Assessment of Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Cd, and Pb Concentrations in Gluten-free Foods From Saudi Arabia by Inductively Coupled Plasma Mass Spectrometry

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INTRODUCTION

The determination of trace element concentrations in food samples is of great importance for human health (1-5). For proper function of the organs, cobalt (Co), zinc (Zn), and copper (Cu) are necessary, while elements such as lead (Pb) and cadmium (Cd) are toxic at traces levels. Essential trace elements become problematic in excess (6-8). The accurate and precise determination of these elements is generally performed using the inductively coupled plasma mass spectrometry and atomic absorption spectrometry techniques (9-13).

Celiac disease is classified as intolerance for gluten in genetically predisposed individuals and is characterized by an inappropriate immune response of the T-lymphocytes in the small intestines to gluten peptides (14). This disease was generally considered to start in childhood, but the profile has changed and today one out of five newly diagnosed individuals is over 65 years old. Celiac disease is a worldwide phenomenon. Approximately 2% of the world's population has celiac disease (15), also called gluten-sensitive enteropathy which causes immunological gluten intolerance. Gluten is found in foods containing wheat, barley, and rye. Thus, these individuals should be on a gluten-free diet to solve their health problems (14-18).

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ABSTRACT

The levels of arsenic, cadmium, chromium, cobalt, copper, iron, lead, manganese, nickel, and zinc in some gluten-free food samples used for celiac disease patients have been determined after microwave digestion by inductively coupled plasma mass spectrometry (ICP-MS). The concentrations were found in the range of 0.09–0.66 (As), 2.9–6.6 (Cd), 4.7–100.3 (Cr), 866–2009 (Co), 0.043–0.26 (Cu), 3.2–17.4 (Fe), 1.4–10.5 (Pb), 12.9–41.3 (Mn), 0.35–0.46 (Ni) and 0.021–0.268 (Zn) mg kg⁻¹. The detection limits for As, Cd, Cr, Co, Cu, Fe, Pb, Mn, Ni, and Zn were 0.33, 0.009, 0.26, 0.041, 0.17, 1.36, 0.025, 0.061, 0.042, and 0.29 mg kg⁻¹, respectively. The accuracy of the method was confirmed by analysis of the standard reference material SRM 1568a Rice Flour. The results were compared with related works published for gluten-free foods used around the world and it was found that the Mn and Fe levels obtained in this study were at higher levels. The highest Ni, Co, Fe, and Cr levels were in Rice Flakes. The lowest Mn, Co, Zn, As, and Cd levels were in the Rice Thins samples.

A hierarchical cluster analysis of the results was performed to identify similarities between the food samples based on element component.

Symptoms of celiac disease are diarrhea, bloating, abdominal pain, constipation, muscular disturbances, headaches, migraines, and bone or joint pain (18).

Inductively coupled plasma mass spectrometry (ICP-MS) is a powerful instrumental detection technique for trace elements in environmental samples including food samples. This technique is preferred to atomic absorption spectrometry (AAS) and inductively coupled plasma atomic emission spectrometry (ICP-AES) due to its lower detection limits for analyte elements in comparison to AAS and ICP-AES (14, 19, 20).

According to our literature survey, no study has been reported on the metal content of gluten-free food samples from Saudi Arabia after microwave digestion. This pilot study is the first on this subject.

In the present work, the trace element concentrations of some gluten-free foods from Saudi Arabia were determined by ICP-MS after microwave digestion. The accuracy of the method was confirmed by analysis of the standard reference material SRM 1568a Rice Flour. The hierarchical cluster analysis of the results was also investigated to identify similarities between food samples based on element components.

EXPERIMENTAL

Instrumentation

An Agilent 7500a inductively coupled plasma mass spectrometer (Agilent Technologies, Palo Alto, CA, USA) was used for the determination of the analytes. The instrument was optimized daily before measurement and operated as rec-

ommended by the manufacturer. The instrumental parameters are listed in Table I.

