2023

Breakfast is the Most Important Meal of the Day: An Investigation of the Levels of Cadmium in Breakfast Cereal

LiLi MacQuarrie

Breakfast is the Most Important Meal of the Day:

An Investigation of the Levels of Cadmium in Breakfast Cereal

LiLi MacQuarrie

Faculty Advisor: Brian Niece, Ph.D.

A Thesis Submitted to Fulfill the Requirements of the Honors Program at Assumption University

Fall 2022

Abstract

Cadmium (Cd) is a transition metal that offers no nutritional value to human beings. Humans' main exposure to Cd is through consumption. Cd is extremely soluble, leading to plants readily absorbing it through contaminated water. Plants containing the absorbed Cd are consumed, and the metal accumulates in the body and is toxic. Effects of Cd in the body include renal tubular damage, pulmonary emphysema, epigenetic changes, and carcinogenesis. Previous studies have looked at Cd in cereal based products, and their results revealed low, varied amounts of Cd in the samples. However, most of these studies were performed in Asian countries. This leaves a gap in data for foods in the United States. This study looks at three different rice cereal brands from grocery stores in the Worcester, MA area. In a 2 g sample, the results ranged from 0.04 ± 0.03 μg in Rice Chex (General Mills), 0.06 ± 0.04 μg in Signature Select's Rice Pockets (Shaws), and 0.09 ± 0.06 μg in Food Club's Rice Squares (Big Y). These results were all above the LOD of 0.015 μg. The amounts of Cd found were comparable with the amounts found in previous literature. Since the levels of Cd were below the TWI of 2.5 μg/kg body weight, it can be concluded that the amount of Cd in these brands do not pose a health risk.

I. Introduction

It is important to know the ingredients in food products. That is the reason for food labels, which give a list of ingredients and nutritional information. These labels help consumers make informed choices in what they purchase and what they are going to feed their families. However, there are some ingredients that go unknown. Potential trace contamination in food is a risk that is slowly being addressed by the FDA and other countries' governments. From industrialization and poor disposal of waste, toxic elements can end up in food products. Well-known contaminants like mercury, which has been a major contaminant found in fish, have been analyzed in depth. However, other lesser-known contaminants, have not. Cadmium is one such metal.

Cadmium

Cadmium is a transition metal that has no nutritional value to the human body. From the International Agency for Research on Cancer (IARC), the most common oxidation state for Cd is Cd^{2+} with a few compounds containing Cd^{1+}.[1] It enters the environment through natural sources and human activities. The uptake into food, however, comes from cadmium exposed soil. The cadmium contaminated soil is mainly due to fertilizers, manure, sewage, and coal combustion. Cadmium from mining, also used in product manufacturing of item such as batteries, spreads into the environment. Cadmium is more soluble than other metals, which causes it to be readily taken up by plants. Due to the high transfer factor properties of plants (from soil to plants), most of the cadmium exposure in humans is through consumption of plant-based food.[2] A review concluded that cadmium first enters the plant by its roots. The acidification of the soil and high solubility allow the roots to readily take up the metal. Cadmium can then be translocated to shoots in ionic form due to its high mobility. The review also mentioned that more than 40% of cadmium may be absorbed and transported to the upper part of wheat. This part of the plant is what grain is produced from.[3]

Consumption of Cadmium

In the United States, the population was found to consume an average of 4.63 μg cadmium per day, or 0.54 μg/kg body weight per week in 2013.[4] This data was collected by matching intake data with the cadmium database of the Food and Drug Administration (FDA)'s Total Diet Study 2006 through 2013. Males with higher incomes and education levels consumed a greater cadmium intake than individuals with lower education levels. Lower cadmium intake was also seen in those underweight, current smokers, and non-consumers of alcohol. The highest intakes on a body weight basis were children ages 10 and below and those who were underweight.[5]

An assessment was performed in 2011 by the Panel on Contaminants in the Food Chain of the European Food Safety Authority for the tolerable weekly intake (TWI) of cadmium. It was determined that the food groups that contributed most to the cadmium intake were cereals and bread at 34% of the cadmium intake. This was determined by looking at the Total Diet Study taken from the FDA. The cadmium concentrations were summed, giving an estimate of the cadmium contents in complex food.[4] Using two different approaches, the panel concluded that there was no need for change for the TWI of cadmium at 2.5 μg/kg body weight.[5] From this information, it can be calculated that the average intake that the U.S. population consumption of cadmium is 22% of TWI.

