In Vitro Investigation of the Therapeutic Effects of Coriander Powder Extract in the Detoxification of Pb and Cd Exposure*

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Abstract

Aim: This study was conducted to investigate the effect of coriander seed powder extract on the chelation rate of cadmium (Cd) and lead (Pb) in saliva, stomach and intestine using an in vitro digestion model.

Method: The method recommended by the Dutch National Institute for Public Health and the Environment (RIVM) was used as an in vitro digestion model. 5 different concentrations (50, 100, 200, 300 and 500 mg) of coriander and garlic powder extracts, to which 100 ppm Cd and Pb were added, were digested in saliva, stomach and intestine. Cd and Pb ratios in each medium were measured by ICP- OES device.

Results: As the amount of coriander (50, 100, 200, 300 and 500 mg) increased, the bioavailability of Cd similarly decreased in saliva to 73.09%, 69.72%, 68.86%, 69.71% and 64.70%, respectively, in the stomach environment to 35.93%, 38.40%, 38.46%, 37.06% and 34.44%, and in the intestinal environment to 16.45%, 15.09%, 11.89%, 4.69% and 3.70%. The bioavailability of Pb decreased in saliva to 72.72%, 67.16%, 69.46%, 68.31% and 64.06%, respectively, in the stomach it decreased to 37.50%, 35.97%, 37.07%, 34.93% and 33.81% respectively, and in the intestine it decreased to 16.83%, 14.94%, 9.86%, 4.26% and 3.10% respectively. Coriander was found to be effective in reducing the bioavailability of both Pb and Cd. In the medium-based comparison, the availability of Cd was highest in saliva and lowest in the intestine. In coriander extracts, Cd availability was significantly reduced compared to the control group ($p < 0.01$). A statistically significant decrease in availability was detected as the concentration increased ($p < 0.01$). In the medium-based comparison, the bioavailability of Pb was highest in saliva and lowest in the intestine. A significant decrease in the bioavailability of Pb was detected.

Conclusion: This study has demonstrated that coriander possesses the capacity to bind cadmium and lead in an in vitro digestion model. Furthermore, this study has determined that coriander can be used as an alternative to chemical chelators (e.g. D-penicillamine) that may be harmful to the body in cases of chronic heavy metal exposure. Therefore, as an alternative, it is recommended to regularly provide coriander tablets or coriander consumption to prevent Cd and Pb exposure.

Keywords: Heavy metal, lead, cadmium, medicinal, aromatic plant, coriander.

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Pb ve Cd Maruziyetinin Detoksifikasyonunda Kişniş Toz Ekstraktının Terapötik Etkilerinin in Vitro İncelenmesi

Öz

Amaç: Bu çalışma, in vitro sindirim modelini kullanarak, kişniş tohumu toz ekstarktının tükürük, mide ve bağırsak ortamında kadmiyum (Cd) ve kurşunu (Pb) şelatlama oranı üzerindeki etkisini incelemek amacıyla yapılmıştır.

Yöntem: İn vitro sindirim modeli olarak Hollanda Ulusal Halk Sağlığı ve Çevre Enstitüsü'nün (RIVM) önerdiği metot kullanılmıştır. 100 ppm Cd ve Pb ilave edilmiş, 5'er farklı konsantrasyonda (50, 100, 200, 300 ve 500 mg) kişniş toz ekstresi, tükürük, mide ve bağırsak ortamında sindirim işlemine tabi tutulmuştur. Her bir ortamdaki Cd ve Pb oranları ICP-OES cihazı ile ölçülmüştür.

