Biochemical profiling of metabolomics in heavy metal-intoxicated impaired metabolism

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Abstract (300 word limit)

Lead (Pb) being a heavy metal is a common toxicant present in the environment. Yet only a limited number of studies are available describing the effect of Pb on metabolomics. This study aimed to investigate the toxic effects induced by Pb, through biochemical profiling. The levels of antioxidant enzymes such as GPx, SOD, MDA, and CAT were detected in the liver tissue homogenates. The effect of Pb on lipid and amino acid metabolism was also determined in serum and plasma of experimental mice by MS/MS and AAA respectively. The alteration in the gene expression of CPT I, CPT II, LCAT, CROT, CACT, and MTR under the influence of Pb was also determined by qRT-PCR. The effect of Pb on hepatic morphological changes was also analyzed by histopathology. To investigate these parameters 25 male Wister albino mice were taken and randomly divided into five groups. Group 1 was the control group that received normal saline, group 2 was the diseased Pb group that received PbAc (120 mg/kg) after dissolving in water, and group 3 was the treated group (Pb + Q-CRN) that received Que (50 mg/kg) blended in corn oil as a treatment against Pb toxicity, group 4 was Q-CRN group that received Que blended in corn oil to investigate the effect of Que alone on metabolomics, group 5 was CRN group that received corn oil only to investigate any interference in the biochemical profiling due to the administration of corn oil. After 4 weeks of study, it was concluded that Pb caused impairment in the metabolism of amino acid metabolism by significantly increasing the level of serine, threonine, and asparagine and decreasing the level of valine, lysine, and glutamine amino acids in mice plasma. However, the administration of Que significantly restored the level of free amino acids. The lipid metabolites, L-carnitine, sphinganine, phytosphingosine, and lysophosphatidylcholine belonging to the fatty acid ß-oxidation, sphingolipid metabolism, and lysolipid metabolism sub-pathway of lipid metabolism were also qualified in mice serum. The scanning mass range was selected between 50-2000 m/z because the selected lipid metabolites had the molecular weight within this range. The significant decline in the GPx, SOD, GSH, and CAT level and elevation in the MDA level in the Pb intoxicated mice group confirmed the Pb induced oxidative stress and lipid peroxidation as compared to the CON group. The antioxidant effect of Que was elucidated in Pb + Q-CRN group. Pb exposed group showed significant upregulation in the expression of CPT I, CPT II, LCAT, CROT, CACT, and MTR genes in liver tissue homogenates. The administration of Que significantly improved the mRNA expression of these genes. Histology of the liver evaluated the morphological changes in the Pb group. Hence the findings of this study proved that Pb exposure caused weight gain, oxidative stress, upregulation in gene expression, and impairment in lipid and amino acid metabolism in mice.

Recent Publications (minimum 5)

1. **AKASH MSH***, Sumbal R, Rehman K, Ibrahim M, Imran M, Assiri MA. Biochemical Activation and Regulatory Functions of Trans-Regulatory KLF14 and Its Association with Genetic Polymorphisms. ***Metabolites***. 2023, 13(2): 199. https://doi.org/10.3390/metabo13020199. (**IF= 5.581, *Corresponding author**).
2. Yaqoob A, Rehman K, **AKASH MSH***, Akash MSH, Alvi M, Shoaib SM. Biochemical profiling of metabolomics in heavy metal-intoxicated impaired metabolism and its amelioration using plant-based bioactive compound. ***Front Mol Biosci***. 2022; 9:1029729. https://doi.org/10.3389/fmolb.2022.1029729. (**IF= 6.113, *Corresponding author**).
3. Alvi M, Rehman K, **AKASH MSH***, Akash MSH, Yaqoob A, Shoaib SM. Determination of metabolomics profiling in BPA-induced impaired metabolism. ***Pharmaceutics***. 2022: 14(11): 2496. https://doi.org/10.3390/pharmaceutics14112496. (**IF= 6.525, *Corresponding author**).
4. Shahid M, Rehman K, **AKASH MSH***, Suhail S, Kamal S, Imran M, Assiri MA. Genetic Polymorphism in Angiotensinogen and Its Association with Cardiometabolic Diseases. ***Metabolites***. 2022; 12(12):1291. https://doi.org/10.3390/metabo12121291. (**IF= 5.581, *Corresponding author**).
5. Qader A, Rehman K, **AKASH MSH***. Biochemical profiling of lead-intoxicated impaired lipid metabolism and its amelioration using plant based bioactive compound. ***Environ Sci Pollut Res***. 2022; 29(40):60414-60425. https://doi.org/10.1007/s11356-022-20069-5. (**IF= 5.19, *Corresponding author**).



Biography (150 word limit)

Dr. Muhammad Sajid Hamid Akash is currently working as associate professor at Department of Pharmaceutical Chemistry, Government College University Faisalabad (GCUF), Pakistan. Currently, he is focusing on investigating the effect of environmental contaminants (ECs) on various molecular and metabolic pathways that are involved in cardiometabolic disorders and their treatment strategies. His Research work is the cutting edge and worthy of extension in developing countries like Pakistan, where it can be most beneficial and cost-effective especially for diabetic patients. He has published 180 research articles in peer-reviewed journals, 60 book chapters in Springer, Elsevier, CRC Press, Wiley and 6 books (2 books with Elsevier and 4 books with Springer). Besides this, he is also serving as Associate Editor in Cellular Biochemistry (sections of Frontiers in Molecular Biosciences, Frontiers in Chemistry and Frontiers in Cell and Developmental Biology) and Academic Editor in Biochemical genetics, BMC Endocrine Disorders and PLOS ONE, Section Editor in Endocrine, Metabolic & Immune Disorders - Drug Targets, Review Editor in Frontiers in Endocrinology - Diabetes: Molecular Mechanisms. Moreover, Dr. Akash has also edited three special issues as Guest Editor in Metabolites, Frontiers in Toxicology and BIOCELL journals. Additionally, Dr. Akash has also voluntarily served as a reviewer in more than 100 peer-reviewed journals. Dr. Akash has been awarded PAS Gold Medal in Health Sciences from Pakistan Academy of Sciences, PROF AR Shakoor Gold Medal in Biological Sciences from Zoological Society of Pakistan and Productive Scientist of Pakistan from Pakistan Council for Science and Technology.

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