Cadmium Toxicity

There are many health risks involved in the consumption of cadmium. Due to a half-life of 10-30 years, the metal accumulates in the body instead of the body breaking it down and excreting it. It mainly accumulates in the kidneys which causes renal tubular damage and pulmonary emphysema. Chronic exposure to cadmium may also lead to carcinogenesis in the lungs, prostate, kidneys, breast, urinary bladder, nasopharynx, pancreas, and hematopoietic system. The toxicity of cadmium blocks the mitochondrial electron-transport chain which, when normally functioning, produces molecules of adenosine triphosphate (ATP), an energy molecule necessary for bodily functions. The blocking of the transport chain via complex III (cytochrome bc1 complex) decreases the synthesis of ATP. Cadmium also induces various epigenetic changes in the cells. These changes present themselves as chemical modifications of DNA methylation, histone post-translational modifications, and miRNAs. After absorption, a metal-binding protein called metallothionein is synthesized to protect against toxic metals like cadmium. However, cadmium increases the production of reactive oxygen species (ROS), which damages biological molecules like DNA.[6] The long-term effects on children lead to a potential of low IQ as well as impaired neurological and physical development.[7]

The excretion rate of cadmium is about 0.005% of the body weight.[8] This means that though cadmium does leave the body, it leaves very slowly while still building up in the system.

Itai-itai disease is also caused by exposure to cadmium. It causes osteomalacia, a softening of the bones, along with renal tubular dysfunction. Itai-itai disease caused an increase in mortality with a study conducted showing that 67.6% of participants died within the first 10 years of observation. The most common cause of death among those affected by the disease was pneumonia and renal diseases in renal tubular dysfunction cases. This disease was endemic in Japan starting in the 1960s. Itai-itai disease mainly affects women who live in rice farming areas near the Jinzu River in Toyama, Japan. This river is contaminated but still irrigates the rice fields allowing the rice to absorb the cadmium contents.[9] The health risks that are caused by cadmium consumption pose a large concern.

Cadmium Studies in Food

Several studies have been done, similar in nature, that analyze cadmium in food products. A study conducted in Brisbane, Australia was concerned with the daily intake of lead and cadmium of young children, which analyzed levels of these metals in breakfast cereals, rice products, and diets of young children.[7] The cause for concern comes from the long-term effects on children that cadmium poses. Samples of various ready-to-eat breakfast cereals and rice samples were collected from several different markets in Brisbane and Gold Coast in Queensland, Australia. The rice samples included products made in Australia and imported rice samples. To analyze the amount of lead and cadmium in cereals and rice, the researchers digested the samples by microwave digestion and used inductively coupled plasma mass spectrometry (ICPMS) to examine the levels. ICPMS is a method of analysis that atomizes and ionizes a sample so that the ions produced can be measured by a detector.[10] The results showed that levels of cadmium (<10 to 110 μg/kg) and lead (< 10 to 250 μg/kg) in cereals were low but varied. In the discussion, the researchers described that the levels of cadmium and lead were comparable with the reported values in cereal products from studies performed in Italy, Spain, and Japan.[7]

Another, similar study was done in Japan performed between 1998-2000. The main cause for concern that this research was focused on was cadmium causing Itai-itai disease. Like the research done in Brisbane, the researchers used ICPMS to examine both lead and cadmium in rice (polished), bread (loaf), noodle and flour (wheat) samples. The samples were collected from 63 cities from across Japan. Researchers also compared the products against one another to see the differing levels of metal. The results showed variation in levels of cadmium in the products tested. In polished uncooked rice the grand geometric mean was 50 μg/kg, whereas it was 19 μg/kg for flour. The levels of cadmium were much higher than the levels of lead, 2-3 μg/kg in rice and flour, however, they were still very low.[11] These results fall within the rage of results from the Brisbane study. Though these levels are low, the buildup of cadmium is what poses the threat. In the discussion, it was mentioned that reported cadmium contents in other areas in Asia and outside of Asia were lower than those found in Japan. The inter-area differences could be due to the marketing system of rice in Japan. Therefore, kitchen bought boiled rice samples would be the best indication of local conditions rather than store bought.

