

## Review

# The Effect Of Micronutrients on Lead (Pb) Toxicity

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## Abstract

There is increasing data that micronutrient ingestion has a noteworthy consequence on the harmfulness as well as oncogenesis initiated by numerous elements. This review scrutinizes the influence of micronutrient eminence on the harmfulness of unnecessary metals like lead. Regrettably, insufficient research has rightly inspected the consequence of dietary insufficiency or else supplementation on metal harmfulness. More usually, the consequence of nutritional variation should be gathered or derived by the outcomes of research done to recognize physiology or how a cell responds, or pathogenesis of a condition, interface or interaction taking place in living cells. We have selected three groups to distinguish the consequence of nutritional status on heavy metals: interface among essential micronutrients as well as lethal elements in the course of ingestion, attachment, as well as elimination; the impact of trace elements on the breakdown as well as absorption of heavy elements; and the influence of trace elements on additional harmful results of heavy elements. Based on evidence derived by mechanistic clinical trials, the capacity of trace elements to modify heavy elements' harmfulness is assured. Trace elements work together among heavy elements at numerous parts in the body: intake as well as the elimination of heavy elements; the passage of elements in the body; the attachment to marked proteins; breakdown as well as isolation of heavy elements; lastly, during additional outcomes of toxicity like free radical formation. As a result, subjects consuming a food deficient of trace elements will be susceptible to injury from heavy elements like Lead (Pb).

**Keywords:** Lead, Micronutrients, Metal Toxicity.

## Introduction

Studies on the influence of trace elements on harmfulness as well as oncogenesis initiated by numerous elements ensured to create increasing proof in the role of micronutrient consumption as well as decline in ill effects of heavy metals. It is ensured that we have gone through the collected works concerning this matter; conversely, limited work rightly inspected the influence of nutritional insufficiency on heavy element poisoning. Generally, the influence of nutritional concentration should be gathered from the outcomes of research done to recognize physiology or how cell re-

sponds, or pathogenesis of a condition, or interface or interaction taking place in living cells.

The present review scrutinizes the influence of micronutrients on the harmfulness of a heavy element like lead. The interactions of trace elements are divided into three sections. The first category considers the interaction among important trace elements as well as a heavy element like Pb in the process of intake, attachment, as well as elimination. The second category considers the interaction of trace elements during the breakdown and absorption of heavy elements like lead. The last category deals with the role of trace elements in decreasing the adverse effects of heavy metals in the human body.



Micronutrients are capable of modifying the lethal effects of elements by binding on the heavy element at its central spot of action. Cases of such kind of interference consist of the interaction of calcium with Pb. In such conditions, the heavy metals apply their impact by restricting the action of the trace elements. This concludes that improving the vital trace elements' accessibility must reduce the adverse effects of heavy elements. Increased lead content is taken up by subjects consuming calcium-deficient food compared to people that consume calcium-rich food.

Therefore, trace elements play an essential role in reducing adverse effects like an increased release of free radicals caused by heavy element accumulation.

### Influence of Micronutrients on Lead Toxicity

Pb produces several unfavorable health conditions, causing damage to the nervous and blood-forming cells, kidney, thyroid regulation, as well as bone tissues, the nervous system being the mainly affected organ. Currently, damage and delayed intellectual, mental and communication skills in babies and young children are the most adverse influences that are of utmost interest. The adverse effect, which is influenced by exposure duration and determined by Pb dosage, is initiated after ingestion from different environmental sources, such as air, food, and water. On the other hand, banning Pb-containing fuels in developed countries and the exclusion of Pb-components in food containers, significantly showed a decline in the amount of toxicity from these products. Pb present in dyes painted on buildings constructed previously in the 19th century in different cities was the main cause of Pb ingestion among the school-going age group. These young people from a low-income background and suffering from calcium and iron deficiency show increased signs of Pb toxicity [1]. Adverse effects of Pb and its damage to the nervous system happen at a serum Pb value in the range of 0.48 and 0.72 pmol/l; besides, more than one million children in America have a blood Pb level in this range or even a little higher [2]. Among the subjects aged above 18 years, bone disorders are reported as well [3]. Conditions like pregnancy, breastfeeding, and old age increase the incidence of nervous system disorders due to Pb intoxication [4].