Bulgular: Kişniş miktarı (50, 100, 200, 300 ve 500 mg) arttıkça Cd'nin biyoerişilebilirliği benzer şekilde tükürükte sırasıyla %73,09, %69,72, %68,86, %69,71 ve %64,70'e, mide ortamında %35,93, %38,40, %38,46, %37,06 ve %34,44'e ve bağırsak ortamında ise %16,45, %15,09, %11,89, %4,69 ve %3,70 ' e düşmüştür. Pb'nin biyoerişilebilirliği ise tükürükte sırasıyla %72,72, %67,16, %69,46, %68,31 ve %64,06'e, midede sırasıyla %37,50, %35,97, %37,07, %34,93 ve %33,81'e ve bağırsakta sırasıyla %16,83, %14,94, %9,86, %4,26 ve %3,10' a düşmüştür. Kişnişin hem Pb hem de Cd'nin biyoerişilebilirliğini azaltmada etkili olduğu görülmüştür. Ortam bazlı karşılaştırmada, Cd'nin erişilebilirliği en yüksek tükürükte, en düşük ise bağırsakta gözlemlenmiştir. Kişniş ekstraktlarında, kontrol grubuna kıyasla Cd erişilebilirliği anlamlı düzeyde azaldığı görülmüşür ($p<0.01$). Konsantrasyon arttıkça erişilebilirlikte istatistiksel olarak anlamlı bir azalma tespit edilmiştir ($p<0.01$). Ortam bazlı karşılaştırmada, Pb'nin biyoerişilebilirliği, en yüksek tükürükte, en düşük değerler bağırsakta gözlemlenmiştir. Pb'nin biyoerişilebililiğinde anlamlı azalma tespit edilmiştir.

Sonuç: Bu çalışma kişnişin in vitro sindirim modelinde Cd ve kurşunu bağlama kapasitesine sahip olduğunu göstermiştir. Ayrıca bu çalışma ile kişnişin, kronik ağır metal maruziyetinde vücut için zararlı olabilecek kimyasal şelatörlerin (örn. D-penisilamin) yerine kullanılabileceği belirlenmiştir. Bu nedenle, alternatif olarak, Cd ve Pb maruziyetini önlemek için düzenli olarak kişniş tabletlerinin veya kişniş tüketiminin sağlanması önerilmektedir.

Anahtar Sözcükler: Ağır metal, kurşun, kadmiyum tıbbi aromatik bitki, kişniş.

Introduction

Heavy metals refer to metals and semi-metals with a density greater than 5 g per cubic centimetre, which can exhibit toxic properties even at low concentrations. In medicine, these are known as toxic metals[1].

Among toxic heavy metals, Pb is widely used due to its ease of extraction and processing. The reason for Pb's extensive industrial use is its structural properties, low cost, and ease of processing. Due to these characteristics, Pb has found widespread use in many sectors, primarily mining and battery manufacturing[2,3]. The main cause of increased Pb content in the environment is human activity. Lead is released into the air as a result of mining, factories using lead compounds, alloys, vehicle exhaust, and the burning of fossil fuels. It is also used in the composition of pesticides. Lead-containing waste products, lead-based paints, batteries, and industrial waste cause lead accumulation on the soil surface. Lead in the soil mixes with rainwater, entering water sources or lakes, thus continuing the cycle from air to water to soil to plants and animals, and ultimately to humans[3,4].

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Long-term exposure to low levels of lead can cause accumulation in the body and lead poisoning. The half-life of Pb in the blood is 30 days. It accumulates particularly in the brain, kidneys, liver, teeth, hair and bones[5]. The World Health Organisation's guideline value for Pb in drinking water is 0.01 mg/L[6].

The toxic effects of Pb may vary depending on the degree of exposure. In general, the structures most adversely affected by poisoning are red blood cells, the nervous system, kidneys and bones, followed by the immune system, reproductive systems and cardiovascular system[7]. In Japan, non-occupational Pb poisoning was once caused by Pb-based cosmetic face powder.

A study on the Pb concentration in the ambient air of a battery manufacturing plant found that a total of 15 points exceeded the Pb exposure limit value of 0.15 mg/m^3[8]. The researchers emphasise that there is a correlation between the Pb concentration in the workplace ambient air and the blood Pb levels of workers.

In a similar study, the average blood Pb level was determined to be 26.806 µg/100 ml for workers in enclosed car parks and 18.153 µg/100 ml for workers in open car parks. The researchers emphasised that the blood Pb levels of both indoor and outdoor car park workers were above standard values[9].

