel extract (Group E) and jamun seed extract (Group F) exposed rats there was no change in serum phosphate levels as compared to control rats (Group A). Analysis of Variance (ANOVA) indicated that treatment was significant (7 day - F= 5.642, P< 0.0009; 14 day - F = 16.037, P< 0.0001).

Discussion

In present study, Cd treated rats exhibited hypocalcemia. This is in agreement with the report of Tripathi and Srivastav (2011b) who have also noticed hypocalcemia in rats after exposure to

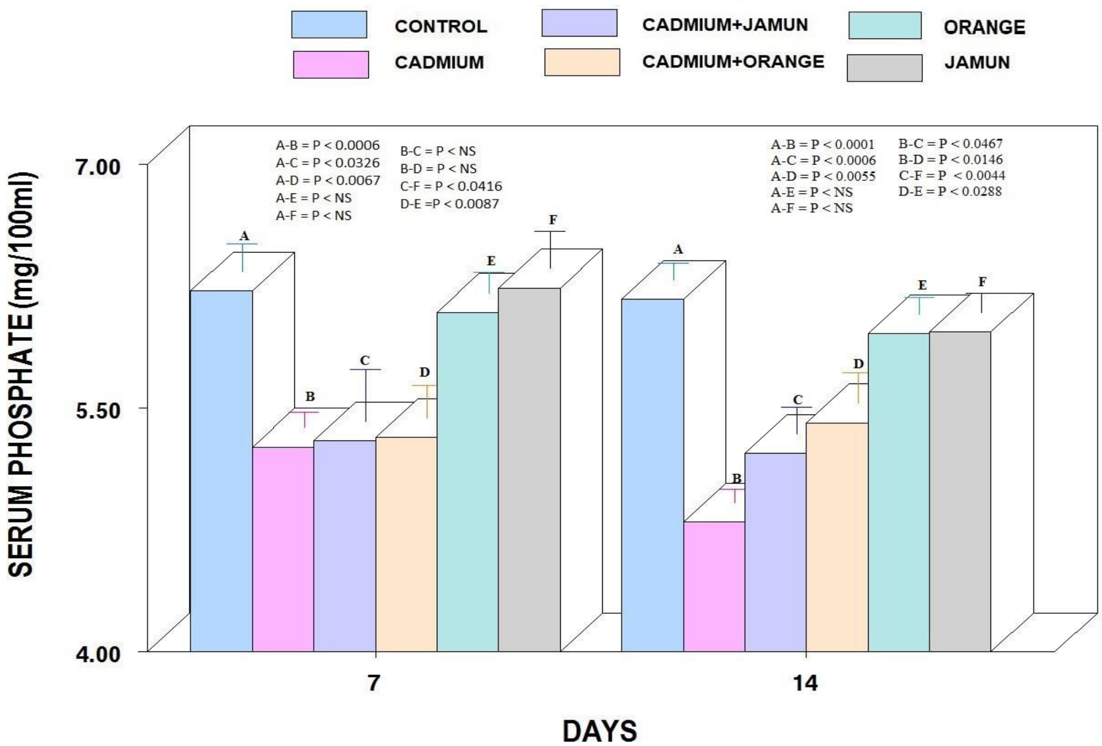

Fig. 2: Serum phosphate levels (mg/100 ml) of Wistar rat: control (group A); cadmium (group B), cadmium + jamun seed extract (group C), cadmium + orange peel extract (group D), orange peel extract (group E) and jamun seed extract (group F) extract. All values indicate mean + S.E. of five specimens.

