Review Article

A BRIEF REVIEW: HEAVY METAL AND THEIR ANALYSIS

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ABSTRACT

The research development of heavy metal is not a new area of science, having existed for around more than a century. The study of heavy metal is called heavy metal science. It is a provocative field of science, having experienced steady and strong growth over its history, with many companies investing large amounts of money into the development of new method to estimating and eliminating heavy metal from the different house hold thing, cosmetics, food and drug formulation. This review was focused on the heavy metal toxicity and its estimating different analytical technique that are now in development.

Keywords: Heavy metals, Analysis, Development.

INTRODUCTION

The mineral nutrition of higher plants is of fundamental importance to agriculture and human health, yet many basic questions remain unanswered, particularly in relation to the accumulation of essential heavy metals. Heavy metal ions such as Cu₂, Zn₂, Mn₂, Fe₂, Ni₂ and Co₂ are essential micronutrients for plant metabolism but when present in excess, these, and non-essential metals such as Cd_2 , Hg_2 , Ag_2 and Pb_2 , can become extremely toxic.¹ Pollution of different environments is due to human activities in recent years. One of such pollution is marine pollution by heavy metals. The heavy metals are accumulated in the marine environment then transfer to the marine organisms e.g. fishes by different ways. When their concentrations exceed the required levels, they become toxic and cause several health problems. The fishes became sick then die when too much contamination is happened² Herbs, minerals, and metals are used in Ayurvedic HMPs. Lead toxicity has been associated with use of Ayurvedic HMPs, including status epileptics, fatal infant encephalopathy, congenital paralysis and sensor in euraldeafness, and developmental delay. Since 1978, at least 55 cases of heavy metal intoxication associated with Ayurvedic HMPs in adults and children have been reported in the United States and abroad.³ Pesticide and heavy metals are persistent and non biodegradable and they can be bio accumulated through the biologic chains. For this reason, accurate monitoring of their concentration plays an important role. Population can be contaminated with organic pollutants and heavy metals by ingestion of contaminated or polluted food and water. The gravity of toxic effect depends on nature, concentration, body resistance and presence of other contaminants. The concentration of this element in food products is varied, depending of their origin, storage conditions and processing technologies.⁴ These metals have peculiar characteristics including that (1) they do not decay with time (2) They can be necessary or beneficial to plants at certain levels but can be toxic

when exceeding specific thresholds, (3) they are always present at a background level of non-anthropogenic origin, their input in soils being related to weathering of parent rocks and paedogenesis and (4) they often occur as cations which strongly interact with the soil matrix, consequently, heavy metals in soils can become mobile as a result of changing environmental conditions. This situation is referred to as Chemical timing bomb" Sources of these elements in soils mainly include natural occurrence derived from parent materials and human activities It is necessary then to evaluate the relationship among these.⁵ In support of the toy industry, many laboratories are being called up onto analyze a wide variety of sample matrices for metal content. The primary element of interest is lead, but a number of other toxic elements pose a considerable threat, especially for children. This subset of elements, known as heavy metals, includes antimony, arsenic, barium, cadmium, chromium, selenium, mercury and lead as they are all known to accumulate in the body and cause detrimental effects over time. Some plastic and wooden toys, particularly those with painted surface shave demonstrated elevated levels of Pb and other elements. Regulations exist which provide limits in materials for which surface contact with children can result in possible ingestion.⁶ The U.S. Environmental Protection Agency, the Agency for Toxic Substances and Disease Registry (ATSDR) has complied priority list in 2001 called the "Top 20Hazardous Substances". The heavy metals Arsenic, Lead, Mercury, and Cadmium ranked 1st, 2nd, 3rd, and 4th in the list, respectively. Since Arsenic, Lead, and Mercury ranked as the top three most hazardous substances in the said priority list, there searchers formulated this study to determine the presence or absence of these toxic heavy metals in selected samples of infant formula milk using Atomic Absorption Spectrophotometry (AAS). Presence of these heavy metals is to be measured in parts per million (ppm), and the obtained values are to be compared to the Provisional Tolerable Weekly Intake (PTWI) for toxic metals as set by the Food and Agriculture



Organization/World Health Organization Joint Expert Committee on Food Additives (JECFA)⁷

Limitation of few heavy metal as per WHO⁸

Lead (WHO limit 10 ppm)

Cadmium (WHO limit 0.3)

Mercury (WHO limit 1)

Arsenic (WHO limit 10)

Pathway of heavy metals intake in human⁹

Heavy metals are individual metals and metal compounds that can impact human health. Eight common heavy metals are: arsenic, barium, cadmium, chromium, lead, mercury, selenium, and silver. These are all naturally occurring substances which are often present in the environment at low levels. In larger amounts, they can be dangerous. Generally, humans are exposed to these metals by ingestion (drinking or eating) or inhalation (breathing).