Cd is an inorganic, toxic, odourless, white, soft, malleable metal belonging to group II B of the periodic table. Cd has an atomic mass of 112. There are areas in nature with naturally high Cd content. In addition, it is the most common environmental toxic metal, largely due to human activities, particularly the smelting of Cd-mixed Zn, Pb and Cu ores. As an element, Cd is widely used in soldering, alloys and battery production, while its compounds are commonly used in the paint, plastics, and printing industries. Over the last 50 years, the rate of Cd-related environmental pollution has increased in line with its growing use[10].

There is no mechanism for conversion to a less toxic structure in the body, and in the absence of effective chelating agents, excretion is very poor. The International Agency for Research on Cancer has classified Cd as a Group I carcinogen[11]. Cd causes oxidative stress by generating reactive oxygen species (ROS) and disrupts the body's antioxidant defence system. These free radical structures, which have lost their electrons, cause cell death by affecting carbohydrates, enzymes and proteins, impair the body's immune system by causing changes in the number and function of T cells, and cause cancer by leading to DNA mutation and DNA damage[12-15].

In humans, Cd exposure occurs mainly through respiration, food, and smoking. Chronic Cd exposure can cause damage to the respiratory tract, loss of smell, respiratory distress, chronic obstructive pulmonary disease, chronic rhinitis, impaired lung function and emphysema[12,14,15].

Cd crosses the placenta and causes damage to the foetus and placenta[16,17]. In addition, it is known to damage the liver, bones, urogenital organs, and other vital organs. Increased mortality rates from cancer and cardiovascular disease in males have been associated

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with Cd exposure[18-20].

Cd causes infertility by leading to foetal death, embryonic abnormalities, and sometimes structural and functional damage to the male or female reproductive system. Toxic effects of Cd in males include decreased sperm motility, testicular damage, organ degeneration and dysfunction, vacuolisation of seminiferous tubules, and prostate cancer[21]. In females, Cd toxicity can cause haemorrhage in the ovaries and changes in hormone production.

Chelation therapy is used in acute and chronic heavy metal poisoning. The basis of the treatment is the formation of chelates with metals[22]. Sulphur-containing compounds are of great importance in preventing poisoning and facilitating the excretion of heavy metals by forming chelates with them, calcium disodium ethylenediaminetetraacetic acid (EDTA), and D- penicillamine (DPA) are the most commonly used chemical chelation agents in cases of heavy metal poisoning. These substances bind with heavy metals in the blood and soft tissues, forming excretable compounds that enable the removal of these elements from the body[23].

Heavy metals cause free radicals and disrupt the cellular antioxidant defence system. Various antioxidants derived from plants are currently being evaluated. Plant extracts have a potential chelation effect on certain metals and prevent damage caused by heavy metals in various tissues[24,25]. Some vegetables, fruits, and spices contain multiple compounds with antioxidant properties. Among these natural antioxidants, flavonoids, phenolic compounds, isoflavones, lutein, lycopene carotenoids, and tocopherols can inhibit oxidation and function as chelators and reducers of free radicals[26-28].

Certain plant-derived compounds are being presented as potential alternatives to traditional chelators. Academic studies have revealed that these substances, when administered parenterally, reduce heavy metal absorption in the digestive tract[29]. Natural chelators reduce or completely eliminate the toxic effects of heavy metals. The components synthesised by plants to protect themselves against external factors: anthocyanins, flavonols and flavonoids have been found to exhibit a protective property against heavy metal-induced toxic effects[30,31]. Compounds in plants facilitate the elimination of toxic heavy metals from the body. They form chelates with compounds containing sulphur (S) in their structure, preventing the absorption of these elements from the intestines[32]. In this context, coriander, which contains organosulphur compounds in its structure, can be considered a biologically active compound with these properties.

This study was carried out to determine the effect of coriander on the bioavailability of cadmium (Cd) and lead (Pb) in an in vitro digestion model.

Material and Methods

Material

Coriander seed powder extract (*Coriandrum sativum*) (Alfasol) was used as the material in this study**.**

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Method

At this stage, a laboratory-scale gastrointestinal system model was established. The gastrointestinal system model was created by preparing mouth, stomach, and intestinal solutions in a stirring water bath at body temperature (37°C).

