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Alteration of Ca/P Ratio and Hydroxyapatite Stability in Human Teeth Exposed to Lead: An In Vitro Experimental Study

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Abstract

Background: Lead (Pb) contamination in aquatic environments has been associated with increased dental health problems in exposed populations. One proposed mechanism underlying this association is the disruption of dental hydroxyapatite (HAp) stability through calcium (Ca) substitution and phosphate (P) degradation, which may alter the Ca/P ratio and mineral integrity. Therefore, this study was conducted to experimentally evaluate the impact of Pb exposure on Ca, P, and Ca/P ratio in human teeth under in vitro conditions. **Objective:** this study aimed to evaluate the effect of Pb exposure on changes in Ca, P, and Ca/P ratio, as well as the degradation kinetics of HAp in vitro. **Methods:** This true experimental study employed a completely randomized factorial design. Extracted human teeth were immersed in $PbSO_4$ solutions at concentrations of 0.01, 0.1, and 1 ppm for 30, 60, and 90 minutes. Ca and P levels were measured, and the Ca/P ratio was calculated. Degradation kinetics were analysed using linear regression to determine reaction order and rate constants. **Result:** Pb exposure resulted in a consistent reduction of the Ca/P ratio across all concentrations and exposure durations, with values below the stoichiometric hydroxyapatite ratio (1.67), indicating increased mineral instability. Both Ca and P degradation followed zero-order reaction kinetics, with higher degradation rate constants observed at 0.01 and 1 ppm. **Conclusion:** these findings provide experimental evidence that Pb exposure can destabilize dental hydroxyapatite by accelerating Ca and P degradation, thereby potentially increasing susceptibility to mineral loss.

Keywords: Calcium-Phosphate Ratio, Dental Mineral, Heavy Metal, Hydroxyapatite Lead

INTRODUCTION

Dental caries remains one of the most prevalent oral health problems worldwide, particularly in developing countries. In Indonesia, these diseases rank first out of the top 10 list of diseases (Anitasari & Rahayu, 2005; Herliwati et al., 2022). The World Health Organization (WHO) states that the incidence of dental caries in children is 60% - 90% (Kazeminia et al., 2020). In Indonesia, the prevalence of dental caries according to age group is as follows: at age three years, 60%; at age four years, 85%; and at age five years, 86.4%. This shows that the prevalence of caries in preschool children is still relatively high (Achmad et al., 2020; Ramadhany et al., 2020).

Beyond behavioural and dietary determinants, growing evidence suggests that environmental contaminants may contribute to mineral instability in hard tissues, including tooth enamel and dentin (Djinu et al., 2025). In regions where river water is used for daily activities, including oral hygiene, chronic exposure to heavy metals in aquatic systems may represent an underappreciated risk factor for dental mineral degradation (Nadia et al., 2018; Yusfarani et al., 2023).

South Kalimantan is characterized by extensive river and wetland systems that are closely connected to community life. Environmental assessments in the Barito River basin and its estuarine area have highlighted pollution pressures linked to domestic and upstream anthropogenic activities, raising concerns about metal contamination in aquatic environments that may affect exposed populations (Nusantara et al., 2025). Such context supports the importance of evaluating Pb-related mechanisms using experimental approaches that can clarify causally plausible pathways.

The mechanism of tooth decay due to heavy metals is still an interesting research topic. This is due to several facts, such as several studies in South Kalimantan revealing Pb pollution in the estuary waters of the Barito Watershed of 0.2039 mg/L (Sofarini et al., 2010). The Pb level has exceeded the threshold value set through Governor's Decree No. 4/2007, which is less than 0.1 mg/L. In addition, the results of research by Abdurrahman et al. (Santoso et al., 2022) stated that with the STORET Method, the water quality in the Barito Watershed is included in the category of heavily polluted, with the measured parameters being the heavy metals mercury (Hg), cadmium (Cd), and Pb (Santoso et al., 2024; Sudarningsih et al., 2023).