cadmium. The present study is in agreement with the reports of earlier workers who have noticed hypocalcemia after exposure to different toxicants in -- (i) rats – cypermetrin (Srivastava *et al.,* 2021); microcystin LR (Srivastava *et al.,* 2020), chlorpyrifos (Tripathi *et al.,* 2013), diazinon (Rangoonwala *et al.*, 2005), mipcin (Rangoonwala *et al.,* 2007), cypermethrin (Rangoonwala *et al.,* 2008), heroin (Barai *et al.,* 2009); (ii) in chickens: gamma benzene hexachloride and quinalphos (Agarwal *et al.,* 2009); and (iii) in frogs: chlorpyrifos (Srivastav *et al.,* 2018) and cadmium (Srivastav *et al.,* 2019). In toxicant exposed fish hypocalcemia has also been reported-- deltamethrin (Srivastav *et al.*, 1997b, 2010); aldrin (Singh *et al.*, 1996); malachite green (Srivastava *et al.,* 1995); formothion (Singh *et al.*, 1997); cadmium (Rai and Srivastav, 2003, Chowdhary *et al.*, 2004, Suzuki *et al.*, 2004), cypermethrin (Mishra *et al.,* 2010), herbal pesticides (Kumar *et al.*, 2011 a, b; Prasad *et al.,* 2011 a,b) and dimethoate (Pandey and Das, 2015). Treatment with nickel to *Cyprinus carpio* caused no significant changes in serum calcium levels (Bozorgzahed *et al.,* 2023).

In the present study rats exposed to cadmium exhibited hypophosphatemia. In past, other investigators have also reported hypophosphatemia after toxicant exposure to rats- microcystin LR (Moreno *et al.,* 2003; Srivastava *et al.,* 2020), cypermetrin (Srivastava *et al.,* 2021); cadmium (Tripathi and Srivastav, 2011b), chlorpyrifos (Tripathi *et al.,* 2013), in chickens- gamma benzene hexachloride and quinalphos (Agarwal *et al.,* 2009). After treatment with chlorpyrifos hypophosphatemia was recorded in frog (Srivastav *et al.,* 2018). Hypophosphatemia was noticed in fish after exposure to chlorpyrifos (Srivastav *et al.,* 1997 a), deltamethrin (Srivastav *et al.,* 1997 b), cypermethrin (Mishra *et al.,* 2001), cadmium (Rai and Srivastav, 2003), *Nerium indicum* leaf extract (Prasad *et al.,* 2011a), *Euphorbia royleana* (Prasad *et al*., 2011 b), azadirachtin (Kumar *et al*. 2011 a), *Euphorbia tirucalli* (Kumar *et al*., 2011b), lead (Srivastav *et al*., 2013) and microcystin LR (Prakash *et al.,*2015, 2016). In contrast, no alteration was noticed in blood phosphate of rats treated with heptachlor (Rangoonwala *et al.,* 2004), diazinon (Rangoonwala *et al.,* 2005) and mipcin (Rangoonwala *et al.,* 2007). In heroin administered rats, Barai *et al.* (2009) noticed hyperphosphatemia.

The hypocalcemia induced by cadmium in rats may due to the degeneration of kidney in cadmium exposed rats (our unpublished data). In mammals various toxicants caused degeneration of kidney (Chmielnicka *et al*., 1989; Prozialeck *et al*., 2009; Tripathi and Srivastav, 2010, 2011 a). Increased efflux of calcium may occur due to kidney damage by toxicants (Chmielnicka *et al.,* 1989; Prozialeck *et al*., 2009) which can be attributed to the observed hypocalcemia in present study. Few investigators have attributed toxicant induced hypocalcemia to the degenerative changes in the renal tubules in fishes (Koyama and Itazawa, 1977; Roch and Maly, 1979; Larsson *et al.,* 1981; Haux and Larsson, 1984). Hypocalcemia in mipcin (Rangoonwala *et al.,* 2007) and heroin (Barai *et al.,* 2009) treated rats has been attributed to the degeneration of parathyroid glands.

Conclusion

It is concluded that cadmium exposure adversely affects the serum calcium and phosphate levels of the rats. The fluctuation observed in these parameters after cadmium exposure could be protected by the supplements obtained from extracts of jamun seed and orange peel. It is suggested that living beings after their exposure to cadmium should intake supplements of these given extracts which would help in the reduction of the cadmium toxicity.