	Form Entering Body	Major Route of Absorption	Distribution	Major Clinical Effects	Key Aspects of Mechanism	Metabolism and Elimination
Arsenic	Inorganic arsenic salts	Gastrointestinal, respiratory (all mucosal surfaces), skin	Predominantly soft tissues (highest in liver, kidney). Avidly bound in skin, hair, nails	Cardiovascular: shock, arrhythmias. CNS: encephalopathy, peripheral neuropathy. Gastroenteritis; pancytopenia; cancer (many sites)	Inhibits enzymes; interferes with oxidative phosphorylation; alters cell signaling, gene expression	Methylation. Renal (major); sweat and feces (minor
Lead	Inorganic lead oxides and salts	Gastrointestinal, respiratory	Soft tissues; redistributed to skeleton (> 90% of adult body burden	CNS deficits; peripheral neuropathy; anaemia; nephropathy; hypertension; reproductive toxicity	Inhibits enzymes; interferes with essential cations; alters membrane structure	Renal (major); feces and breast milk (minor
	Organic (tetraethyl lead	Skin, gastrointestinal, respiratory	Soft tissues, especially liver, CNS	Encephalopathy	Hepatic de alkylation (fast) →tri alky metabolites (slow) →dissociation to lead	Urine and feces (major); sweat (minor
Mercury	Elemental mercury	Respiratory tract	Soft tissues, especially kidney, CNS	CNS: tremor, behavioral (erethism); gingivostomatitis; peripheral neuropathy; acrodynia; pneumonitis (high-dose	Inhibits enzymes; alters membranes	Elemental Hg converted to Hg ²⁺ . Urine (major); feces (minor
	Inorganic: Hg ⁺ (less toxic); Hg ²⁺ (more toxic)	Gastrointestinal, skin (minor	Soft tissues, especially kidney	Acute tubular necrosis; gastroenteritis; CNS effects.	Inhibits enzymes; alters membranes	Urine
	Organic: alkyl, aryl	Gastrointestinal, skin, respiratory (minor	Soft tissues	CNS effects, birth defects	Inhibits enzymes; alters microtubules, neuronal structure	Deacylation. Fecal (alkyl, major); urine (Hg ²⁺ after deacylation, minor)

Toxicology of Selected Arsenic, Lead, and Mercury Compounds¹⁰

Effect of heavy metals in our body⁹

Arsenic

Aside from occurring naturally in the environment, arsenic can be released in larger quantities through volcanic activity, erosion of rocks, forest fires, and human activity.

Health effects

Arsenic is odourless and tasteless. Inorganic arsenic is a known carcinogen and can cause cancer of the skin, lungs, liver and bladder.

• Ingestion of very high levels can possibly result in death.

• Long-term low level exposure can cause a darkening of the skin and the appearance of small "corns" or "warts" on the palms, soles, and torso.

Regulatory limits

• Environmental Protection Agency (EPA) - 0.01 parts per million (ppm) in drinking water.

• Occupational Safety and Health Administration (OSHA) - 10 micrograms per cubic meter of workplace air (10 μ g/m3) for 8 hour shifts and 40 hour work weeks

Barium

Barium is a very abundant, naturally occurring metal and is used for a variety of industrial purposes.



Health effects

Barium is not known to cause cancer.

• Large amounts of barium intake can cause, high blood pressure, changes in heart rhythm or paralysis and possibly death.

Regulatory limits

• EPA - 2.0 parts per million (ppm) in drinking water.

• OSHA - 0.5 milligrams of soluble barium compounds per cubic meter of workplace air for 8 hour shifts and 40hour work week

Cadmium

Cadmium is a very toxic metal. All soils and rocks, including coal and mineral fertilizers, contain some cadmium. It is used extensively in electroplating.