Calcium tablets, grape juice, glass containers and glazed pots can contain Pb and are considered causes of Pb contact [5]. Ceramics traded worldwide can release

vast quantities of Pb into consumable items [6]. Pb pollution of these containers is an essential health-associated issue among the Mexican community [7]. A remarkable rise in the serum Pb level was traced among children belonging to the Mexican community who consumed food items stored in Pb-containing containers [8].

### Lead-Calcium Interactions

The wide range of *in vivo*, *in vitro*, and clinical trial reports signifies the importance of the Pb-calcium interaction [9] that takes place by modifying the expression of nucleic acids and proteins present within the living cell which occurs due to the capability of Pb to represent or replace calcium during metabolic processes. Reports show evidence that Pb prevents the discharge of neurotransmitters by inhibiting the transport of calcium to the peripheral nerves [10], by competing with calcium ions during the process of movement through calcium canals [11], restricting calcium ion transport by additional calcium canals [12]. It is known that Pb prevents calcium movement through the cells by interacting with the  $\text{Ca}^{2+}/\text{Na}^{+}$  adenosine triphosphate (ATP) pumps. This process of interdependence might probably explain in what way Pb interferes with calcium in the digestive system [13].

The further significant interaction among Pb and calcium occurs inside the cells, where Pb obstructs the calcium attachment to a specific protein having the property of a signaling molecule intracellularly [14]. This interaction creates a fight between Pb and calcium for calcium specific proteins like calmodulin and protein kinase C (PKC). Pb works by replacing the calcium combined with calmodulin and disturbing the released amount of calcium within the nerve ends, which causes activation of neurotransmitter discharge [15]. Pb exhibits an enhanced capability to trigger protein kinase C, thus initiating an upsurge in its action. This can cause an increase in cell multiplication, differentiation and increased cellular activity to PKC such as cell-cell interaction, cytoskeletal structure, as well as the discharge of neurotransmitters [16]. Currently, it is illustrated that Pb modifies inositol polyphosphate specific protein attachment in the rat brain, probably causing alterations in the concentration of calcium within the cell and thus impacting neuronal action [17]. Considering these interactions, it is recommended that Pb should be interrupted promptly since an imbalance in calcium levels within the growing brain cells might impede healthy growth [18].

## Calcium Interferes with Lead Concentration.

Gastrointestinal Pb ingestion and retention represent the essential Pb consumption pathway [9], and it is influenced by the micronutrient level of the gastrointestinal lining. Grown-ups retain about 10% of consumed Pb, but young individuals retain about 50% of the consumed Pb. This variance might be the outcome of a higher concentration of intestinal carriage receptors throughout increased growth [19].

Consumed Pb is released into blood deposits, skeletal tissues, and soft tissues, also the liver, through which it is expelled [20]. Longitudinal research shows that Pb is not excreted at a similar frequency as it is taken up by the body [21]. Pb, which is also excreted in urine and feces, continually collects in the body muscles with age [22].

Nutritional matters are believed to play a significant part in Pb retention in the body. Higher amounts of Pb are traced in the blood of subjects consuming food with little calcium concentration; it also results in an upsurge of intestinal uptake and a rise in Pb concentration [23].

Calcium and Pb get attracted to the same attachment spots on intestinal mucosal proteins, which are most required in the process of uptake [24]. These common attachment spots on receptors likely enlighten us why enough calcium in food reduces lead intake. Research by Six and Goyer [25] has reported that rodents subjected to a low calcium diet and variable quantities of Pb had a higher blood level and tissue concentrations of Pb than rats that ingested a diet with an average level of calcium. This report explains that a shortage in the calcium component from food upsurges the Pb level in vital organs [26].