A study performed in China examined the cadmium and lead contents produced by Chinese rice cultivators. Samples of grain from all major Chinese production regions were collected. Grains collected included both *indica* (n=70) and *japonica* (n=40) type grains. Southern China grew exclusively *indica* type grain, central and south-western China grew both types, and northern China grew exclusively *japonica* type grain. The mill that was used produced both white and wholemeal flour. Samples were broken down by microwave digestion, and graphite furnace atomic absorption was used to assay the levels of cadmium and lead. Almost all flours contained below 200 μg/kg of both metals. Three rice samples went above the maximum allowable concentration of 200 μg/kg. The cadmium content in white flour ranged from <0.0025 to 253 μg/kg while the lead content ranged from <25.0 to 383 μg/kg. The wholemeal flour tended to be higher (GM of Cd: 67.6 μg/kg) than the white flour (GM of Cd: 0.0567 mg/kg) in heavy metal content.[12] These levels fall within the range of the cadmium and lead content in other studies. Like the other studies, the heavy metal content of the samples varied in range. In this study, it was said that the variance of flour was not attributed to cultivator or location, but rather from differences in the pH of the soil, in the way the flour was fertilized and/or in the quality of the irrigation water that was used.

A separate study conducted in northeastern China focused on the level of cadmium in cereal and pulses (legumes). Again, using inductively coupled plasma mass spectrometry, the researchers analyzed cereals and pulses from open markets in north-eastern China. The results revealed that there was not a significant variation of levels of lead between the five cereals that were tested. With limited samples of pulses, the levels of lead in the four types of pulses were not significantly different. Between pulses (25.7 μg/kg) and cereals (31.3 μg/kg), the average amount of lead did not differ significantly. For cadmium, the overall average of cadmium in cereal (9.2 μg/kg) was significantly lower than the overall average in pulses (55.7 μg/kg). In cereal, cadmium in maize was significantly lower than in other cereals with glutinous rice having more cadmium than in non-glutinous rice. Cowpeas had the most cadmium content, followed by soybeans and kidney beans. The discussion of possible public health implications that these levels of cadmium and lead pose was examined by a national report of nutritional survey in China. This survey revealed that north-eastern Chinese citizens tend to eat more wheat products than those in the south. Pulses showed no difference between the north and the south.[13] Though the levels of cadmium and lead are low, the high intake of these cereals and pulses in north-eastern China pose great danger. Along with the high intake of cereals and pulses, the half-life of cadmium is extensive which causes a buildup of cadmium in the body.

Using hybrid plasma mass spectrometry, a study conducted in the United Arab Emirates examined heavy metal toxins in breakfast cereal. Samples were collected from local outlets in the United Arab Emirates of different brands. These samples were digested and diluted into an aqueous solution where the cadmium and other metals were converted into ions. The toxins that were examined for were arsenic, cadmium, mercury, and lead. The results revealed that the cereals contained 100-900 μg/kg arsenic, 8-50 μg/kg cadmium, 270-370 μg/kg mercury, and 115-30000 μg/kg lead. In the article, a discussion was made about the range that cadmium had. Researchers discuss the environment and condition in which the plants were growing are responsible for the origin and trace of the toxic metals. They concluded that these levels, except for lead, fell within the acceptable limit with the EU permissible levels.[14] The cadmium content fell within the range of the previous studies. Just as in the other studies, the range varied.