In Vitro Digestion Method

The in vitro digestion method recommended by the Netherlands National Institute for Public Health and the Environment (RIVM) was used[33]. This recommended model is the best model used to determine the bioavailability and bioaccessibility of heavy metals in the digestive tract because it closely resembles the physiological conditions in the human body. Compared to other

in vitro digestion models, this model involves quick and simple steps and is considered helpful in determining bioavailability and predicting the health risks of heavy metals[34,35]. The model consists of three parts: the mouth, stomach, and small intestine. The chemicals used for artificial enzymes represent saliva, gastric juice, and a mixture of duodenal and bile juices in the mouth, stomach, and small intestine, respectively. The compositions of the artificially prepared digestive fluids are based on human physiology[29].

The in vitro digestion model system simulating the human gastrointestinal system, including the saliva, stomach, and small intestine stages, was prepared based on the method applied by Yang et al.[29]. Five different concentrations of coriander seed powder extract were added to each medium at 50, 100, 200, 300, and 500 mg. A phosphate buffer (20 mM) was used for pH adjustments. A standard solution of heavy metals (Cd and Pb) at the same concentration (100 ppm) was added to the samples.

Amylase (Sigma Chemical Co.) was used for the salivary phase. Pepsin (Sigma Chemical Co.) was used for the gastric phase. A mixture of bile extract/ pancreatin/ lipase (Sigma Chemical Co.) was used for the intestinal phase.

Artificial Digestion Model

In the first stage of the digestion process, five different concentrations of coriander digestion models were prepared. The aromatic plant (dissolved in 20 mM phosphate buffer) at the ratios mentioned above and heavy metals (Cd and Pb) were added to 9 ml of saliva solution so that each standard solution would be 100 ppm, and the stirring process was applied in a stirring water bath at 37°C at 55 rpm for 5 minutes. Then, 5 ml samples were taken from the liquid part of each sample and stored for ICP-OES analysis.

In the second stage, 13.5 ml of gastric fluid was added to the samples, the pH was adjusted to pH 1.7 using HCl, and the samples were shaken in a stirring water bath at 55 rpm and 37°C for 2 hours. At the end of the 2-hour stirring process, 5 ml was taken from each sample and stored for ICP-OES analysis.

In the final stage, 27 ml of intestinal fluid was added to the samples, the pH was adjusted

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to 8 using 1N NaOH, and the samples were subjected to stirring at 55 rpm for 2 hours in a stirring water bath. After the 2-hour stirring process, 5 ml was taken from each sample and stored for ICP-OES analysis.

The negative control was prepared by adding only Cd and Pb at 100 ppm each, without adding coriander extract, and subjected to digestion procedures as described above. The percentage bioavailability of heavy metals was determined by dividing the concentration of dissolved heavy metals in the liquids by the total heavy metal content in the control group and multiplying by 100.

$$Bioavailability\ \% = \frac{Metal\ content\ in\ the\ aqueous\ phase}{Metal\ content\ in\ the\ control\ group} x\ 100$$

Cd and Pb quantity determinations were performed using ICP-OES (Inductively Coupled Argon Plasma-Optical Emission Spectrometer). To measure the Pb and Cd contents in the supernatants obtained from the digestions, 5 mL of 1 N nitric acid (HNO_3) was added to the samples. Argon (Ar) was used as the carrier gas, auxiliary gas and plasma gas in the ICP-OES. The emission line wavelengths were set to 214.438 nm for Cd and 220.353 nm for Pb.

All measurements were performed in triplicate, and data were expressed as the mean±standard deviation (SD). ANOVA was used for the statistical analysis of the effects of coriander, and regression analysis was used to determine the relationship between them.

