Acta Scientific CANCER BIOLOGY (ISSN: 2582-4473)

Volume 6 Issue 3 March 2022

Research Article

Study of Oxidative Stress Effect in Pathophysiology of Cancer Induced by Lead Toxicity

Derouiche Samir[1,2]*, Kenioua Achouak[1], Benaoun Khadidja[1]

[1]*Department of Cellular and Molecular Biology, Faculty of Natural Sciences and Life, University of El Oued, Algeria*

[2]*Laboratory of Biodiversity and Application of Biotechnology in the Agricultural Field, University of El Oued, Algeria*

***Corresponding Author:** Derouiche Samir, Department of Cellular and Molecular Biology, Faculty of Natural Sciences and Life, University of El Oued, Algeria.

Received: February 28, 2022

Published: March 24, 2022

Abstract

Introduction: Lead is a chemical element that exists in nature. It is recognized as one of the most toxic and harmful heavy metals, even in low quantities.

Objective: This review focuses on the effect of oxidative stress in the developement of cancer by lead.

Methods: The data were collected by searching Science Direct, Google Scholar, PubMed, Scopus, Springer and National Center for Biotechnology Information (NCBI). The Keywords used as search terms were "Lead", "Acute and Chronic toxicity", "lead and Oxidative stress" and "free radical induced cancer".

Results: Lead is a genotoxic agent causes genotoxicity by oxidative stress in exposed cells, tissues and organs. Lead is also reported to cause impairment in DNA synthesis process and cause chromosomal aberrations and destabilization of DNA. Many of lead genotoxic effects in mammal cells are mediated by ROS and/or the lipids soluble by products of oxidative stress. In a cellular system, it has been demonstrated that singlet oxygen is the major species participating in the induction of DNA strand breakage which promotes genetic damage and cancer disease.

Conclusion: Lead toxicity can be determined by the oxidative stress status of the cells which can be the main cause of the development of cancer related to the complications of acute and chronic toxicity by lead.

Keywords: Lead; Oxidative Stress; Cancer; Toxicity

Introduction

Lead is a chemical element that exists in nature [1], It is included in heavy metals designates for chemists high atomic number metals [2], it has the atomic number is 82 [3] (Bozdağ., *et al*. 2019), It is recognized as one of the most toxic and harmful heavy metals, even in low quantities [4] and is an environmental pollutant [5]. It is a widely used metal since the ancient period, and it is used in many industrial applications [6]. Lead is a multi-target toxicant, capable of causing different alterations during exposure, its persistence in the body thus presents a great risk for human health. Lead is a naturally occurring heavy metal [7] nonessential, inorganic and is primarily absorbed by the respiratory system and the digestive tract extremely toxic, widely distributed in the environment and exposure to this element is still a major public health problem [8]. It can accumulate in the body and disrupt the body, especially the system nervous system, blood, gastrointestinal tract, cardiovascular system and kidneys [9]. This toxicity is explained by the formation of reactive oxygen species (ROS) which causes an imbalance between the pro-oxidant and antioxidant

systems [10]. This imbalance potentially leads to structural damage and functional at the level of the organism. All of this translates that the lead toxicity causes oxidative stress [11]. Cells under oxidative stress exhibit various dysfunctions due to damage have various dysfunctions due to damage caused by ROS to lipids, proteins and DNA. the toxicity associated with this metal could be due to oxidative tissue damage [12]. There may be an independent source of oxidative damage related to the direct effect of lead on membrane lipids. Considering that lead toxicity is currently one of the world's serious problem, there is still no specific, reliable and safe treatment [13]. In light of these data, the aim of this review was to identify the role of oxidative stress as factors associated with acute and chronic toxicity of lead.

Methods

The data were collected by searching Science Direct, Google Scholar, PubMed, Scopus, Springer and National Center for Biotechnology Information (NCBI). The Keywords used as search terms were "lead", "Acute and Chronic toxicity", "lead induced inflammatory reaction", "lead and Oxidative stress" and "free radical induced cancer".