A broader study compared the cadmium contents in rice from various areas in the world. The samples were collected from ten areas in Asia (Australia, continental China, Taiwan, Indonesia, Japan, Korea, Thailand, Malaysia, Philippines, and Vietnam) and eight areas outside of Asia (Canada, Colombia, Finland, France, Italy, South Africa, Spain, and U.S.A). The analysis done in this experiment was done differently than the previous analyses. The method was electrothermal atomic absorption spectrometry (graphite furnace atomic absorption). There were small sample sizes from areas outside of Asia. While Asian rice samples were well accounted for (1460), the samples outside of Asia were only 86 samples. There were several comparisons made that included variations between countries and variations within an area. From the data collected, it was concluded that there is a difference in cadmium contents in rice depending on the area from which consumers buy the rice. From Asia, the highest geometric mean was 55.70 μg/kg in Japan and in Australia the lowest was 2.67 μg/kg. From areas outside of Asia, the highest and lowest were 133.30 μg/kg in Colombia and 0.85 μg/kg from Spain. This makes sense due to different levels of contamination between areas. Different areas have different manufacturing practices, which would account for the variations in contamination. Within the paper, another comparison was done of cadmium content in rice throughout the last ten years in Japan. The results show that there has been no significant change in levels of cadmium in Japan during the last ten years. Though it is a positive note that cadmium levels have not risen, they have also not dropped.[15]

Summary

The toxic transition metal cadmium is extremely soluble, allowing the uptake of the metal into plants. These plants are thus turned into food products. The toxicity of cadmium poses many health problems including renal damage, carcinogenesis, reduction in production of mitochondrial ATP, and development issues in children. Therefore, it is pertinent that food products be analyzed for cadmium contamination. The studies that have been performed concluded that there are small, varied amounts of cadmium in cereal and rice products. However, cadmium builds up in the system and consuming small amounts daily will cause health issues. These analyses were also area focused, mostly in Asia. This leaves a need for more analysis performed in areas less studied.

Previous studies on cadmium in cereal have been mainly focused on areas in Asia, data from other areas outside of Asia were very limited. The FDA mentions Cd in their report, but it is not detailed. The following research was conducted to look at U.S. rice cereal brands. The three samples were collected from separate brands in grocery stores in the Worcester, MA area.

II. Procedure

Samples

Three samples of cereal were collected from three different brands: General Mill's Rice Chex, Signature Select's Rice Pockets (Shaws), and Food Club's Rice Squares (Big Y).

Digestion

Samples were digested using wet ashing. To a 250 mL Erlenmeyer flask, 2 g of sample was added with 8 M TraceMetal™ Grade nitric acid (Fisher, catalog no: A509P212). The mixture was boiled for 5 minutes and then cooled. Once the mixture cooled, 10 mL deionized water was added. The whole mixture was filtered through 12.5 cm glass fiber filter paper (Fisherbrand, at:09-804-125A) into a 50 mL volumetric flask and diluted.

Each sample was then diluted by a factor of 5 in a 50 mL volumetric flask. The sample was then diluted to volume.

Matrix Modifier

In a 25 mL volumetric flask, 2.5 mL ____% diammonium phosphate, $(NH_4)_2HPO_4$ (Baker & Adamson, code:1311), was added with 0.25 mL 10% magnesium nitrate (PerkinElmer, part no: B0190634). The mixture was then diluted.

Cadmium Standard

In a 100 mL volumetric flask, 100 µl of 1 mg/ml cadmium stock solution (ACROS organics, catalog no: 195871000) was added and diluted. From this dilution, 100 µL was added to a new 100 mL volumetric flask and diluted to make a 1 ppb Cd standard.

Graphite Furnace Atomic Absorption Spectrometry

A new calibration curve was created each day. The calibration curve was created using the autosampler. The total volume of the standard and diluent was 20 μL. The volumes for the diluent and Cd stock are found in Table 1. To each injection, 5μL of matrix was also added.

Table 1. Amount of Cd stock and diluent that is taken up by the autosampler for each concentration of the calibration curve.

Concentration (ppb)	Standard (μL)	Diluent (μL)
0.1	2	18
0.2	4	16
0.4	8	12
0.6	12	8
0.8	16	4
1.0	20	0

The temperature parameters and the amount of time the temperature is held at is shown is Table 2. Samples were measured in triplicate. The two lowest temperatures dried the sample. At 500ºC, the nonmetal material was burned off. The measurement occurred at 1500ºC, which evaporated the metal for its absorbance to be read. The light source was a hollow cathode Cd lamp (PerkinElmer, part no: N3051020). The detector measured at a wavelength of 228.8 nm. The graphite tube was THGA with end caps (PerkinElmer, part no: B3000653).