A Hettich Universal 320 centrifuge (Tuttlingen, Germany) was used to separate the undissolved parts of the samples. A Speedwave MWS microwave oven (Berghof, Germany) was used for sample digestion.

Reagents and Solutions

Analytical grade reagents and chemicals (Merck, Darmstadt, Germany) were used. Ultra-pure water was obtained using a Milli-Q® system (18.2 MΩ-cm resistivity) (Millipore Corporation, USA). Stock standard solutions (1000 mg L⁻¹) of the analyte elements were obtained from Merck, Darmstadt, Germany. Working standards of the corresponding metal ions were prepared from dilution of the stock standard solutions with distilled water. Certified standard reference material NIST SRM 1568a Rice Flour was obtained from the National Institute of Standards and Technology (NIST), Gaithersburg, MD, USA.

Sampling and Sample Preparation

For this study, gluten-free food samples were purchased at local

markets in Jeddah, Saudi Arabia. The samples were dried at 105 °C, ground with a mortar, and then stored in plastic bags. Prior to analysis, the samples were kept away from sand dust to avoid element contamination.

The samples were placed in closed Teflon® vessels and digested in the microwave oven (18, 21). An amount of 100 mg gluten-free food sample was accurately weighed into the PTFE digestion vessels, 10 mL of concentrated HNO₃ was added, and then left standing for about 20 minutes before closing the vessels. The decomposition of the samples was carried out in a microwave digestion system using a two-step program (see Table II). The undissolved parts were separated by centrifugation at 4000 rpm for 10 minutes. The extract was transferred into volumetric flasks and made up to 25-mL volume with double distilled water. Blank experiments were also carried out in the same way. The analyte elements were determined by ICP-MS.

The standard reference material SRM 568a Rice Flour was digested with the same microwave digestion procedure as given above and analyzed by ICP-MS.

RESULTS AND DISCUSSION

Accuracy of the digestion method was verified by using the certified reference material SRM SRM 1568a Rice Flour. The results listed in Table III were found to be within the certified values. The digestion method was chosen due to its accuracy with respect to both recovery and time values. A comparison of these results shows that the current digestion procedure is free from the interference of matrix components in the food samples.

The detection limits for As, Cd, Cr, Co, Cu, Fe, Pb, Mn, Ni, and Zn were 0.33, 0.009, 0.26, 0.041, 0.17, 1.36, 0.025, 0.061, 0.042, and 0.29 mg kg⁻¹, respectively. The concentrations of the analyte elements in gluten-free food samples from Saudi Arabia are given in Table IV as dry weight. The concentration levels for all samples were at the mg kg⁻¹ level. The level of Fe was the highest, while the As and Cd levels were lowest.

TABLE II
Microwave Oven Heating Program for the Decomposition of Gluten-free Food Samples

Step	Program 1	Program 2
T (°C)	145	190
P (bar)	50	50
Power (%)	70	90
Ta (min)	10	5
Time (min)	5	10

TABLE III
Concentrations of Analyte Elements in SRM 1568a Rice Flour

Element	Concentration (mg kg ⁻¹)		
	Certified Value	Found	Recovery (%)
Cu	2.4±0.3	2.4±0.3	99
Fe	7.4±0.9	7.5±0.2	101
Mn	20.0±1.6	19.2±0.2	96
Zn	19.4±0.5	18.5±0.6	95
Cd	0.022±0.002	BDL ^a	-

^a BDL: Below the detection limit.

TABLE I
Operating Conditions for Agilent 7500a ICP-MS

Nebulizer	Babington
Spray Chamber	Quartz, Double pass
RF Power	1220 W
Frequency	27.12 MHz
Sampling Depth	7.0 mm
Plasma Gas Flow Rate	15 L min ⁻¹
Auxiliary Gas Flow Rate	1.0 L min ⁻¹
Carrier Gas Flow Rate	1.15 L min ⁻¹
Sample Uptake Rate	0.3 mL min ⁻¹
Detector Mode	Auto
Integration Time	3 s
Internal standards	⁹ Be, ⁴⁵ Sc, ¹⁰³ Rh, ²⁰⁸ Bi (200 ppb)