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References

Agarwal S, Batra M and Chauhan S. (2009) Effects of gamma benzene hexachloride and quinalphos on serum calcium and phosphorus levels in experimentally fed broiler chickens. J Immuno Immunopathol. 11(1): 57-59

Ahmed OM, Fahim HI, Ahmed HY, Al-Muzafar HM, Ahmed RR, Amin KA, El-Nahass E and Abdelazeem WH. (2019) The preventive effects and the mechanisms of action of navel orange peel hydroethanolic extract, naringin, and naringenin in N-acetyl-p-aminophenol-induced liver injury in Wistar rats. Oxidative Med Cell Longe. 2019: 2745352.

Arafa HMM, Aly HAA, Abd-Ellah MF and ElRefaey HM. (2009) Hesperidin attenuates benzol[a]pyrene-induced testicular toxicity in rats via regulation of oxidant/antioxidant balance. Toxicol Ind Health 25: 417-427.

Barai SR, Suryawanshi SA and Pandey AK. (2009) Response of parathyroid gland, C cells and plasma calcium and inorganic phosphate levels in rat to sublethal heroin administration. J Environ Biol. 30: 917-922.

Bashandy SAE, Ahmad-Farid OAH, Omara EA, El-Toumy SA and Salib JY. (2019) Protective effects of *Citrus reticulata* peel extract against potassium dichromate-induced reproductive toxicity in rats. Asian Pacific J Reprod. 8: 267-275.

Bozorgzadeh P, Shamsaie MM, Pourang N and Hosseini SSP. (2023) Effects of nickel on liver and bone metabolic functions, biochemical and histopathological responses in common carp (*Cyprinus carpio*). Iranian J Fish Sci. 22(3): 526-546.

Chagas VT, Coelho RMRS, Gaspar RS, da Silva SA, Mastrogiovanni M, Mendonça CJ, Ribeiro MNS, Paes AMA and Trostchansky A. (2018) Protective effects of a polyphenol-rich extract from *Syzygium cumini* (L.) skeels leaf on oxidative stress-induced diabetic rats. Oxid Med Cell Longev. 2018: 5386079.

Chen CY, Zhang SL, Liu ZY, Tian Y and Sun Q. (2015) Cadmium toxicity induces ER stress and apoptosis via impairing energy homoeostasis in cardiomyocytes. Biosci Rep. 35(3): e00214.

Chmielnicka J, Halatek T and Jedlinska U. (1989) Correlation of cadmium-induced nephrology and the metabolism of endogenous copper and zinc in rats. Ecotoxicol Environ Saf. 18: 268-276.

Chowdhury MJ, Pane FF and Wood CM. (2004) Physiological effects of dietary cadmium acclimation and waterborne cadmium challenges in rainbow trout: respiratory, ionoregulatory and stress parameters. Comp Biochem Physiol. 139: 163-173.

Genchi Giuseppe, Maria SS, Graziantonio L, Alessia C and Alessia C. (2020) The effects of cadmium toxicity. Int J Environ Res Public Hlth. 17(11): 3782.

Guo L, Ganguly A, Sun L, Suo F, Du LL and Russell P. (2016) Global fitness profiling identifies arsenic and cadmium tolerance mechanisms in fission yeast. G3 (Bethesda) 6(10): 3317-3333.

Haux C and Larsson A. (1984) Long term sublethal physiological effects on rainbow trout, Salmo gairdneri, during exposure to cadmium and after subsequent recovery. Aquat Toxicol. 5: 129-142.

He L, He T, Farrar S, Ji L, Liu T and Ma X. (2017) Antioxidants maintain cellular redox homeostasis by elimination of reactive oxygen species. Cell Physiol Biochem. 44(2): 532-553.

Heather RS, Dennis S and Fitzpatrick S. (2020) Cadmium: Mitigation strategies to reduce dietary exposure. J Food Sci. 85(2): 260-267.

Jagetia GC. (2018) A review on the role of jamun, syzygium cumini skeels in the treatment of diabetes. Int J Complement Alt Med. 11(2): 91-95.

Jeon SM, Bok SH, Jang MK, Kim YH, Nam KT, Jeong TS, Park YB and Choi MS. (2002) Comparision of antioxidant effects of naringin and probucol in cholesterol-fed rabbits. Clin Chim Acta 317: 181-190.