Additional work has also reported that the ingestion of Pb by the gastrointestinal tract is negatively interrelated to the calcium level in food [27]. An investigation on expecting women of the Mexican population observed that consuming food served on Pb-glazed ceramics was related to increased serum Pb concentrations; also, ingestion of foods high in calcium reduced serum Pb concentration in female subjects with a low income. This reduction was not noteworthy, but the intake of milk substances reduced serum Pb concentrations significantly among females having a high income [28].

Reports on the relation between calcium-fortified food and Pb intoxication show that a small reduc-

tion in Pb uptake can decline the blood Pb level; however, these results were not that significant considering the effect of calcium deficiency on Pb intake as well as its absorption. Hence, maintaining normal calcium levels instead of the consumption of calcium-fortified food is considered beneficial in fighting Pb toxicity [27].

## Lead and Bone Metabolism

The majority of the deposition of Pb is in the bones. Thus, bone remodeling proves to be a significant part of the uptake and excretion of Pb from the human system [29]. Reports on the impact of calcium, phosphorous, as well as vitamin D on the absorption of Pb by bone, are extensive [30]. Literature states that breastfeeding mothers of the Mexican population using a ceramic container with Pb that also consume low calcium-rich food had a high level of Pb in the hard tissues [31]. Animal studies have demonstrated that food with a small amount of phosphorous had raised Pb levels and foods having low calcium and phosphorous components lead to increased Pb concentrations [31]. Thus, these reports suggest that calcium and phosphorous rich food could have a beneficiary inhibitory consequence on the intake and collection of Pb [32].

Vitamin D does not merely increase the absorption of calcium but also phosphate, stimulates the absorption of additional essential elements like magnesium, iron, and zinc, and also the absorption of heavy elements like Pb [33]. The significant influence of vitamin D associated with enhanced absorption of Pb by the digestive system is prompted by calcium-combined enzymes by intestinal tissues [34]. Reports also determine that the unique lead interaction on such calcium-combined proteins will definitely result in vitamin D increase of Pb absorption in addition to deposition in the renal tissues and bone [35]. Likewise, while calcium levels are very low, the blood level of vitamin D, 1,25-dihydroxy-vitamin D, is elevated to raise the absorption of calcium and production of calbindin-D, a calcium attached protein [35]. Therefore, a further process of lead absorption can happen in the situation of calcium insufficiency [35]. After depositing in the bone, Pb will be released because of bone remodeling during bone fractures or arthritis. The release of a long-standing Pb collection via hard tissues of an expecting mother is a major cause in stimulating Pb via placental transfer [31].

Investigations in rodents describe that Pb deposited in hard tissues as a result of previous exposure in expecting women should be quantified as an essential basis for self ingestion and milk contamination among lactating mothers [36]. A study in the Swedish population exhibited a drop in serum calcium level and an increase in blood Pb concentration in lactating women, mostly because of the discharge of Pb through the bone [37]. After reaching menopause, a noteworthy release of calcium by the bones and also estrogen reduces the discharge of the existing Pb from the cell into blood [38].

### Lead-Iron Interactions

Iron insufficiency and a shortage of iron intake in the phase of development among young animals causes increased Pb ingestion and concentration. Hence, it is alarming to report that young individuals and expecting women are more prone to Pb consumption from the diet [39]. Conversely, contrasting to calcium insufficiency, iron insufficiency in animals does not seem to lead in the relocation of Pb into soft tissues [39]; it merely disturbs the movement of Pb through the digestive system [40]. An inverse association among the iron level in food and serum Pb concentration was mentioned in a clinical investigation conducted on children younger than 5 years old [41]. Awareness of iron-related malnutrition existing among young children is well known, but the damage to the perceptive and mental development among such individuals is more noteworthy [42]. However, it is not well known why the lack of iron supply leads to adverse effects on young people's communication skills. The effects of Pb and iron on the heme biosynthetic pathways have been extensively investigated and characterized. Heme production is a biochemical process that involves numerous stages, biological catalysts, and enzymes. A shortage in an enzyme or biological catalysts advances to a build-up of by-products of heme synthesis in the human system. Pb inhibits such biological catalysts during this important biochemical reaction, and a significant amount of delta-aminolevulinic acid dehydratase (ALAD), a biological catalyst, remains concentrated in the body. In addition, Pb interferes with mitochondria during the production of ATP, the energy currency of the cells; ATP is required for the breakdown of elements, prior to the attachment of iron into the