Table 2. Temperature parameters for each absorbance measurement.

Temperature (ºC)	Ramp Time (sec)	Hold Time (sec)
110	1	30
130	15	30
500	10	20
1500	0	5
2450	1	3

III. Results

A typical calibration curve is shown in Figure 1. All the calibration curves demonstrated a close correlation, indicating that the data was linear all the way down to 0.1 ppb.

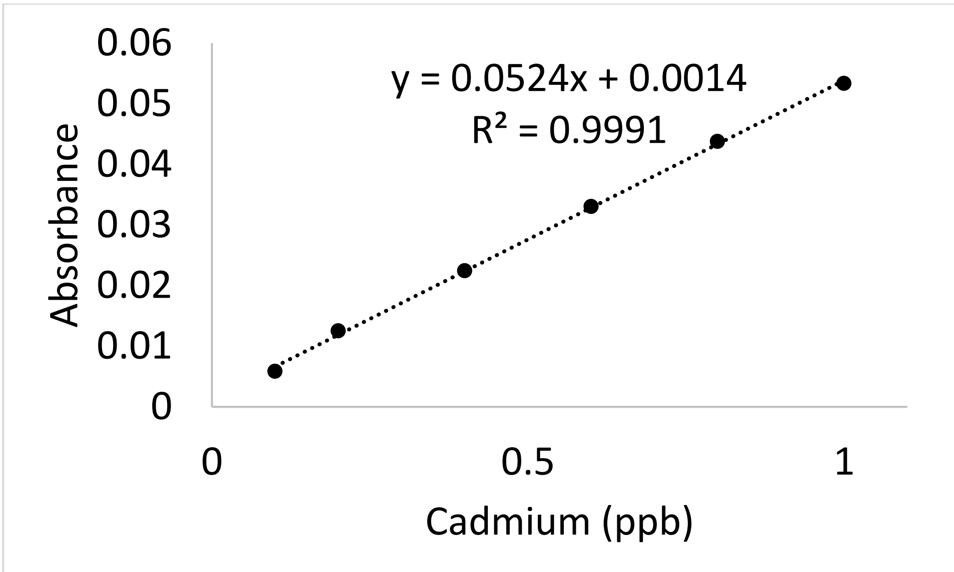

Figure 1. Typical calibration curve.

Concentrations of Cd in rice cereal are summarized in Table 3 in terms of µg/g of cereal. Samples were measured across a period of 10 days with 4 different sample groups. Day 1-5 were tested from sample group 1, day 6-7 were from sample group 2, day 8-9 were from sample group 3, and day 10 was sample group 4.

Table 3. The measured amount of Cd (µg/g) in samples of Chex, Signature Select, and Food Club.

Sample Group	Chex (µg/g)	Signature (µg/g)	Food Club (µg/g)
1	0.035	0.047	0.067
2	0.012	0.025	0.028
3	0.003	0.007	0.006
4	0.003	0.018	0.017

The average Cd across the three cereals from the 10 days of measurements is summarized in Figure 2. On average, Food Club had the highest amount of Cd with an average of 0.04 µg/g.

Signature Select followed with an average of 0.03 μg/g. The brand with the lowest average of Cd was Chex with an average of 0.02 μg/g.