Physico-chemical properties of lead

Lead has atomic number Z = 82 [14], and the atomic mass is 207.21g, for its melting point is 327°C and their boiling point is 1720°C [15], it is a dense metal (d = 11.34 at 20°C) and its specific heat capacity at 20°C is 0.125J/g, and presented by resistivity is 20.65 μΩ/cm [16].

Metabolism of lead

Absorption

The lead mainly enters the body through three routes through the digestive and pulmonary routes and also through the skin. Digestive route is the main route of contamination (intoxication plomb Sites). It can be direct by ingestion of food (contaminated water or food) or by contact of soiled hands with the mouth [17]. The percentage of lead resorbed by the digestive route is 10% in adults; it is 50% in young children, diets enriched with these minerals decrease its absorption, and the iron deficit is associated with a greater absorption for lead and diets low in protein or high in fat which support increased lead absorption [18]. The respiratory tract is the second possible route of contamination lead vapors, oxides or pulverulent salts, very fine dust or fumes or lead dust found in the air [19], it is also to blame for the lead fixed on the particles suspended in the air: only the very fine particles can penetrate into the pulmonary alveoli, the larger ones are rejected, or raised by the mucociliary carpet and swallowed (then borrowing the digestive tract). Lead can also enter the body following skin lesions on the other hand The transcutaneous passage of inorganic lead derivatives is very low compared to organic lead (liposolubility) [20].

Distribution

Blood lead represents only 1 to 2% of the quantity present in the body, the half-life of lead in the blood can be as short as 20-40 days, for distribution Lead absorbed by the digestive tract passes into the bloodstream [21] where it is distributed between red blood cells (90%) and plasma (less than 10%) probably due to its affinity for thiol groups [22] therefore the compartment with very rapid exchanges: plasma proteins, and the second compartment with rapid exchanges: soft tissues (kidneys, brain, spleen, liver, bone marrow, but also red blood cells, etc.) The last compartment with intermediate exchanges: muscles, trabecular bone [23].

Elimination

Lead excretion is mainly urinary (> 75%) and it not absorbed by the gastrointestinal tract is eliminated by faeces faecal (15-20%) [24]. Lead can also be eliminated through saliva, sweat, hair and nails. Negligible under normal conditions, exposure to heat can lead to sweat excretion in humans greater than urinary elimination [25], elimination life is greatly increased in the event of renal failure. Lead is found in the urine from the daily ingestion of at least 1 mg of dd lead acetate, essentially in free ionized form when blood lead levels are within normal limits [26].

Toxic effects of lead on human health

Occur by inhalation or absorption in accidental situations. These effects generally appear for blood lead levels of between 1000 and 2000 μg/l, but can occur in certain subjects at much lower levels of between 400 and 600 μg/l, [27] in children for intoxications leading to blood lead levels that can vary from 900 to 8000 μg/l, Their symptoms are Digestive disorders are among the earliest symptoms. They result in the appearance of severe colic associated with abdominal pain and cramps [28]; Anorexia from vomiting in intermittent phases; Renal failure the appearance of

tubular lesions characterized by oliguria, albuminuria, glycosuria and hyperphosphaturia [29]; Lesions to the central nervous system (headache, agitation, delirium, hallucinations) are clinically manifested by convulsive encephalopathy and coma which can lead to death; Severe neurological or psychomotor (psychomotor delay, epilepsy, blindness and hemiparesis); Effects on hepatic metabolism [30]. The two routes of exposure to lead by ingestion, and inhalation for symptoms of poisoning are Neurological effects; The first signs of central neurological damage are headache, asthenia, sleep disturbances (insomnia, nightmares), difficulty concentrating, irritability, decreased libido and depressive thoughts; encephalopathy and cardiovascular effects; peripheral neuropathy and abdominal syndrome; renal and hepatic effects; haematological effects, carcinogenicity, Signs of impregnation; metabolic and endocrine effects and effect on reproduction [31].