Health effects

Cadmium and cadmium compounds are known human carcinogens. Smokers get exposed to significantly higher cadmium levels than non-smokers.

• Ingesting very high levels severely irritates the stomach, leading to vomiting and diarrhea.

• Long-term exposure to lower levels leads to a buildup in the kidneys and possible kidney disease, lung damage, and fragile bone

Regulatory limits

• EPA – 5 parts per billion (ppb) or 0.005 parts per million (ppm) of cadmium in drinking water

• Food and Drug Administration (FDA) – concentration in bottled drinking water should not exceed 0.005ppm (5 ppb).

• OSHA – an average of 5 micrograms per cubic meter of workplace air for an 8-hour workday, 40-hour work week

Chromium

Chromium is found in rocks, animals, plants, and soil and can be a liquid, solid, or gas.

Health effects

Chromium (VI) compounds are toxins and known human carcinogens, whereas Chromium (III) is an essential nutrient.

• Breathing high levels can cause irritation to the lining of the nose; nose ulcers; runny nose; and breathing problems, such as asthma, cough, shortness of breath, or wheezing

• Long term exposure can cause damage to liver, kidney circulatory and nerve tissues, as well as skin irritation.

Regulatory limits

• EPA- 0.1 ppm (parts per million) in drinking water.

• FDA – should not exceed 1 milligram per liter (1ppm) in bottled water.

• OSHA – an average of between 0.0005 and 1.0 milligram per cubic meter of workplace air for an 8-hourworkday, 40-hour workweek, depending on the compound

Lead

As a result of human activities, such as fossil fuel burning, mining, and manufacturing, lead and lead compounds can be found in all parts of our environment.

Health effects

EPA has determined that lead is a probable human carcinogen. Lead can affect every organ and system in the body

• Exposure to high lead levels can severely damage the brain and kidneys and ultimately cause death.

• In pregnant women, high levels of exposure to lead may cause miscarriage.

Regulatory limits

• EPA – 15 parts per billion (ppb) in drinking water, 0.15 micrograms per cubic meter in air

Mercury

Mercury combines with other elements to form organic and inorganic mercury compounds.

Health effects

The EPA has determined that mercuric chloride and methyl mercury are possible human carcinogens.

• The nervous system is very sensitive to all forms of mercury.

• Exposure to high levels can permanently damage the brain, kidneys, and developing fetuses. Effects on brain functioning may result in irritability, shyness, tremors, changes in vision or hearing, and memory problems.

Regulatory limits

• EPA – 2 parts per billion parts (ppb) in drinking water

• FDA – 1 part of methyl mercury in a million parts of seafood.

• OSHA – 0.1 milligram of organic mercury per cubic meter of workplace air and 0.05 milligrams per cubic meter of metallic mercury vapor for 8-hour shifts and40-hour work week

Selenium

Selenium is a trace mineral widely distributed in most rocks and soils. Radioactive selenium is used in diagnostic medicine.

Health effects

The Tolerable Upper Intake Level is 400 micrograms of selenium per day. Consumption above that level can lead to selenosis.



• Brief exposures to high levels in air can result in respiratory tract irritation, bronchitis, difficulty breathing, and stomach pains. Longer-term exposure can cause respiratory irritation, bronchial spasms, and coughing

Regulatory limits

 \bullet EPA – 50 parts per billion of selenium (50 ppb) in drinking water.

• OSHA – 0.2 mg per cubic meter of workroom air for an 8-hour work shift.

Silver

Silver usually combines with other elements such as sulfide, chloride, and nitrate.

Health effects

According to EPA, silver is not classifiable as a human carcinogen

• Exposure to high levels for a long period may result in a condition called arygria, a blue-gray discoloration of the skin and other body tissues. Argyria appears to be a cosmetic problem that may not be otherwise harmful to health.

• Exposure to high levels of silver in the air has resulted in breathing problems, lung and throat irritation, and stomach pains.

• Skin contact with silver can cause mild allergic reactions such as rash, swelling, and inflammation in some people.

Regulatory limits

• EPA – recommends concentration in drinking water not to exceed 0.10 parts per billion (ppb). Requires that spills or accidental releases of 1,000 pounds or more be reported.

 \bullet OSHA – in workplace air, 0.01 milligrams per cubic meter (0.01 mg/m³) for an 8-hour workday, 40-hourworkweek.