Pb can enter the body through the digestive tract, respiration, and skin. When lead enters through the digestive tract, it is distributed to various parts of the body: bones (60%), liver (25%), kidneys (4%), reticuloendothelial system (3%), intestinal wall (3%), and other tissues [12]. Previous research showed that mice exposed to 100 mg of Pb/kg body weight for 30 days can result in a 16% decrease Ca levels in their bones and teeth. This decrease occurs because Pb has a higher affinity than Ca, leading Pb to replace Ca in the bone and tooth mineral matrix, resulting in decreased Ca levels in bones and teeth (Rădulescu & Lundgren, 2019). This phenomenon is supported by research conducted by Leonas et al. (Leonas et al., 2017), which indicates that inhalation exposure to Pb nanoparticles can significantly impact the size of hydroxyapatite molecules.

From a materials and mechanistic perspective, tooth mineral is dominated by HAp, and Ca P phase in which the stoichiometric Ca/P ratio (≈1.67) is considered a hallmark of structural stability under physiological conditions (Lubojański et al., 2024). Changes in Ca/P ratio are widely interpreted as indicators of altered mineral balance and increased susceptibility to dissolution. Recent enamel-surface experimental work further supports that chemical deposition/ion interaction can measurably shift Ca/P ratio, reinforcing Ca/P as a sensitive proxy for mineral integrity (Kopp et al., 2024).

Pb is a divalent cation that can interact strongly with apatite materials, and the broader apatite literature increasingly emphasizes how ion substitution and doping can modify apatite physicochemical properties, including stability and functional behaviour (Marques et al., 2025). Importantly, recent mechanistic and characterization studies indicate that Pb uptake by Hap can proceed through pathways such as dissolution–precipitation and surface-associated processes, potentially leading to phase alteration and mineral property changes. These insights strengthen the biological plausibility that Pb exposure may destabilize dental mineral by perturbing CA–P balance. In contrast to systemic effects involving the body's circulation and metabolic pathways, this in vitro study was designed to specifically observe the direct physicochemical interactions between Pb and dental tissue. This emphasis on local exposure and mechanistic understanding aims to reassure researchers and students that the findings are based on clear, controlled interactions, free from systemic biological variability (Kong et al., 2025).

However, while many studies discuss Pb contamination and mineral interactions, direct experimental evidence in the context of human dental tissue that quantifies Ca, P, and Ca/P ratio changes under controlled Pb exposure—particularly including kinetic interpretation of mineral degradation—remains limited. Most available reports focus on adsorption/remediation performance of HAp in water treatment rather than dental mineral degradation mechanisms (El Hammari et al., 2023). Consequently, there is a clear research gap regarding how Pb exposure may alter dental HAp mineral integrity through measurable changes in Ca, P, and Ca/P ratio and whether such changes follow identifiable kinetic behaviour.

Therefore, this study aimed to experimentally investigate the impact of Pb exposure on Ca, P, and Ca/P ratio in extracted human teeth under in vitro conditions. In addition, this study evaluates the degradation kinetics of Ca and P to better describe the reaction order and rate behaviour associated with Pb-induced mineral alteration. By integrating mineral compositional change and kinetic modelling, this work provides a mechanistic framework to explain how environmental Pb exposure may compromise dental HAp stability.

MATERIALS AND METHODS

Study Design

This study was a true experimental laboratory study using a completely randomized factorial design. The independent variables were Pb concentration (0.01, 0.1, and 1 ppm) and exposure duration (30, 60, and 90 minutes). The dependent variables were Ca and P levels, and Ca/P ratio in dental HAp.

Sample Preparation

Extracted non-carious human teeth were used as research samples. Teeth were cleaned with distilled water to remove surface contaminants, air-dried, and stored under sterile conditions before treatment. Each tooth was randomly allocated into experimental groups. The study employed a 3×3 factorial design (three Pb concentrations × three exposure durations). Each treatment condition was conducted in duplicate to ensure measurement reliability.