Koyama J and Itazawa Y. (1977) Effects of oral administration of cadmium on fish-I. Analytical results of the blood and bones. Bull Jap Soc Sci Fish. 43: 523-526.

Kumar A, Prasad M, Mishra D, Srivastav SK and Srivastav Ajai K. (2011a) Botanical pesticides, azadirachtin attenuates blood electrolytes of a fresh water catfish *Heteropneustes fossilis*. Pest Biochem Physiol. 99(2): 170-173.

Kumar A, Prasad M, Mishra D, Srivastav SK and Srivastav Ajai K. (2011b) Effects of Euphorbia tirucalli latex on blood electrolytes (calcium and phosphate) of a freshwater air-breathing catfish *Heteropneustes fossilis*. Toxicol Environ Chem. 93: 585-592.

Kumari B, Sharma V and Yadav S. (2017) The therapeutic potential of *Syzygium cumini* seeds in diabetes mellitus. J Med Plant Stud. 5: 212-218.

Larsson A, Bengtsson BE and Haux C. (1981) Disturbed ion balance in flounder Platichthys flesus L., exposed to sublethal levels of cadmium. Aquat Toxicol. 1: 19-35

Lordan R and Zabetakis I. (2022) Cadmium: A focus on the brown crab (*Cancer pagurus*) industry and potential human health risks. Toxics 10(10): 591.

Macvanin MT, Gluvic Z, Zafirovic S, Gao X, Essack M and Isenovic ER. (2023) The protective role of nutritional antioxidants against oxidative stress in thyroid disorders. Front Endocrinol (Lausanne). 13: 1092837.

Markiewicz-Górka I, Pawlas K, Jaremków A, Januszewska L, Pawłowski P and Pawlas N. (2019) Alleviating effect of α-lipoic acid and magnesium on cadmium-induced inflammatory processes, oxidative stress and bone metabolism disorders in Wistar rats. Int J Environ Res Public Hlth. 16(22): 4483.

Mishra D, Srivastav S, Srivastav SK and Srivastav Ajai K. (2001) Plasma calcium and inorganic phosphate levels of a freshwater catfish, *Heteropneustes fossilis* in response to cypermethrin treatment. J Ecophysiol Occup Hlth. 1: 131-138.

Mishra D, Tripathi S, Srivastav SK, Suzuki N and Srivastav Ajai K. (2010) Corpuscles of Stannius of a teleost *Heteropneustes fossilis* following intoxication with a pyrethroids (cypermethrin). North-Western J Zool. 6(2): 203-208.

Moreno IM, Mate A, Repetto G, Vazquez CM and Camean AM. (2003) Influence of microcysin-LR on the activity of membrane enzymes in rat intestinal mucosa. J Physiol Biochem. 59: 293-300

Mossa AH, Ibrahim FM, Mohafrash SMM, Baker DHA and Gengaihi SE. (2015) Protective effect of ethanolic extract of grape pomace against the adverse effects of cypermethrin on weanling female rats. Evidence-Based Comp Alter Med2015: 381919.

Pandey RK and Das VK. (2015) Dimethoate induced changes in serum Ca2 and corpuscles of Stannius in freshwater catfish *Heteropneustes fossilis*, after short-term and long-term exposure. American J Life Sci. 3(1):17-21

Prakash C, Kumar A, Prasad M, Srivastav SK and Srivastav Ajai K. (2015) Microcystin-LR attenuates blood calcium and phosphate levels in stinging catfish *Heteropneustes fossilis*. Int J Pharm Biol Sci. 6: 1147-1153.

Prakash C, Prasad M, Kumar A, Mishra D, Chaudhary A and Srivastav SK. (2016) Protective effect of ZnCl2 on toxicity produced by Microcystin–LR on serum calcium and phosphate levels of freshwater catfish *Heteropneustes fossilis*. Int J Pure App BioSci. 4:

111- 117.

Prasad M, Kumar A, Mishra D, Srivastav SK and Srivastav Ajai K. (2011 a) Alterations in blood electrolytes of a freshwater catfish *Heteropneustes fossilis* in response to treatment with a botanical pesticide, Nerium indicum leaf extract. Fish Physiol Biochem. 37: 505-510.