Discussion and Conclusion

Stress oxidative defined as "A disturbance in the pro-oxidant and anti-oxidant balance in favor of the former, leading to potential damage" [32]. Under normal physiological condition, oxidants are removed through antioxidant defense mechanism. If incompletely cleared by antioxidants, oxidants will cause accumulation of ROS. In efficiency and insufficiency of antioxidant defense system are concerned in some pathological conditions induced by ROS [33]. ROS has been implicated in a wide array of diseases such as neurodegenerative disorders, autoimmune diseases, complex life style diseases and cancer. DNA is the memory of the entire bio-chemical composition of living beings, it is a molecule that is very susceptible to attack by oxygen radicals [34]. ROS can create various types of DNA damage; modification of all bases, deletions, frame shifts, strand breaks, DNA-protein cross-links, and deoxyribose backbone and chromosomal rearrangements. •OH and ONOO– in particular can react with all components of DNA and form several new compounds [35]. One of these will generate 8-hydroxydeoxyguanosine (8-OHdG), which has been implicated in carcinogenesis and is considered a reliable marker for oxidative DNA damage [36]. Since Lead is a non-essential element for the life of eukaryotic cells, the mechanisms responsible for lead toxicity are multiple and potentially affect all the cells of the body. To this end, we were interested in the oxidative stress generated by lead at the level of different organs (hematopoietic system, liver, kidney and brain) [37], the free ionized state that lead exerts its toxic effects in the cell according to several mechanisms: interaction with many proteins through their thiol groups and inhibition of the initiation of protein synthesis at the ribosome level; direct or indirect oxidative effect through the accumulation of heme precursors, disruption of calcium homeostasis and interference on many cytoplasmic or membrane cell processes mediated by calcium [38]. Lead is a genotoxic agent causes genotoxicity by oxidative stress in exposed cells, tissues and organs. Beside this, lead is also reported to cause impairment in DNA synthesis process and cause chromosomal aberrations [39] and destabilization of DNA, abnormal base pairing, formation of micronuclei, chromosome aberration, and sister chromatid exchanges [40]. Many of lead genotoxic effects in mammal cells are mediated by ROS and/or the lipids soluble byproducts of oxidative stress such as MDA [41]. In a cellular system, it has been demonstrated that singlet oxygen is the major species participating in the induction of DNA strand breakage and 8-hydroxydeoxyguanosine adduct induced by lead [42]. In addition, OH^{*} is considered to be the ultimate reactive oxygen species which interacts with DNA and promotes genetic damage. The OH radical attacks DNA on the sugar residue and induces DNA fragmentations, base loss and strand breaks with a terminal sugar residue fragment [43]. In conclusion, Lead toxicity can be related by oxidative stress of cells, which can be the main cause of the development of acute and chronic toxicity, and the most dangerous of them remains related to the emergence of cancer, and therefore it is necessary to take into account these phenomena in any approved treatment program, which may contribute to the prevention lead exposure.

Authors' Contribution

KA participated in search and analysis of the paper. SD is the corresponding author. KA, BK and SD conducted the final edit and finalized the manuscript. All authors read and signed the final paper.

Conflicts of Interest

The authors declare that they have no competing interests.

Ethical Issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Funding/Support

None.

Bibliography

1. Derouiche S and Zeghib K. "Evaluation of the Chelating Efficacy of Aquilaria malaccensis and Aristolochia longa Against Biochemical Alterations Induced by Lead Bioaccumulation in Rats". *Pharmaceutical and Biosciences Journal* 7.2 (2019): 11-15.

2. Tchounwou PB., *et al*. "Heavy metal toxicity and the environment". *EXS* 101 (2012): 133-164.

3. Assi MA., *et al*. "The detrimental effects of lead on human and animal health". *Veterinary World* 9.6 (2016): 660-671.