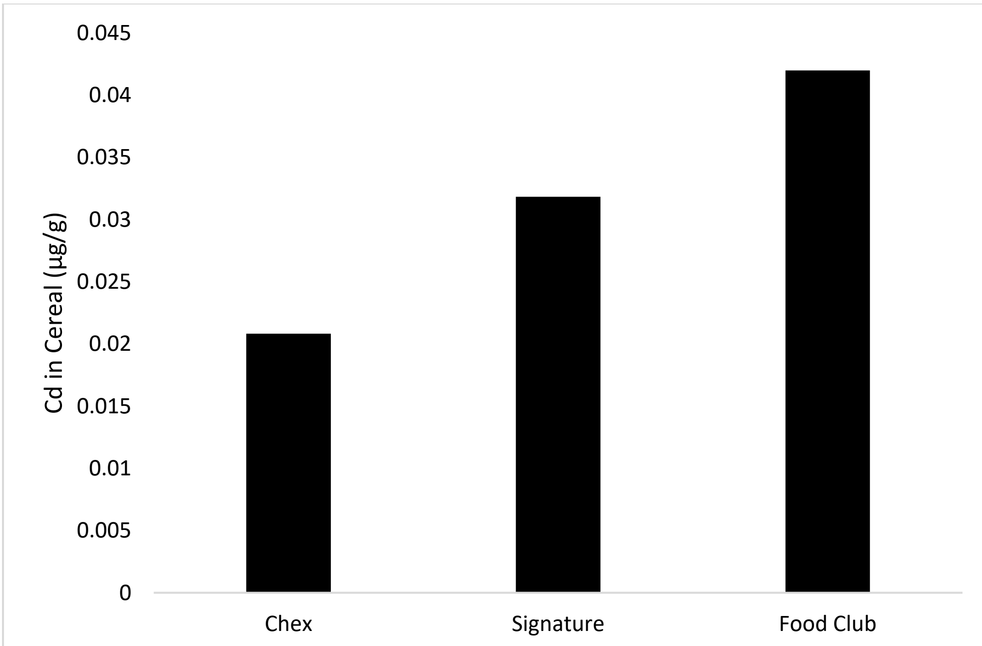

Figure 2. The average of amount of Cd (μg/g) in samples of Chex, Signature Select, and Food Club from 10 days of analysis.

The average concentrations of Cd found in the three brands in μg per 2 g portion is summarized in Table 4. A method blank (0.013 ± 0.009 μg) was used to calculate the limit of detection (LOD) and the limit of quantification (LOQ). The LOD was 0.015 μg while the LOQ was 0.051 μg.

Table 4. Average amount of Cd (μg) found in samples per 2 g Chex, Signature Selection, Food Club, and the method blank ± the standard deviation.

	μg
Chex	0.04 ± 0.03
Signature	0.06 ± 0.04
Food Club	0.09 ± 0.06
Method blank	0.013 ± 0.0006
LOD	0.015
LOQ	0.051

IV. Discussion

This study succeeded in finding measurable amounts of Cd in rice cereal. The limit of detection (LOD) is the lowest concentration of an analyte in a sample that can be consistently detected with a suitable degree of confidence. The limit of detection is 3 times the standard deviation of the blank plus the method blank. In the case of this study, the LOD was 0.015 μg. With the average concentration of Cd in the three samples being above the LOD, it can be concluded that there was a measurable amount of Cd in each. The limit of quantification (LOQ) is the lowest concentration that an analyte can be quantitatively detected with a stated accuracy and precision. The limit of quantification is the 10 times the standard deviation of the blank plus the method blank, which was measured to be 0.051 μg. Both Signature Select and Food Club were above this value.

While this data was collected in small sample sizes, there is something to be said about the low levels at which the samples were measured. With a limit of detection of 0.015 μg, this means that extremely low levels of Cd can be detected using the GFAAS. Assuming the 2 gram sample of cereal, the instrument was able to measure 7 ppt Cd in the cereal sample.

When it comes to acceptable levels of Cd in food, the cereals analyzed are well below the limit. There is no mention from the Food and Drug Administration (FDA) on Cd limit in cereal except in a plan called “Closer to Zero,” an action plan to reduce toxic metals in baby food. In this action plan, the limit for Cd in baby cereal would be 10 ppb (0.01 μg/g) if the plan is adopted. While the issue of Cd in cereal is on the FDA’s radar, it has not yet been fully researched. The total diet study report written by the FDA for the fiscal years 2018-2020, discussed the amounts of cadmium in different foods. In this study, it was determined that leafy greens, potatoes, and other root vegetables have the highest level of Cd.[17] There was mention that cereal was analyzed as well, but there was no data presented. This was a study to test levels of toxic metals, but there was no mention of limits. From Hong Kong's Centre for Food Safety, regulatory control put in place for cadmium in vegetables and carrots is 100 ppb (0.1 μg/g).[18] When comparing the data found in this study to the action plan proposed for "Closer to Zero," the levels would exceed the limit.