Prasad M, Kumar A, Mishra D, Srivastav SK and Srivastav Ajai K. (2011 b) Blood electrolyte of a freshwater catfish *Heteropneustes fossilis* in response to treatment with a botanical pesticide, Euphorbia royleana latex. Integ Zool. 6: 150-156.

Prozialeck WC, Edwards JR, Vaidya VS and Bonventre JV. (2009) Preclinical evaluation of novel urinary biomarkers of cadmium nephrotoxicity. Toxicol Appl Pharm. 238: 301-305.

Rai R and Srivastav Ajai K. (2003) Effects of cadmium on the plasma electrolytes of a freshwater fish *Heteropneustes fossilis*. J Ecophysiol Occup Hlth. 3: 63-70.

Rangoonwala SP, Kazim M and Pandey AK. (2005) Effects of diazinon on serum calcium and inorganic phosphate levels as well as ultrastructures of parathyroid and calcitonin cells of *Rattus norvegicus.* J Environ Biol. 26(2): 217-221.

Rangoonwala SP, Suryawanshi SA and Pandey AK. (2004) Response of serum calcium and inorganic phosphate levels, parathyroid gland and C cells of *Rattus norvegicus* to heptachlor administration. J Environ Biol. 25: 75-80.

Rangoonwala SP, Suryawanshi SA and Pandey AK. (2007) Response of serum calcium and inorganic phosphate levels as well as parathyroid gland, calcitonin producing C cells of *Rattus norvegicus* to mipcin administration. J Environ Biol. 28(2): 475-481.

Rangoonwala SP, Suryawanshi SA and Pandey AK. (2008) Effects of sublethal cypermethrin and fenvalerate administration on serum calcium and inorganic phosphate levels as well as parathyroid gland and thyroid C cells of *Rattus norvegicus*. In: Perspectives Anim Ecol Reprod., (eds.) Gupta V.K. and Verma A.K., Vedams eBooks (P) Ltd (New Delhi, India). ISBN 10: 817035563X

Raza A, Butt MS, Ul-Haq I and Suleria HA R. (2017) Jamun (*Syzygium cumini*) seed and fruit extract attenuate hyperglycemia in diabetic rats. Asian Pacific J Tropical Biomed. 7: 750- 754.

Roch M and Maly EJ. (1979) Relationship of cadmium induced hypocalcemia with mortality in rainbow trout (*Salmo gairdneri*) and the influence of temperature on toxicity. J Fish Res Bd Can. 36: 1297-1303.

Sandbichler AM and Höckner M. (2016) Cadmium Protection Strategies--A Hidden Trade-Off? Int J Mol Sci. 17(1):139.

Simon U, David O, Peter R, Joseph R, Ijeoma C and Celestine N. (2018) Pathological effects of cypermethrin on the testes and accessory sexual glands of Yankasa rams. Arch Pathol Clinical Res. 2: 6-12.

Singh AK, Tiwari MN, Prakash O and Singh MP. (2012) A current review of cypermethrin-induced toxicity and nigrostriatal dopaminergic neurodegeneration. Curr Neuropathol. 10: 64-71.

Singh NN, Das VK and Singh S. (1996) Effect of aldrin on carbohydrate, protein and ionic metabolism of a freshwater catfish, *Heteropneustes fossilis*. Bull Environ Contam Toxicol. 57: 204-210.

Singh NN, Das VK and Srivastav AK. (1997) Formathion and propoxur induced ionic imbalance and skeletal deformity in a catfish, *Heteropneustes fossilis*. J Environ Biol. 18: 357-363.

Srivastav Ajai K, Rai R, Suzuki N, Mishra D and Srivastav SK. (2013) Effects of lead on plasma electrolytes of freshwater fish, *Heteropneustes fossilis*. Inter Aquat Res. 5: 4.

Srivastav Ajai K, Srivastava SK , Mishra D and Srivastav S K. (2010) Deltamethrin-induced alterations in serum calcium and prolactin cells of a fresh water teleost *Heteropneustes fossilis*. Toxicol Environ Chem. 92(10): 1857-1864.