4. Djouadi A and Derouiche S. "Study of fluoride-induced haematological alterations and liver oxidative stress in rats". *World Journal Pharmacy and Pharmaceutical Science* 6.5 (2017): 211-221.

5. Derouiche S., *et al*. "Heavy metals, Oxidative stress and Inflammation in Pathophysiology of Chronic Kidney disease - A Review". *Asian Journal of Pharmacy and Technology* 10.3 (2020): 202-206.

6. Sachdeva C., *et al*. "Lead: Tiny but Mighty Poison". *Indian Journal of Clinical Biochemistry* 33.2 (2018): 132-146.

7. Kumar A., *et al*. "Lead Toxicity: Health Hazards, Influence on Food Chain, and Sustainable Remediation Approaches". *International Journal of Environmental Research and Public Health* 17.7 (2020): 2179.

8. Genchi G., *et al*. "Nickel: Human Health and Environmental Toxicology". *International Journal of Environmental Research and Public Health* 17.3 (2020): 679.

9. Derouiche S., *et al*. "Epidemiological study and role of zinc and lead on breast cancer in el oued (algerian) population". *Advances in Bioresearch* 11.1 (2020): 123-130.

10. Pizzino G., *et al*. "Oxidative Stress: Harms and Benefits for Human Health". *Oxidative Medicine and Cellular Longevity* 2017 (2017): 8416763.

11. Atoussi O., *et al*. "Biological properties and Acute Toxicity Study of Copper oxide nanoparticles prepared by aqueous leaves extract of Portulaca oleracea (L)". *Asian Journal of Pharmaceutical Research* 10.2 (2020): 89-94.

12. Uttara B., *et al*. "Oxidative Stress and Neurodegenerative Diseases: A Review of Upstream and Downstream Antioxidant Therapeutic Options". *Current Neuropharmacology* 7.1 (2009): 65-74.

13. Derouiche S., *et al*. "Effectiveness of a Novel SeNPs synthetized by Aquilaria malaccensis extract compared to selenium acetate on lead induced metabolic disorder and oxidative stress in pregnant rats". *International Journal of Chemical and Biochemical Science* 19 (2021): 50-57.

14. Tafti D and Banks KP. "Nuclear Medicine Physics". In: StatPearls. Treasure Island (FL): StatPearls Publishing (2022).

15. Sposito G., *et al*. "Trace metal chemistry in arid-zone field soils amended with sewage sludge: I. Fractionation of Ni, Cu, Zn, Cd and Pb in solid phases". *Soil Science Society of America Journal* 46 (1982): 260-264.

16. Chantal B. "Toxicologie Clinique". Ed. Flammarion Médecine Science. Paris (2002): 638.

17. Kaminsk YP., *et al*. "Physiopathologie de I'intoxication par le plomb inorganique; MISE AU POINT". *RevMed Interne* 14 (1993): 163-170.

18. Derouiche S., *et al*. "Protective effects of Aristolochia longa and Aquilaria malaccensis against lead-induced oxidative stress in rat cerebrum". *Asian Journal of Research in Pharmaceutical Sciences* 9.1 (2019): 57-63.

19. Lauwerys R. "Toxicologie industrielle et intoxication professionnelles". 3éme Ed. Masson. Paris (1992): 123-131.

20. Alexander J., *et al*. "Scientific Opinion on Lead in Food". *European Food Safety Authority (EFSA), European Food Safety Authority Journal* 8.4 (2013): 1-151.

21. Wani AL., *et al*. "Lead toxicity: a review". *Interdisciplinary Toxicology* 8.2 (2015): 55-64.

22. Ajsuvakova OP., *et al*. "Sulfhydryl groups as targets of mercury toxicity". *Coordination Chemistry Reviews* 417 (2020): 213343.

23. Derouiche S., *et al*. "Triazinone herbicide metribuzin induced acute liver injury: A study of animal model". *Journal of Acute Disease* 7.4 (2018): 152-157.