Pb Exposure Procedure

Teeth samples were immersed in $PbSO_4$ solutions prepared at concentrations of 0.01 ppm, 0.1 ppm, and 1 ppm. Exposure durations were set at 30, 60, and 90 minutes at room temperature. After exposure, the samples were rinsed with distilled water to remove residual Pb solution, dried, and ground into fine powder using a clean mortar and pestle for mineral analysis.

Determination of Ca/P Ratio

The Ca/P ratio was calculated by dividing the molar concentration of Ca by the molar concentration of P for each treatment group. A Ca/P ratio of 1.67 was used as the reference value for stoichiometric HAp stability.

Kinetic Analysis of Mineral Degradation

To evaluate the degradation behaviour of Ca and P after Pb exposure, concentration changes over time were analysed using linear regression. Zero-order kinetics was assessed using the equation:

$$[A] = \left[A_0\right] - kt$$

where:
[A] = concentration at time t
[A_0] = initial concentration
k = degradation rate constant
t = exposure time (minutes)

The reaction order was determined based on the linearity (R^2 value) of concentration versus time plots.

Ca Level Analysis

Ca levels were determined using a titrimetric method adapted from Sarifudin et al. (Sarifudin et al., 2022). Briefly, 2 g of ashed sample was dissolved and subjected to precipitation using oxalic acid and ammonium oxalate. The precipitate was filtered, washed until chloride-free, dissolved in sulfuric acid, and titrated with 0.1 N $KMnO_4$. Ca concentration was calculated based on titration volume using the established formula. Each measurement was performed in duplicate, and the mean value was used for analysis.

P Level Analysis

P levels were measured spectrophotometrically at a wavelength of 880 nm following the method described by Khairuddin et al. (Khairuddin et al., 2022). One gram of homogenized sample was reacted with a mixed reagent solution, and absorbance was recorded within 10–30 minutes. P concentration was calculated using a standard calibration curve. All measurements were conducted in duplicate.

Statistical Analysis

All statistical analyses were performed using SPSS version 19 (IBM Corp., Armonk, NY, USA). Data were presented as mean values from duplicate measurements. Differences between Pb concentration groups and exposure durations were evaluated using two-way ANOVA to determine the effects of Pb concentration and exposure time on Ca and P level, and Ca/P ratio. Correlation and regression analyses were conducted to determine degradation rate constants. Statistical significance was established at $P < 0.05$.

RESULTS

The Ca/P ratio decreased across all Pb concentration groups over time (**Table 1**).

Table 1. Ca/P ratio in teeth exposed to different concentrations and exposure durations of Pb

Pb Concentration (ppm)	Time Exposure (minute)		
	30	60	90
	Ca/P Ratio		
0.01	2	0.754	0.752
0.1	0.460	0.358	0.397
1	0.571	0.475	0.365

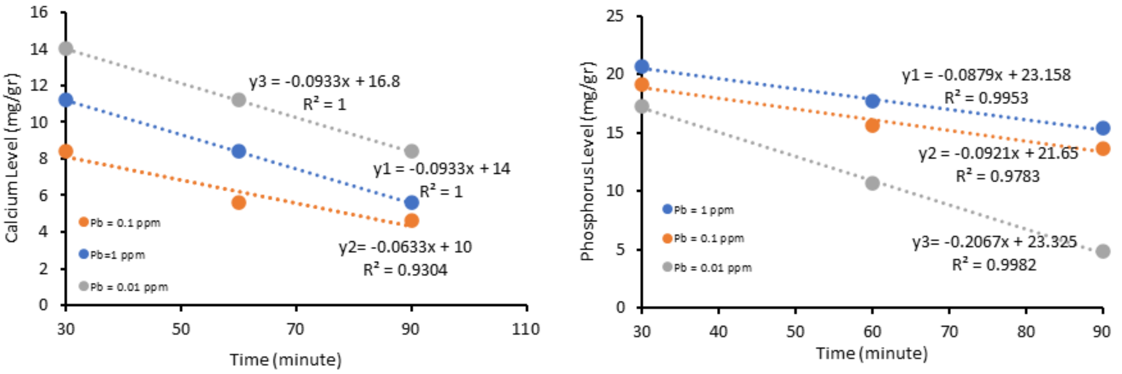
Table 1 shows that at 0.01 ppm, the Ca/P ratio decreased from 0.810 to 0.752. At 0.1 ppm, the ratio decreased markedly from 0.460 to 0.397. At 1 ppm, the ratio declined from 0.571 to 0.365. All Ca/P ratios were substantially lower than the stoichiometric HAp reference value (1.67), indicating mineral imbalance following Pb exposure. The most pronounced reduction in Ca/Ph ratio was observed at 0.1 ppm and 1 ppm concentrations after 90 minutes of exposure.