Ethical Statement

This study was carried out with the approval of the Ethics Committee of Istanbul Gedik University, dated 25.06.2025 and numbered E-11470191-050.4-2025.17334048

Results

Table 1. Average Cd levels and percentage Cd bioavailability in saliva, stomach, and intestinal environments with different rates of coriander extract added

Coriander Extract (mg)	Control	Saliva		Stomach		Intestine	
	Cd ppm	Cd ppm ±SD	Bioavailability %	Cd ppm ±SD	Bioavailability %	Cd ppm ±SD	Bioavailability %
50	99.95	73.05±2.44	73.09	35.92±9.66	35.93	16.44±4.67	16.45
100	99.95	69.68±2.54	69.72	38.38±8.33	38.40	15.08±4.48	15.09
200	99.95	68.83±2.58	68.86	38.44±8.71	38.46	11.88±1.74	11.89
300	99.95	69.68±7.92	69.71	37.04±9.08	37.06	4.69±0.83	4.69
500	99.95	64.67±3.88	64.70	34.43±8.37	34.44	3.70±0.44	3.70

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Although a decrease in the amount of accessible Cd was observed as the coriander concentration increased in the saliva environment, no significant difference was found in the Cd accessibility ratio at the concentration level ($p \leq 0.05$). Although the percentage bioavailability of Cd decreased in the gastric environment compared to the salivary environment, no significant difference was observed between coriander concentrations in the gastric environment ($p \leq 0.05$). Compared to the salivary and gastric environments, the bioavailability of Cd in the intestinal environment decreased significantly depending on the coriander concentration. However, coriander extracts did not create a significant difference in the Cd availability rate.

Table 2. Average Pb levels and percentage Pb bioavailability in saliva, stomach and intestinal environments with different levels of coriander extract added

Coriander Extract (mg)	Control	Saliva		Stomach		Intestine	
	Pb ppm	Pb ppm±SD	Bioavailability %	Pb ppm±SD	Bioavailability %	Pb ppm±SD	Bioavailability %
50	98.90	71.92±7.77	72.72	37.09±9.02	37.50	16.64±5.50	16.83
100	98.90	66.43±2.84	67.16	35.58±7.55	35.97	14.78±4.94	14.94
200	98.90	68.70±8.90	69.46	36.66±6.97	37.07	9.75±0.47	9.86
300	98.90	67.56±3.16	68.31	34.54±7.31	34.93	4.21±1.21	4.26
500	98.90	63.36±5.28	64.06	33.43±7.90	33.81	3.07±0.74	3.1

As the coriander concentration increased in the saliva environment, a decrease in the accessible Pb concentration was observed. However, when considering the accessible Pb concentration, no significant difference was found between the coriander concentration levels ($p \leq 0.05$). Although the percentage bioavailability of Pb decreased in the gastric environment compared to the salivary environment, there was no significant difference in coriander ratios in the gastric environment. No significant difference was observed in Pb availability between coriander ratios in the gastric environment ($p \leq 0.05$).

The effect of different coriander concentrations in the saliva environment on the accessible amount of Cd and Pb was not found to be significant ($p \leq 0.05$). In the regression analysis, a weak decreasing trend in metal ratio was observed as concentration increased; however, this effect did not reach a statistically significant level ($p = 0.0676$). The difference in the interaction between metal type and extract concentration was also not significant ($p=0.9290$ and $p=0.5670$, respectively). These findings indicate that coriander extract may be effective in reducing heavy metal levels, but this effect is limited (Figure 1).