24. Garnier R. "Toxicité du plomb et de ses dérivés". *EMC - Toxicologie-Pathologie* 2.2 (2005): 67–88.

25. Piechalak A., *et al*. "Lead uptake, toxicity and accumulation in Phaseolus vulgaris". *Biologia Plantarum* 52.3 (2008): 565-568.

26. Satarug S., *et al*. "Cadmium and Lead Exposure, Nephrotoxicity, and Mortality". *Toxics* 8.4 (2020): 86.

27. Charkiewicz AE and Backstrand JR. "Lead Toxicity and Pollution in Poland". *International Journal of Environmental Research and Public Health* 17.12 (2020): 4385.

28. Jouhadi Z., *et al*. "Lead poisoning in children: a case report". *Pan African Medical Journal* 24 (2016): 316.

29. Bennett WM. "Lead nephropathy". *Kidney Intern* 28 (1985): 212-220.

30. Swarup D and Maitis K. "Changes in some biochimical constituents in blood and cerebrospinal fluid of lead intoxicated calves". *Indian journal of Animal Sciences* 61.9 (1991): 942-945.

31. Abdel-Bakky MS., *et al*. "Mental depression: Relation to different disease status, newer treatments and its association with COVID-19 pandemic (Review)". *Molecular Medicine Reports* 24.6 (2021): 839.

32. Alfonso V B., *et al*. "Natural antioxidants in functional foods: from food safety to health benefits". *Grasas y Aceites* 54.3 (2001): 295-303.

33. Sarawoot P and Phanit K. "Oxidative Stress-Associated Pathology: A Review (Patologi berkaitan Tekanan Oksidatif: Suatu Kajian)". *Sains Malaysiana* 44.10 (2015): 1441-1451.

34. Shilpa B and Rima D. "Oxidative stress: Major executioner in disease pathology, role in sperm DNA damage and preventive strategies". *Frontiers in Bioscience* 9 (2017): 420-447.

35. Derouiche S., *et al*. "The Study of Socioeconomic and Clinic Risk Factors of Breast Cancer in Algerian Women Population". *Frontiers in Biomedical Technologies* 5.3-4 (2018): 51-57.

36. Saroj SG., *et al*. "Free Radicals and Antioxidants in Human Health: Current Status and Future Prospects". *Journal of the Association of Physicians of India* 52 (2004): 794-804.

37. Flora G., *et al*. "Toxicity of lead: A review with recent updates". *Interdisciplinary Toxicology* 5.2 (2012): 47-58.

38. Chetehouna S., *et al*. "Biological Activity and Toxicological Profile of Zinc Oxide Nanoparticles Synthesized by Portulaca oleracea (L) Leaves Extract". *Advances in Nanomedicine and Nanotechnology Research* 2.2 (2020): 125-133.

39. Aftab A., *et al*. "Cytotoxic and Genotoxic Effect of Arsenic and Lead on Rat Mesenchymal Stem Cells (rMSCs)". *Pakistan Journal of Zoology* 47.1 (2015): 41-47.

40. Clement GY., *et al*. "DNA Damage, Cell Cycle Arrest, and Apoptosis Induction Caused by Lead in Human Leukemia Cells". *International Journal of Environmental Research and Public Health* 13.1 (2015): 56.

41. Bertrand P., *et al*. "Lead-induced DNA damage in Vicia faba root cells: Potential involvement of oxidative stress". *Mutation Research - Genetic Toxicology and Environmental Mutagenesis* 726.2 (2011): 123-128.

42. Jia-Ling Y., *et al*. "Singlet Oxygen Is the Major Species Participating in the Induction of DNA Strand Breakage and 8-Hydroxydeoxyguanosine Adduct by Lead Acetate". *Environmental and Molecular Mutagenesis* 33.3 (1999): 194-201.

43. Derouiche S. "Current Review on Herbal Pharmaceutical improve immune responses against COVID-19 infection". *Research Journal of Pharmaceutical Dosage Forms and Technology* 12.3 (2020): 181-184.