Table 1 also shows that the Ca/P ratio is less than 1.67. This indicates that Ca-orthophosphate is solubilized. The dissolution of Ca-orthophosphate due to Pb exposure follows the law of zero-order kinetics, with the formula:

$$[A] = -kt + [A_0]$$

[A] = current concentration; [Ao]= initial concentration; k = zero-order reaction speed constant; t = time (minutes).

Thus, the amount of Ca and PO_4 degradation rate on HAp can be determined by the linear graph method, as shown in **Figure 1a** and **1b**, respectively. Based on **Figure 1a** and **1b**, the reaction rate constant and the initial concentration of both Ca and PO_4 can be determined, which can be seen in **Table 2** and **3**.



(a) **(b)**

Figure 1. Degradation rate of **(a)** Ca and **(b)** PO_4 due to Pb exposure

Ca levels decreased progressively over time in all Pb concentration groups (**Table 2**). At 0.01 ppm Pb, Ca levels declined from 14 mg/gr (30 minutes) to 8.4 mg/gr (90 minutes). At 0.1 ppm Pb, Ca decreased from 8.4 mg/gr to 4.6 mg/gr. At 1 ppm Pb, Ca levels declined from 11.2 mg/gr to 5.6 mg/gr. Zero-order kinetic modelling showed strong linearity in the 0.01 ppm and 1 ppm groups ($r = -1.000$; $p = 0.000$), indicating a highly consistent degradation pattern. The 0.1 ppm group demonstrated a slightly weaker but still negative correlation ($r = -0.965$; $p = 0.170$). The degradation rate constant (k) was 0.0933 for both 0.01 ppm and 1 ppm groups, while the 0.1 ppm group showed a lower rate constant ($k = 0.0633$).

Table 2. Initial concentration [A0] of Ca, rate constant (k) in Ca degradation reaction, and correlation coefficient and P value of Ca level in several Pb concentrations and time durations of Pb exposure

Pb Concentration (ppm)	Time of Exposure (minute)			Rate constant (k)	Initial concentration [Ao]	Correlation Coefficient (r)	P Value
	30	60	90				
	Ca level (mg/gr)						
0.01	14	11.2	8.4^{*}	0.0933	16.8	- 1.000	0.000
0.1	8.4	5.6	4.6	0.0633	10	-0.965	0.170
1	11.2	8.4	5.6^{*}	0.0933	14	-1.000	0.000

*Statistically significant (P < 0,05)

Table 3. Initial concentration [A0] of P, rate constant (k) in Ph degradation reaction, and correlation coefficient and P value in several Pb concentrations and time durations of Pb exposure

Pb Concentration (ppm)	Time of Exposure (minute)			Rate constant (k)	Initial concentration [Ao]	Correlation Coefficient (r)	P Value
	30	60	90				
	Ph level (mg/gr)						
0.01	17.275	10.625	4.875^{*}	0.1108	23.25	- 0.999	0.027
0.1	18.250	15.650	11.600	0.2067	21.65	-0.941	0.156
1	17.275	17.675	15.350^{*}	0.0713	23.158	- 0.999	0.032