Arsenic (As)

Arsenic is one of the most toxic elements (22-24) and has serious health effects on humans, animals, and plants. It is an environmental and food chain contaminant as well as a carcinogen; drinking water and foodstuffs are the two main common sources of As. Arsenic levels were found below the detection limit of ICP-MS in 13 samples (Table IV). The As content of gluten-free samples from Saudi Arabia ranged from 0.35 to 0.46 mg kg⁻¹ (highest in bread mix and lowest in chocolate balls). Munera-Picazo et al. reported that the As concentrations in rice-based gluten-free food samples for children and adults with celiac disease ranged from 16.8–256 µg kg⁻¹ (17) and 6.2–120 µg kg⁻¹ (15). The As content of the gluten-free food samples

from Italy were in the range of 4x10⁻⁴ to 0.088 mg kg⁻¹ (14). The As levels of the analyzed samples of this study were lower than the maximum corresponding levels set by the World Health Organization (WHO) (24).

Cadmium (Cd)

Cadmium is also most serious, hazardous, and carcinogenic to health (25, 26). Consumption of contaminated food is the main source for human exposure to Cd. The Cd levels found in four samples (Chocolate Balls, Rice Thins, Cereal Balls, and Corn Thins) are below the ICP-MS detection limits (Table IV). As can be seen, while the lowest level of Cd was in Crispy Bread (0.021 mg kg⁻¹), the highest level was in Coconut Biscuit (0.268 mg kg⁻¹). Hernández-Martínez and Navarro-Blasco (26) reported Cd

levels of conventional and organic infant cereals from Spain to contain levels of 4.7 µg kg⁻¹ and 25.5 µg kg⁻¹, respectively. The Cd content of the food samples from Palermo, Italy, ranged from 0.002 to 0.12 mg kg⁻¹ (14). The Cd levels of the samples of this study, except for Coconut Biscuit and Bread Mix, were lower than the maximum corresponding levels as set by the EC (1881/2006) (27).

Chromium (Cr)

Chromium is an essential element at very low levels for some body functions (28, 29). For instance, Cr(III) is essential for glucose tolerance functions, while Cr(VI) is very toxic. The minimum level of Cr was found in the Milky Biscuit sample (mean 2.9 mg kg⁻¹), maximum was found in the Rice

TABLE IV
Concentrations of Some Elements in Gluten-free Food Samples (N=3)