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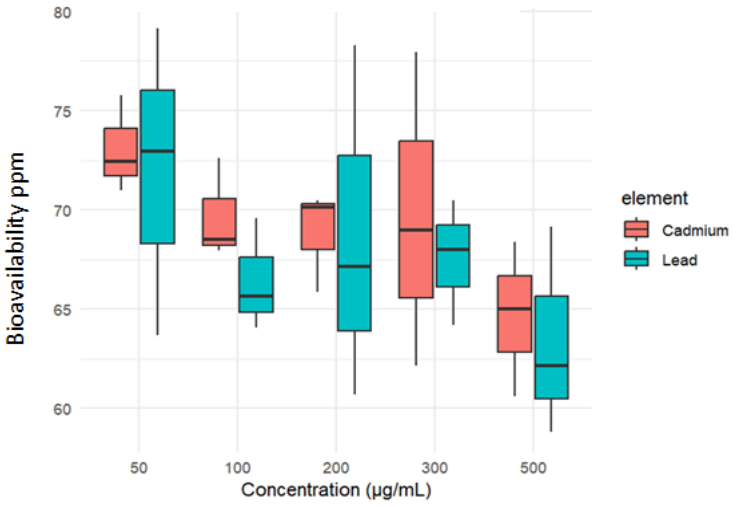
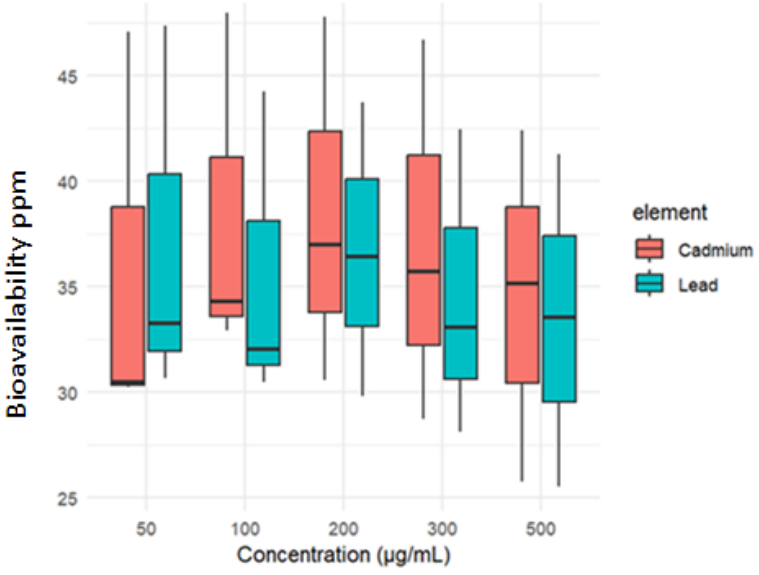
Figure 1. Comparison of the bioavailability of Cd and Pb in coriander in the saliva phase of in vitro digestion



In the stomach phase, no significant difference was found between Cd and Pb at the extract concentrations ($p \leq 0.05$). These findings reveal that coriander extract does not have a selective effect on reducing Cd and Pb levels. Furthermore, linear regression analysis also showed that the interaction was not significant ($p=0.914$) and that the p-value of the overall model was also not significant ($p=0.8303$). The model's R^2 value was negative (-0.07895), confirming that coriander extract did not have a significant effect on the reduction of Cd and Pb ratios. In conclusion, it is observed that coriander extract does not have a significant effect on the Cd and Pb binding ratio under gastric conditions (Figure 2).

Figure 2. Comparison of the bioavailability of Cd and Pb in the stomach phase of in vitro digestion



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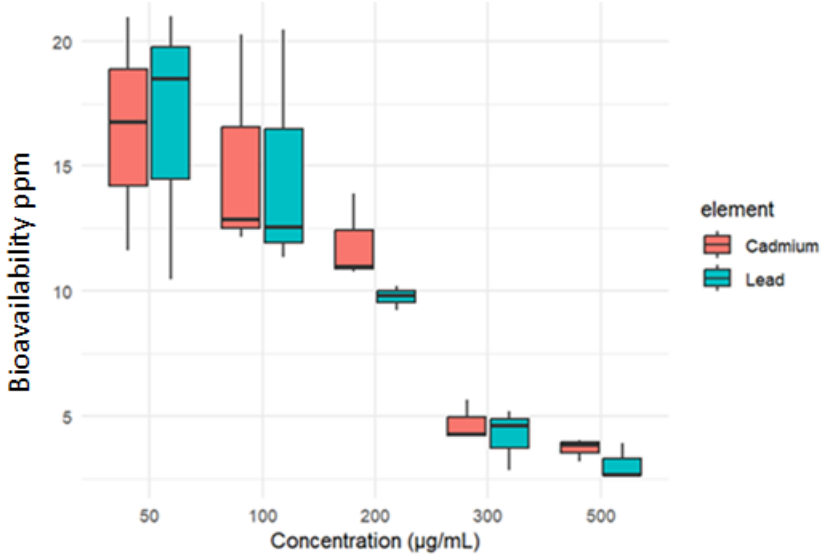
In the intestinal phase, there was no significant difference in the chelation rate of Cd and Pb by coriander extracts and a similar decrease trend was observed in the available amounts of both metals. It was observed that as the coriander concentration increased, there was a significant decrease in the available metal ratio, and this effect was similar for both metals. This situation also shows that the chelation rate of metals increased as the coriander extract concentration increased. As a result, the chelation rate of Cd and Pb increased similarly in extracts, but no significant difference was observed between the metal types (Figure 3).