porphyrin ring [43]. When iron insufficiency is present, ferrochelatase is more prone to such consequences of lead [43], and this causes a reduction in the production of blood cellular components. Thus, iron-rich food can prevent such injury occurring on blood cellular components caused by Pb. Additional studies demonstrate the capacity of metallothionein to attenuate the Pb-induced inhibition of 6-ALAD [44].

### Additional Nutrients that Interfere with Lead

Some additional nutritive constituents influence Pb's concentration; elements such as calcium, iron, and vitamin D provide assurance in reducing the lethal effect of Pb, especially in young kids. The important interaction among Pb and trace elements, besides additional food components, are abridged [45]. Miller et al. exhibited a broad assessment of interactions between Pb and trace elements and performed supplementary and new investigations [46]. Foods rich in nutritional components show a reduction in the intake of lead through the digestive tract [47]. Zinc affects the concentration of lead at the cellular level and decreases Pb toxicity chances because delta-aminolevulinic acid dehydratase is suppressed by Pb [48]. Research proves a negative correlation between zinc and lead concentration, demonstrating that zinc interacts and inhibits Pb absorption in the digestive system [49]. Also, Flora et al. [49] clarified that synchronized intake of zinc and a Pb chelator, calcium disodium EDTA, leads to increased chelation of Pb. Animal studies have reported selenium's defensive action on the damage caused to the central nervous system due to Pb intoxication. Selenium was proved to have a defensive action against Pb to prevent neurotransmission from succinic dehydrogenase, acetylcholine esterase, and the sodium/potassium ATPase in animals [50]. A study reported that adding selenium during deactivation of lead in animals plays a beneficial role in the deactivation of lead saturation, which is possible because lead-deactivator 6-ALAD is produced by selenium [51]. Widespread studies support the beneficial role of trace elements in reducing the lethal effects of Pb, especially in more susceptible subjects. When Pb toxicity is important, nutritive aspects do not stop Pb saturation. Children are highly susceptible even to small amounts of Pb, showing growth anomalies. Thus, the significance and role of trace elements in the protection against the lethal effects of Pb are more prominent

among young individuals and subjects prone to Pb intoxication [45].

## Conclusions

Few studies report the influence of the micronutrient status lethal effects of heavy elements. Depending on the reports from research done to recognize the physiology or how a cell responds, or pathogenesis of a condition, or interaction taking place in living cells, the capacity of trace elements to reduce the lethal effects of heavy elements is certain. Trace elements interfere with heavy elements like Pb at several steps in the body: intake as well as the elimination of heavy elements; the movement of elements through various systems; attachment to the specific receptors; breakdown as well as the isolation of heavy elements; and a role in the reduction of free radicals formation. Thus, subjects consuming food with low nutritional values will be susceptible to injury from heavy elements like Pb. Therefore, consuming food with low nutritional value will play an essential role in the lethal effects of heavy elements and will lead to an increased threat by elements like Pb. Population studies to verify the tolerable concentration of Pb are conducted worldwide. Also, the nutritional value of food consumed varies worldwide.

Determined by the nutritional component of food, the concentration of Pb varies worldwide. Investigations considering the influence of trace elements and metal toxicity are trying to evaluate the threat from heavy metal intoxication. The interference of the trace elements with heavy elements is proved. Overlooking the influence of trace elements, the benefits on the human system should be considered. The usual therapy for lead exposure is to eliminate the providing cause. In conditions where elimination of Pb intoxication can't be avoided, nutritional values of food will be a protective means that should be practiced and recognized.

## Conflict of Interest

The authors declare no conflict of interest.

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