Sample	Concentration (mg kg ⁻¹)									
	As	Cd	Cr	Co	Cu	Fe	Pb	Mn	Ni	Zn
Coconut Biscuit	BDL	0.268±0.035	4.0±0.3	0.15±0.02	8.8±0.7	1597±101	0.14±0.01	67.3±3.5	6.3±0.5	35.2±3.9
Chocolate Balls	BDL	BDL	5.2±0.1	0.19±0.01	BDL	1470±21	0.66±0.02	68.6±0.5	3.2±0.9	12.9±0.9
Rice Thins	BDL	BDL	3.7±0.1	0.043±0.007	1.4±0.1	946±1	0.12±0.01	4.7±0.6	3.8±0.1	BDL
Milky Biscuit	BDL	0.031±0.004	2.9±0.1	0.13±0.05	2.5±0.5	866±96	0.56±0.07	BDL	3.7±0.2	15.2±0.7
Breakfast Rolls	0.35±0.06	0.046±0.002	5.3±0.2	0.18±0.01	5.0±0.2	1689±187	0.39±0.09	10.4±2.0	6.7±0.9	20.0±0.6
Cereal Balls	BDL	BDL	5.4±0.1	0.08±0.001	2.6±0.1	1205±28	0.13±0.01	5.2±0.7	4.3±0.5	12.9±1.7
Rice Flicks	0.44±0.04	0.034±0.001	6.6±0.1	0.26±0.02	9.0±0.2	2009±8	0.42±0.01	15.8±0.5	42.3±3.8	26.0±1.9
Spaghetti	BDL	0.088±0.010	5.2±0.2	0.10±0.01	4.9±0.1	1381±14	0.11±0.01	100.3±0.7	8.9±1.4	18.5±0.8
Crispy Bread	BDL	0.021±0.000	5.5±0.5	0.07±0.01	7.5±0.8	1247±45	0.09±0.01	29.1±0.3	BDL	27.5±7.6
Snacks	BDL	0.021±0.003	5.2±0.1	0.08±0.001	10.2±0.6	1390±9	0.12±0.01	5.1±0.2	5.3±0.2	41.3±0.8
White Loaf	BDL	0.067±0.005	6.5±0.4	0.15±0.01	8.5±0.2	1750±70	0.52±0.15	15.3±0.7	5.6±0.2	18.1±0.4
Corn Thins	BDL	BDL	4.8±0.3	0.20±0.03	9.7±0.1	1562±3	0.15±0.01	43.9±0.4	3.9±0.2	41.3±0.2
Bread Mix	0.46±0.02	0.149±0.011	5.0±0.3	0.17±0.02	9.9±0.9	1875±53	0.17±0.01	51.9±0.8	17.4±2.4	34.7±1.2
Cake Mix	BDL	0.044±0.005	4.9±0.6	0.07±0.01	4.8±0.7	1210±27	0.36±0.02	11.6±2.4	8.7±0.9	14.1±0.5
Brown Loaf	BDL	0.043±0.007	3.5±0.1	0.13±0.01	7.4±0.3	1377±25	0.11±0.01	17.6±0.5	3.4±0.3	19.6±1.8
Chocolate Petals	BDL	0.027±0.002	5.3±0.2	0.25±0.02	10.5±0.6	1518±208	0.21±0.02	11.9±0.2	11.2±1.2	19.6±0.3

BDL: Below the detection limit.

Flicks sample (mean 6.6 mg kg⁻¹). Orecchio et al. (14) reported a Cr concentration in food samples for celiac people from Italy in the range of 0.0091 to 14.4 mg kg⁻¹. While there is no standard maximum limit, The Food and Nutrition Board of the NAS/NRC (30) states that a safe, adequate intake of Cr for an adult is 50–200 µg/day. The Cr levels of analyzed samples were found higher than these values.

Cobalt (Co)

Cobalt is an essential element to improve some of our body functions which includes the brain functions (31–33). In this study, the lowest Co level was found in Rice Thins at 0.043 mg kg⁻¹ and the highest in Rice Flicks at 0.26 mg kg⁻¹. There is limited study in the literature about the Co content of gluten-free foods. Orecchio et al. (14) reported the Co concentration ranging from $3 \cdot 10^{-4}$ to 0.54 mg kg⁻¹ with an average value of 0.084 mg kg⁻¹ in foods given to celiac people from Italy (14). The levels of Co in the samples used for this study are also within the range as reported by Orecchio et al. (14).

Copper (Cu)

Copper is an essential element for human beings (34, 35) and plays various important metabolic functions for proteins and metalloenzymes. The mean concentrations of Cu were in the range of 1.4–10.5 mg kg⁻¹. The lowest level of Cu was in Rice thins, while the highest levels were found in snack samples. Orecchio et al. (14) reported that Cu concentrations of celiac food samples from Palermo, Italy, ranged from 0.14 to 1.8 mg kg⁻¹. It is difficult to assess any health risk of Cu from foods since there are no standard maximum limits for copper. The WHO (World Health Organization) recommends 2–9 mg per day for an adult (36). The Brazilian Ministry of Health recommends 10 mg kg⁻¹ as

the maximum Cu level (37). In general, the Cu levels found in this study were below these recommended values (36, 37).