Figure 3. Comparison of the bioavailability of Cd and Pb from coriander in the ıntestinal phase of in vitro digestion



Discussion

In an experimental study conducted on mice, changes in enzyme activity and haematological and biochemical parameters were observed in mice exposed to Pb and Cd[36]. The researchers report that chelation therapy with garlic can reverse haematological and biochemical changes, thereby preventing the toxic effects of Pb and Cd. The researchers' findings support the method we obtained from our in vitro study. In this context, it can be said that coriander can alleviate toxic effects by both promoting antioxidant activity and removing Pb from tissues and reducing tissue exposure to Pb.

It has been reported that oral administration of garlic reduces Pb concentrations in the blood and tissues of mice, indicating that garlic acts as a chelating agent in the treatment of Pb poisoning[37,38]. The researchers findings were consistent with our in vitro study and demonstrated that the toxic effects associated with Pb and Cd exposure can be significantly prevented with coriander treatment. These values also support the results of our in vitro study. This protective effect of coriander is likely due to the chelation of heavy metals in the body by sulphur compounds and the promotion of their excretion via the intestines.

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Our results are also consistent with previous studies[36-39], which showed that sulphur-containing compounds are effective in heavy metal exposure. This study demonstrated that the use of aromatic plants, such as vitamins, flavonoids, and mineral elements, can provide defence against Pb and Cd in the body.

Conclusions and Recommendations

This study demonstrated that coriander has the capacity to bind Cd and Pb and that the use of an in vitro digestion model reduces the amounts of heavy metals in the digestive tract. Furthermore, it was determined that coriander intake could be as effective as a chemical chelator for chronic exposure to heavy metals. Specifically, regression and ANOVA analyses revealed that coriander could be considered a strong alternative. This study also demonstrated that an in vitro test could be a good indicator for predicting the bioavailability of these heavy metals at a low price and in a quick manner. Coriander has more protective potential than therapeutic potential in heavy metal poisoning. In this context, increasing coriander intake, possibly through dietary supplements, may be encouraged. This study also demonstrated that an in vitro test could be a good indicator for predicting the bioavailability of these heavy metals in a low price and quick manner for people working in occupational settings where heavy metal contamination is prevalent.

In a limited number of studies, health risk assessments have been applied using in vitro digestion models. In health risk assessments, it is essential to consider heavy metal exposures as potential human health indicators and to include them in the studies. This study highlights the importance of health risk assessments and points to their use as a reference in future in vitro digestion model studies.

To prevent health disorders in workers due to heavy metal exposure, it is recommended that the risk of contamination be calculated in advance at each stage and that precautions be taken at the outset to minimise exposure by improving the process accordingly. Necessary precautions must be taken in risk assessments in this context.

The first step in treating heavy metal poisoning should be to eliminate the source of exposure. Chelating agents are then used to facilitate the elimination of heavy metals from the body. Due to economic and social constraints and high unemployment levels, workers do not want to leave their jobs. Therefore, as an alternative, side effects can be prevented by ensuring that coriander tablets are taken regularly to limit exposure to heavy metals.

Heavy metal chelation therapy with herbal agents is a treatment method that requires long-term and very careful application, except in cases of acute poisoning with a risk to life. Plant extracts can also be taken in capsule form and are recommended for use for at least 6 months.

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