As mentioned previously, the Panel on Contaminants in the Food Chain of the European Food Safety Authority determined that the tolerable weekly intake (TWI) for cadmium was 2.5 μg/kg body weight.[5] For a 60 kg man, this would mean that he would be able to consume 150 μg of cadmium per week. If this man consumed one serving size of cereal (40 g) per day, he would be consuming 0.09 μg/kg/week (Chex), .15 μg/kg/week (Signature Select), or 0.19 μg/kg/week (Food Club) of Cd per serving. These are well below the limit that he could consume.

On the lower end of the experimental results, the Chex cereal had 20 μg/kg. Food Club was 20 μg/kg higher with an average concentration of 40 μg/kg. Signature Select was in the middle range with an average concentration of 30 μg/kg. Comparing these experimental results to previously reported values, the results were on par and on the lower end of the spectrum. From the Brisbane study, the measurable amounts of cadmium ranged from <10 to 110 μg/kg.[7] Just as in the Brisbane study, the one of the studies performed in China had a large range of <0.0025 to 253 μg/kg.[12] The other study in northern China had an overall average of 9.2 μg/kg in cereals.[13] The study performed in Japan in 1998 had a grand geometric mean of 50 μg/kg for uncooked rice.[11] With the varied range of Cd in literature values, it is hard to determine a precise average of Cd in cereal. However, the data found in this study is on par with previous studies performed outside of the U.S.

V. Conclusion

This study successfully found a measurable amount of Cd across all three samples. In a 2 g sample, Chex (0.04 ± 0.03 μg), Signature Select (0.06 ± 0.04 μg), and Food Club (0.09 ± 0.06 μg) were all above the LOD of 0.015 μg. Signature Select and Food Club were above the LOQ of 0.051 μg. These results were comparable to the literature values which have a low, but varied range. Due to low concentrations, it is difficult to precisely determine the amount of cadmium in the samples, but it can be confirmed that there is a measurable amount. Since Chex was below the LOQ, more analysis would have to be performed to determine the precise amount of cadmium. Once that is done, further analysis could be performed to determine if the samples are significantly different from each other. These results aligned with other literature values for Cd, having low and varied amounts. The low concentrations in these samples indicate that a person will not eat more than the TWI of 2.5 μg/kg body weight. As far as health risks are concerned, the low levels will not pose an effective risk to the consumer.

References

1. International Agency for Research on Cancer. In A Review of Human Carcinogens; IRC Monographs; International Agency for Research on Cancer: Lyon, **2012**; Vol. 100.
2. Chunhabundit, R. Cadmium Exposure and Potential Health Risk from Foods in Contaminated Area, Thailand. *Toxicological Research* **2016,** 32 (1), 65–72. DOI: 10.5487/TR.2016.32.1.065
3. Abedi T, Mojiri A. Cadmium Uptake by Wheat (Triticum aestivum L.): An Overview. Plants (Basel). **2020**, 9 (4):500. DOI: 10.3390/plants9040500
4. Kim, K.; Melough, M.; Vance, T.; Noh, H.; Koo, S.; Chun, O. Dietary Cadmium Intake and Sources in the US. Nutrients **2018**, 11 (1), 2. DOI: 10.3390/nu11010002
5. Alexander J.; Benford D.; Raymond Boobis A.; Ceccatelli S.; Cravedi J.; Di Domenico A.; Doerge.; Dogliotti E.; Elder L.; Farmer P.; Filipič M.; Fink-Gremmels J.; Fürst P.; Guérin T. Katrine Knutsen H.; Machala M.; Mutti A.; Rudolf Schlatter J.; van Leeuwen R. Statement on Tolerable Weekly Intake for Cadmium. *EFSA Journal* **2011**, 9 (2).
6. Genchi, G.; Sinicropi, M. S.; Lauria, G.; Carocci, A.; Catalano, A. The Effects of Cadmium Toxicity. *International Journal of Environmental Research and Public Health* **2020**, 17 (11), 3782. DOI: 10.3390/ijerph17113782
7. Tinggi, U.; Schoendorfer, N. Analysis of Lead and Cadmium in Cereal Products and Duplicate Diets of a Small Group of Selected Brisbane Children for Estimation of Daily Metal Exposure. J. *Trace Elem. Med. Biol*. **2018**, 50, 671–675. DOI: 10.1016/j.jtemb.2018.06.022