Iron (Fe)

Iron is an essential mineral necessary for many important metabolic functions of the body (32, 38). It is part of hemoglobin, the oxygen-carrying component of the blood. Iron not attached to the hemoglobin in the red blood cells is stored in the liver, bone marrow, spleen, and muscles. A lack of Fe leads to anemia, and the symptoms include severe weakness and fatigue. The mean Fe levels of our samples were in the range of 866–2009 mg kg⁻¹ (highest in Rice Flicks, lowest in Milky Biscuit). Orecchio et al. (14) reported Fe levels in gluten-free food samples ranging from 1.1 to 83 mg kg⁻¹. According to the Turkish Food Codex (39), the maximum Fe level permitted for food is 15 mg kg⁻¹. The iron levels of the analyzed samples of the present work were generally found to be higher than the official values.

Lead (Pb)

Lead is a highly toxic metal when inhaled or ingested and is extremely harmful to the human body systems and organs (40, 41). The main target and damages of Pb toxicity in adults and children is the nervous system. Lead toxicity, especially in middle-aged and elderly people, causes an increase in blood pressure and anemia (42–44). The highest level of Pb was found in Chocolate Balls (0.66 mg kg⁻¹) and lowest in Spaghetti (0.11 mg kg⁻¹). Hernández-Martínez and Navarro-Blasco (26) reported the Pb content of conventional and organic infant cereals marketed in Spain at the 12.4 µg kg⁻¹ and 170 µg kg⁻¹ level, respectively. The Pb concentration in gluten-free food samples from Italy was reported to range from 0.0013 to 1.1 mg kg⁻¹ (14). The

maximum corresponding Pb level for cereals set by the EC (1881/2006) is 0.2 mg kg⁻¹ (27). The Pb levels of Chocolate Balls, Milky Biscuit, Breakfast Rolls, Rice Flicks, White Loaf, Cake Mix, and Chocolate Petals samples were found higher than the maximum allowable levels as set by the EC (1881/2006) (27).

Nickel (Ni)

Nickel plays an important part in overall health of the human body and in particular on the adrenaline and glucose metabolism and the production of the red blood cells (45–46). Nickel is found in many foods and in all animal tissue as well as in most human tissue. Nickel concentration in the Crispy Bread samples was found below the detection limit of the ICP-MS. Minimum and maximum values of Ni in gluten-free samples were found to be 3.2 mg kg⁻¹ (Chocolate Balls) and 42.3 mg kg⁻¹ (Rice Flicks). The concentration of Ni for gluten-free foods from Italy ranged from 0.016 to 15 mg kg⁻¹ (14). The Turkish Official Gazette for Turkish standards (47) reported the maximum allowable Ni levels in some food samples as 0.2 mg kg⁻¹. The Ni levels of the analyzed samples except for Crispy Bread were higher than the reported values (14, 47).

Manganese (Mn)

Trace amounts of Mn are very important for good health (48–50). It makes the bones strong yet flexible, aids the body in absorbing Vitamin B1, and acts as an important activator for the body to use enzymes. The Mn levels in Milky Biscuit samples were found below the detection limit of the ICP-MS. The mean highest levels of Mn were found in the Spaghetti samples (mean 100.3 mg kg⁻¹) and lowest in the Rice Thins (mean 4.7 mg kg⁻¹). In the Orecchio et al. study (14), the Mn concentrations in food samples from Italy for celiac people

ranged from 0.39 mg kg⁻¹ to 4.7 mg kg⁻¹ (14). While there is no standard maximum limit for Mn, the National Research Council's "estimated safe and adequate daily dietary intake" is 2–5 mg (31). The intake of Mn from food, water, and dietary supplements per day should be lower than 11 mg (31). When comparing the Mn levels of the samples of this study with the recommended daily intake, the Mn levels of some samples were higher than the Council's limit (31).

Zinc (Zn)

Zinc is known to be involved in most metabolic pathways in humans (51–53). Zinc deficiency can lead to loss of appetite, growth retardation, skin changes, and immunological abnormalities. Zinc is widespread among living organisms due to its biological significance. As can be seen in Table IV, the Zn level was found below the detection limit of ICP-MS in only one sample (Rice Thins). The concentration range of Zn in our gluten-free food samples was 12.9–41.3 µg/g. The highest level was in snacks, while the lowest level was found in Chocolate Balls. The Zn concentration in gluten-free foods has been reported to range from 1.1 to 137 mg/kg (14). According to the Turkish Food Codex (47), the maximum level of Zn permitted for foods is 5 mg kg⁻¹. The maximum tolerable daily intake of Zn set by WHO is 0.3–1.0 mg kg⁻¹ (54). The Zn levels of our samples were higher than these values.