*Statistically significant (P < 0,05)

Table 3 shows that at 0.01 ppm Pb, P levels decreased from 17.275 mg/gr to 4.875 mg/gr. At 0.1 ppm Pb, P declined from 18.250 mg/gr to 11.600 mg/gr. At 1 ppm Pb, P decreased from 17.275 mg/gr to 15.350 mg/gr. Strong negative correlations were observed at 0.01 ppm (r = -0.999; p = 0.027) and 1 ppm (r = -0.999; P = 0.032), supporting zero-order degradation kinetics. The 0.1 ppm group showed a weaker correlation (r = -0.941; P = 0.156). The highest degradation rate constant for P was observed at 0.1 ppm (k = 0.2067), followed by 0.01 ppm (k = 0.1108) and 1 ppm (k = 0.0713).

DISCUSSION

This study demonstrates that Pb exposure induces measurable degradation of Ca and P in dental tissue under in vitro conditions. Both minerals exhibited time-dependent reductions consistent with zero-order kinetic behaviour in most concentration groups. The results of this study indicate significant alterations in the Ca/P ratio and hydroxyapatite stability, which are crucial for understanding tooth mineralization. In vitro, these findings demonstrate that Pb can directly compromise tooth mineral integrity through dissolution and ion-substitution processes. This explanation provides additional perspective that Pb-induced tooth damage occurs not only through the systemic pathway during odontogenesis but also through direct contact with erupted tooth surfaces.

The Ca degradation pattern showed strong linearity at 0.01 ppm and 1 ppm, suggesting a constant rate of mineral loss over time. Interestingly, the rate constant at 0.1 ppm was lower than at 0.01 and 1 ppm. This non-linear concentration-response pattern may indicate complex mineral surface interactions rather than simple dose-dependent dissolution. Ph degradation also followed a declining trend, with strong correlations at low and high concentrations. Notably, the highest P degradation rate constant occurred at 0.1 ppm (k = 0.2067), suggesting that intermediate Pb concentrations may induce accelerated Ph destabilization (Wiener et al., 2015; Yepes et al., 2020).

The Ca/P ratio findings further support mineral imbalance. The marked reduction in Ca/P ratio across all groups indicates disruption of HAp stability. Since hydroxyapatite stability depends on balanced Ca and P composition, the observed ratios (0.365–0.810) suggest substantial structural alteration (Jeong et al., 2019; Kurniawan et al., 2019).

Mechanistically, Pb^{2+} ions may interact with the mineral lattice through substitution or surface complexation processes. Such interactions may promote dissolution–reprecipitation phenomena, altering mineral stoichiometry and increasing susceptibility to degradation. Interestingly, the highest Ca degradation rate was observed at both low (0.01 ppm) and high (1 ppm) concentrations, while phosphorus degradation peaked at 0.1 ppm. This pattern suggests that Pb-induced mineral destabilization may not follow a simple linear concentration-response model but may involve surface saturation, precipitation phenomena, or competing reaction pathways (Monir et al., 2010; Suhartono et al., 2012, 2019).

From an environmental health perspective, these findings provide mechanistic evidence that Pb exposure can alter dental mineral composition. Although conducted under in vitro conditions, the observed mineral imbalance may help explain increased vulnerability of dental tissues in populations chronically exposed to Pb-contaminated water sources.

CONCLUSION

In conclusion, the results of this study indicate that Pb exposure can trigger tooth decay. This can be seen from the decrease in Ca/P ratio value and the increase in Ca and PO_4 degradation rate in dental hydroxyapatite. However, there are several shortcomings in this study, including that Pb exposure to teeth is still limited to in vitro tests, variations in Pb concentration and duration of Pb exposure are not too much, and it only assesses Ca, PO_4, and their ratios. Further research in vivo with variations in duration and concentration of Pb, as well as other parameters that have not been measured in this study. Further research is expected to explain in more detail the pathomechanisms of Pb exposure to teeth.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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