Factors influencing metal toxicity¹¹

- physical and chemical properties (among others chemical forms of element)

- element interaction

- formation of compounds or complexes among metal and other metalloids

- interchange of metal bounds to proteins

- sources and sinks, environmental transport, and transformation

- influence of concentration and other exposure variables (for example: time, route, pattern of exposure, bioavailability)

- nutritional status

- taking drugs such as alcohol and nicotine

ANALYTICAL METHOD ESTIMATION OF HEAVY METAL

Analysis of toxic heavy metals (arsenic, lead, and mercury) in selected infant formula milk commercially available in the philippines by AAS⁷

To test for the presence of toxic heavy metals, specifically Arsenic, Lead and Mercury in formula milk available in the Philippines for infants aged 6 to through Atomic Absorption Spectrophotometry. And to compare the results an existing standard for allowable amounts of toxic heavy metals in food product by the World Health Organization

Determination of Heavy Metals in Fish Species of the Mediterranean Sea (Libyan coastline) Using Atomic Absorption Spectrometry²

The presence of heavy metals in our environment has been of great concern because of their toxicity when their concentration is more than the permissible level. The accepted values of the concentrations of Co, Cd, Pb, Fe and Cu in fishes as reported in the World Health Organization (WHO) are presented in. The concentrations of Co in different tissues are presented in. It was found that the concentration of this metal was ranged from 0.570mg/kg to 44.693 mg/kg, which means that, the concentrations of Co in all examined tissues were more than the reported level.

Levels of some heavy metals in fishes as reported in $\ensuremath{\mathsf{WHO}}$

Concentration, mg/kg	Heavy metal
0.015	Со
0.030	Cd
0.050	Pb
0.300	Fe
1.000	Cu

Evaluation of essential elements and heavy metal levels in fruiting bodies of wild mushrooms and their substrate by EDXRF spectrometry and FAAspectrometry¹²

The essential elements (Zn, Cu, Fe, K, Mn, Mg, Se) and heavy metals (Cd, Cr, Ni, Pb, Ti, Sr,Co, Bi) contents of eight wild mushrooms (Amanita vaginata, Amanita rubescens, Amanita phalloides, Armillariella mellea, Armillariella tabescens, Agaricus campestris, Hypholoma fasciculare, Hypholoma pudorinus) and soil samples of ten forest sites from Dambovita County, Romania, were determined.. The elements in soil, especially heavy metals, are specific to the acidic soils of the Romanian forest lands and are influenced by industrial pollution. Analytical possibilities of EDXRF and FAAS analytical methods were compared and the heavy metal transfer from substrate to mushrooms was studied. The coefficient of accumulation of essential elements and heavy metals was calculated as well.



Heavy metal analysis for the toy industry by inductively coupled plasma optical emission spectroscopy⁶

In support of the toy industry, many laboratories are being called upon to analyze a wide variety of sample matrices for metal content. The primary element of interest is lead, but a number of other toxic elements pose a considerable threat, especially for children. This subset of elements, known as heavy metals, includes antimony, arsenic, barium, cadmium, chromium, selenium, mercury and lead as they are all known to accumulate in the body and cause detrimental effects over time. Some plastic and wooden toys, particularly those with painted surfaces have demonstrated elevated levels of Pb and other elements. Regulations exist which provide limits in materials for which surface contact with children can result in possible ingestion..

Ion chromatographic and voltammetric determination of heavy metals in soils. Comparison with atomic emission spectroscopy $^{13}\,$

The aim of this paper is to compare different analytical techniques, aspectroscopic, an electrochemical and a chromatographicone to determine total heavy metals concentrations in soils and to establish a correlation between these three techniques even though soil solutions are complex matrices providing a lot of interference problems. Atomic emission spectroscopy is the method of reference for heavy metals concentrations analysis

A titrimetric method for the quantitative estimation of lead in biologicalmaterials¹⁴

The announcement by Fischer in 1929 of the remarkable affinity of dithizone (diphenylthiocarbazone) solutions for lead has stimulated many laboratories to search for practical micro methods that could be applied to the determination of lead in biological materials.