Hierarchical Cluster Analysis (HCA)

Hierarchical cluster analysis (HCA) is used to categorize the objects of a system into classes or clusters based on their similarities. In this study, HCA was used in order to identify similarities between food samples based on element components. The Euclidean distance for similarities

between variables and the Ward linkage algorithm was used to link a group (cluster) of variables with similar distances. The MINITAB-16 program was used for HCA. The dendrogram is presented in Figure 1. Six groups were formed according to the HCA results and are shown in Figure 1.

- The first group consisted of Coconut Biscuit, Corn Thins, Chocolate Balls, and Chocolate Petals,
- The second group, Spaghetti, Snacks, and Brown Loaf,
- The third group, Breakfast Rolls and White Loaf;
- The fourth group, Rice Flicks and Bread Mix,
- The fifth group, Rice Thins and Milky Biscuit,
- The sixth group, Cereal Balls, Cake Mix, and Crispy Bread.

It can be thought that all of the As, Cd, Cr, Co, Cu, Fe, Pb, Mn, Ni and Zn concentrations of the samples have similar impact on the formation of both the first group and

the second group. While the Cr and Fe concentrations in the third group were relatively high in the White Loaf and Breakfast Rolls samples, the Cr, Fe, Ni, and As concentrations in of the fourth group were at high levels in the Rice Flicks and Bread Mix samples (Table IV), This led the researchers to think that these food samples are grouped into the same clusters according to these high concentration levels of the metals. On the other hand, just as all metal concentrations are at low levels in the Rice Thins and Milky Biscuit samples of the fifth group, the Co and Pb concentrations are at low levels in the sixth group, leading us to think that the low concentrations of the metals play a significant role in grouping them (Table IV).

In a nutshell, ICP-MS findings can be a valuable tool in providing extra information about grouping food samples based on heavy metal concentrations through the use of HCA. This information could be especially useful for those who consume these types of foods as well as for researchers wishing to find relevant data with HCA.

Fig. 1. The dendrogram showing the results of hierarchical clustering analysis in food samples according to their element components, similarity level > 80 (x-axis: 1=Coconut Biscuit, 2=Chocolate Balls, 3=Chocolate Petals, 4=Corn Thins, 5=Spaghetti, 6=Snacks, 7=Brown Loaf, 8=White Loaf, 9=Breakfast Rolls, 10=Rice Flicks, 11=Bread Mix, 12=Rice Thins, 13=Milky Biscuit, 14=Cereal Balls, 15=Crispy Bread, 16=Cake Mix).

CONCLUSION

In this pilot study, the levels of the trace elements As, Cd, Cr, Co, Cu, Fe, Pb, Mn, Ni, and Zn found in gluten-free foods sold for consumption by celiac patients from Saudi Arabia were analyzed by ICP-MS. The Fe levels were highest, while the Cd levels were lowest for all samples. The Coconut Biscuit, Bread Mix, Corn Thins, Chocolate Petals, Breakfast Rolls, and Rice Flicks samples show the highest rates of Fe, Mn, Cu, Zn, and Ni. Because of the relatively high metal levels and their high consumption rate, these foods are a very important source of micronutrients for the population of countries with similar dietary habits. A comparison was made of the trace element levels in the gluten-free foods with the maximum corresponding levels or recommended values as set by WHO, the National NAS/NRC, the Turkish Food Codex, the Turkish standards, the Brazilian Ministry of Health, and the EC. This study shows that while the levels of Cr, Fe, and Zn in the analyzed samples were higher than the maximum or recommended values, the levels of As and Cd in the samples analyzed were lower.

Received June 6, 2015.

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