8. Sarwar, N.; Saifullah; Malhi, S. S.; Zia, M. H.; Naeem, A.; Bibi, S.; Farid, G. Role of Mineral Nutrition in Minimizing Cadmium Accumulation by Plants. *Journal of the Science of Food and Agriculture* **2010**, 90 (6), 925–937. DOI: 10.1002/jsfa.3916
9. Nishijo, M.; Nakagawa, H.; Suwazono, Y.; Nogawa, K.; Kido, T. Causes of Death in Patients with Itai-Itai Disease Suffering from Severe Chronic Cadmium Poisoning: A Nested Case–Control Analysis of a Follow-up Study in Japan. *BMJ* Open **2017**, 7 (7). DOI: 10.1136/bmjopen-2016-015694
10. Wilschefski, S.; Baxter, M. Inductively Coupled Plasma Mass Spectrometry: Introduction to Analytical Aspects. *Clinical Biochemist Reviews* **2019**, 40 (3), 115–133. DOI: 10.33176/AACB-19-00024
11. Shimbo, S.; Zhang, Z.-W.; Watanabe, T.; Nakatsuka, H.; Matsuda-Inoguchi, N.; Higashikawa, K.; Ikeda, M. Cadmium and Lead Contents in Rice and Other Cereal Products in Japan in 1998–2000. *Science of The Total Environment* **2001**, 281 (1-3), 165–175. DOI: 10.1016/s0048-9697(01)00844-0
12. Xie, L. H.; Tang, S. Q.; Wei, X. J.; Shao, G. N.; Jiao, G. A.; Sheng, Z. H.; Luo, J.; Hu, P. S. The Cadmium and Lead Content of the Grain Produced by Leading Chinese Rice Cultivars. *Food Chemistry* **2017,** 217, 217–224. DOI: 10.1016/j.foodchem.2016.08.099
13. Zhang, Z.-W.; Watanabe, T.; Shimbo, S.; Higashikawa, K.; Ikeda, M. Lead and Cadmium Contents in Cereals and Pulses in North-Eastern China. *Science of The Total Environment* **1998**, 220 (2-3), 137–145. DOI: 10.1016/s0048-9697(98)00252-6
14. Pillay A.E.; Stephen S.; Xavier G. Heavy Metal Toxins in Breakfast Cereals – a Baseline Study Using Hybrid Plasma Mass Spectrometry. *Journal of Analytical & Pharmaceutical Research* **2018**, 7 (4). DOI: 10.15406/japlr.2018.07.00270

15. Watanabe, T.; Shimbo, S.; Moon, C.-S.; Zhang, Z.-W.; Ikeda, M. Cadmium Contents in Rice Samples from Various Areas in the World. *Science of The Total Environment* **1996,** 184 (3), 191–196. DOI: 10.1016/0048-9697(96)05100-5
16. Center for Food Safety and Applied Nutrition. Closer to zero: Reducing childhood exposure to contaminants from foods. https://www.fda.gov/food/environmental-contaminants-food/closer-zero-reducing-childhood-exposure-contaminants-foods (accessed Jan 31, 2023).
17. Winfield S.; Hoffman-Pennesi D.; Boyer M; Spungen J.; Vonderbrin J.; Councell T.; Nyambok E.; Gavelek A.; Cooper K.; Kato D. Total Diet Study Report - Food and Drug Administration. fda.gov/media/159745/download (accessed Dec 3, 2022).
18. Food Contaminants -Cadmium in Food. https://www.cfs.gov.hk/english/programme/programme_rafs/programme_rafs_fc_02_04.html#:~:text=The%20levels%20are%20set%20at,of%20animal%20and%20poultry%2C%20respectively (accessed Dec 3, 2022).