Estimation of relative bioavailability of lead in soil and soil-like materials using *in vivo* and *in vitro* methods¹⁵

Bioavailability of lead in a particular medium may be expressed either in absolute terms (absolute bioavailability, ABA) or in relative terms (relative bioavailability, RBA). For example, if 100 micrograms (μ g) of lead dissolved in drinking water were ingested and a total of 50 μ g were absorbed into the body, the ABA would be 0.50 (50%).

Trace analysis of heavy metals in groundwater samples by ionchromatography with post-column reaction and ultraviolet–visibledetection¹⁶

In order to quantify the major heavy metals (Pb, Cu, Cd, Co, Zn and Ni), three ionic separation column systems were evaluated: (1) a cationic column (HPIC-CS2, Dionex) tested with two eluents (10 m*M* oxalic acid–7.5 m*M* citric acid; and 40 m*M* D-tartaric acid–12 m*M* citric acid); (2) an anionic column (HPIC-AS4, Dionex) evaluated with 25 m*M* oxalic acid as eluent; and (3) a bifunctional ion-exchange column (lonpac CS5, Dionex).

Speciation of heavy metal binding non-protein thiols in *Agropyronelongatum* by size-exclusion HPLC-ICP-MS¹⁷

In order to quantify the major heavy metals (Pb, Cu, Cd, Co, Zn and Ni), three ionic separation column systems were evaluated: (1) a cationic column (HPIC-CS2, Dionex) tested with two eluents (10 m*M*oxalic acid–7.5 m*M* citric acid; and 40 m*M* D-tartaric acid–12 m*M* citric acid); (2) an anionic column (HPIC-AS4, Dionex) evaluated with 25 m*M* oxalic acid as eluent; and (3) a bifunctional ion-exchange column (Ionpac CS5, Dionex) which was also tested with two eluents (6 m*M* pyridine, 2,6-dicarboxylic acid; and 50 m*M* oxalic acid /95 m*M* lithium hydroxide

Colorimetric Assay for Determination of Lead (II) Based on Its Incorporation into Gold Nanoparticles during Their Synthesis¹⁸

Gold nanoparticles (Au-NPs) were synthesized in one step at room temperature, using gallic acid (GA) as reducer and stabilizer. Pb2+ is added during the gold nanoparticle formation. Analysis of Pb2+ is conducted by a dual strategy, namely, colorimetry and spectrometry. As the Pb2+ concentration increases, the color turns from red-wine to purple, and finally blue. This method offers a sensitive linear correlation between the shift of the absorption band ($\Delta\lambda$) and logarithm of Pb2+ concentration ranging from 5.0 × 10–8 to 1.0 × 10–6 M with a linear fit coefficient of 0.998, and a high selectivity for Pb2+ detection with a low detection limit down to 2.5 × 10–8 M.

CONCLUSION

A heavy metal is a member of a loosely-defined subset of elements that exhibit metallic properties. It mainly includes the transition metals, some metalloids, lanthanides, and actinides. Many different definitions have been proposed—some based on density, some on atomic number or atomic weight, and some on chemical properties or toxicity. The term heavy metal has been called a "misinterpretation" in an IUPAC technical report due to the contradictory definitions and its lack of a "coherent scientific basis". The heavy metals based researcher rapidly becoming very important class of area and are likely to a replace many existing research field in the very near future due to its harmful effect to human being. Raw material used in the production of food, drug and Ayurvedic formulation always tested for the maximum limits of heavy metals specified by WHO (Arsenic not more than 10Jg/kg, cadmium not more than 0.3 mg/kg, and lead not more than 10 mg/kg of raw materials). Different consumable and unconsumeable product containing heavy metals for producing different effects like toxicity, act as a carrier for active ingredients and as a catalysts. Different analytical technique use to performing modern chemical tests on these results clearly indicates the presence of heavy metals which is not safe but according to Ayurveda these metals have been transformed to non toxic forms that are safe for internal use. Our aims to focus on the heavy metal toxicity and its



estimation by different analytical technique those are now in development.