Srivastav Ajai K, Srivastava SK and Srivastava AK. (1997 a) Response of serum calcium and inorganic phosphate of freshwater catfish, *Heteropneustes fossilis*, to chlorpyrifos. Bull Environ Contam Toxicol. 58(6): 915-921.

Srivastav Ajai K, Srivastava SK and Srivastav SK. (1997 b) Impact of deltamethrin on serum calcium and inorganic phosphate of freshwater catfish *Heteropneustes fossilis*. Bull Environ Contam Toxicol. 59(5): 841-846.

Srivastav Ajai K, Srivastav S, Srivastav SK and Suzuki N. (2018) Alterations in the serum electrolytes of the Indian Skipper frog *Euphlyctis cyanophlyctis* caused by an organophosphate pesticides: Chlorpyrifos. Jordan J Biol Sci. 11(4): 395-399.

Srivastav Ajai K, Srivastav S, Srivastav SK, Faggio C, Sekiguchi T and Suzuki N. (2019) Response of ultimobranchial and parathyroid glands of the Indian skipper frog *Euphlyctis cyanophlyctis* to cadmium toxicity. Iranian J Toxicol. 13(3): 39-44.

Srivastava A, Srivastav Sunil K and Upadhyay Ravi K. (2023) Cadmium induced pathological and eco-toxicological effects in animals. World J Pharmaceut Res. 12: 313.

Srivastava BD and Srivastav Ajai K. (2017) Hepatoprotective effects of extracts of *Syzygium cumini* seeds and *Citrus sinensis* peels against microcystin lr-induced toxicity in rat. Intern J Zool Invest. 3(1): 95-105.

Srivastava BD, Srivastava M, Srivastav SK, Urata M, Suzuki N and Srivastav Ajai K. (2021) Cypermethrin induced alterations in serum calcium and phosphate of rats: protective role of jamun seed and orange peel extracts. Jordan J Biol Sci. 14(3): 417-422.

Srivastava BD, Srivastava M, Srivastav SK, Urata M, Suzuki N and Srivastav Ajai K. (2020) Jamun seed and orange peel extracts protects effects of microcystin LR on serum calcium and phosphate of rats. European J Biol Res. 10(3): 198-206.

Srivastava SJ, Singh ND, Srivastav AK and Sinha R. (1995) Acute toxicity of malachite green and its effect on certain blood parameters of a catfish *Heteropneustes fossilis*. Aquat Toxicol. 31: 241-247. 1206

Suzuki N, Yamamoto M, Watanabe K, Kambegawa A and Hattori A. (2004) Both mercury and cadmium directly influence calcium homeostasis resulting from the suppression of scale bone cells: the scale is a good model for the evalution of heavy metals in bone metabolism. J Bone Mineral Metabol. 22: 439-446.

Tripathi S and Srivastav Ajai K. (2010) Nephrotoxicity induced by long-tem oral administration of different doses of chlorpyrifos. Toxicol Indus Hlth. 26: 439-447.

Tripathi S and Srivastav Ajai K (2011 a) Cytoarchitectural alterations in kidney of Wistar rat after oral exposure to cadmium chloride. Tissue Cell 43: 131-136.

Tripathi S and Srivastav Ajai K. (2011b) Alterations in the serum electrolytes, calcitonin cells and parathyroid gland of Wistar rat in response to administration of cadmium. Proc I Con Environ Poll Remediat. 141 Ottawa, Ontario, Canada, 17-19 August 2011 Paper No. 126.

Tripathi S, Suzuki N and Srivastav Ajai K. (2013) Response of serum mineral (calcium, phosphate and magnesium) and endocrine glands (calcitonin cells and parathyroid gland) of Wistar rat after chlorpyrifos administration. Microscopy Res Tech. 76(7): 673-678.

Yamanobe Y, Noriyuki N, Takehisa M, Takaaki I, Kanako NK, Momoko C, Kazuhito Y and Toshihiro T. (2015) Sex differences in shotgun proteome analyses for chronic oral intake of cadmium in mice . PLoS One 10(3): e0121819.