REFERENCES

- 1. Williams Lorraine E., Pittman Jon K., Hall J. L.Emerging mechanisms for heavy metal transport in plants. Biochimica et Biophysica Acta 2000, 1465, 104-126,
- Khalifa K. M., Hamil A. M, Al-Houni A. Q. A., Ackacha M. A. Determination of Heavy Metals in Fish Species of the Mediterranean Sea (Libyan coastline) Using Atomic Absorption Spectrometry. International Journal of PharmTech Research.2010, 2, 1350-1354
- 3. Saper Robert B., Kales Stefanos N, Paquin Janet, Burns Michael J., Eisenberg David M., Davis Roger B, Phillips Russell S., Heavy Metal Content of Ayurvedic Herbal Medicine Products JAMA, 2004, 292, 2868-2873.
- Stanciu Gabriela, Mititelu Magdalena, Gutaga Simona Pesticides and Heavy Metals Determination in Marine Organisms fromBlack Sea. Chem. Bull. "POLITEHNICA" Univ. 2005, 50, 123-126.
- Shiraz, *Qishlaqi* Iran *Afshin and Moore Farid*. Statistical Analysis of Accumulation and Sources of Heavy Metals Occurrence inAgricultural Soils of Khoshk River Banks, American-Eurasian J. Agric. & Environ. Sci. 2007, 2, 565-573.
- 6. Davidowski Lee, Grosser Zoe, Thompson Laura, Heavy Metal Analysis for theToy Industry by Inductively Coupled Plasma Optica IEmission Spectroscopy. www.perkinelmer.com, 1-5.
- Cruz Gian Carlo, Din Zaheer, Feri Christian Dale, Balaoing Angela Mae, Gonzales Eva Marie, Navidad Hannah Mia, Schlaaff Ma. Margot Flor, Winter. Jennifer. Analysis Of Toxic Heavy Metals (Arsenic,Lead, And Mercury) In Selected Infant Formula Milk Commercially Available In The Philippines By AAS.E-International Scientific Research Journal 2009, 1, 40-51.
- 8. Ghosh Amitava, Chakrabarti Piyali, Roy Partha, Bhadury Somnath, Nag Tanushree And Sarkar Simli Bioremediation Of Heavy Metals From Neem (Azadirachta Indica) Leaf Extract By Chelation With Dithizone. Asian Journal of Pharmaceutical and Clinical Research, 2009, 2, 87-92.
- 9. Martin Sabine, Griswold Wendy, Human Health Effects of Heavy Metals www.engg.ksu.edu/CHSR 15, 2009.

- 10. Katzung Bertram g. Basic and Clinical Pharmacology-10th edition.
- 11. Zukowska J. And Biziuk M. Methodological Evaluation of Method for Dietary Heavy Metal Intake. Journal Of Food Science, 2008, 1-9.
- Radulescu Cristiana, Stihi Claudia, Busuioc Gabriela, Popescu Ion V, Gheboianu Anca Irina, Cimpoca Valerica Gh. Evaluation of essential elements and heavy metal levels in fruiting bodies ofwild mushrooms and their substrate by EDXRF spectrometry and FAA spectrometry Romanian Biotechnological Letters, 2010, 15,544 4-5456.
- 13. GunkelP., Fabre B., Prado G. and Baliteau J.Y., Ion chromatographic and voltammetric determination of heavy metals in soils. Comparison with atomic emission spectroscopy.EDP Wiley-VCH Sciences, 1999, *27*, 823-828.
- 14. Horwit. M. K. And Cowgill George R.A. Titrimetric Method For The Quantitative Estimation Of Lead In Biological Materials. www.jbc.org, 2011, 553-564.
- 15. Estimation Of Relative Bioavailability Of Lead In Soil And Soil-Like Materials Using *In Vivo* And *In Vitro* Methods Office of Solid Waste and Emergency Response U.S. Environmental Protection Agency Washington, DC 20460, 9285.7-77.
- 16. Santoyo E, Gutierrez S. Santoyo, Verma Surendra P., Trace analysis of heavy metals in groundwater samples by ionchromatography with post-column reaction and ultraviolet–visibledetection Journal of Chromatography A, 2000, 884,229–241.
- 17. Wei MS Zhenggui, Wong Jonathan Woonchung, Chen Dengyun, Speciation of heavy metal binding non-protein thiols in *Agropyronelongatum* by size-exclusion HPLC–ICP-Microchemical Journal, 2003, 74, 207–213.
- Ding Nan, Cao Qian, Zhao Hong, Yang Yimin, Zeng Lixi, He Yujian, Xiang Kaixiang and Wang Guangwei Colorimetric Assay for Determination of Lead (II) Based on Its Incorporation into Gold Nanoparticles during Their Synthesis, 2010, *10*, 11144-11155.
