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An Overview of Heavy Metals (Arsenic, Lead and Phosphorous) Analysis in Drinking Groundwater and its Cause of Cancer

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Abstract

Globally, almost 2.5 billion people rely on groundwater for drinking, the concentration level of heavy metals in drinking water is a major challenge it may be either low or high and both conditions are the cause of diseases. A high level of heavy metals in the human body alters several biochemical pathways leads to the cause of several diseases and among them is cancer. It is necessary to know the accurate concentration level of heavy metals in drinking water before use. Precise estimation of metals ions presence can be done with an instrumental analytical technique like Atomic Absorption Spectrometry (AAS), Inductively coupled plasma atomic emission spectrometry (ICP-AES), Inductively coupled plasma mass Spectrometry (ICPMS), Capillary Zone Electrophoresis (CZE), HPLC/ICP-DRC-MS and Flame atomic absorption spectrometer, etc. By these instruments, the exact concentration of heavy metals like arsenic, lead and phosphorous can be determined. Heavy metals toxicity (As, Pb, and P) in the human body alter the biochemical pathways, and final it indicates cell damage, cellular membrane damage, inactivation of enzymes, and changes in protein structure these effects cause diseases such as carcinogenesis, cell damage, loss of cellular functions and neurotoxicity respectively. This review article was prepared from several sources for the articles like Pubmed, Google Scholar, Web of sciences, Scopus, and WHO website.

Key words: Heavy metals; Toxicity; Drinking water; Analytical technique; Cancer

Introduction

In the ecosystem, the presence of heavy metals has been confirmed. Their presence is mainly due to daily activities like industrial and agriculture which is called anthropogenic. Pollution in water and soil is due to waste products of the industry that affect the growth of plants and aquatic life. Ultimately, the metals found in the consumable items such as dietary, supplements, cosmetics and various other commercial products. From literature, it confirmed that the heavy metal present in the soil, diet and natural medicine products. Continuous exposure to heavy metals ion in the body can cause many adverse health effects and even can cause toxicity in the body. A very minimum quantity of some heavy metals is essential to maintain the normal physiology of human body functions and a little excess of the heavy metals dangerous or even toxic. Accumulations of heavy metals such as Lead (Pb), Mercury (Hg), Cadmium (Cd) and Arsenic (As) are toxic a resulting in body organ disruption. Heavy metals interact with nuclear proteins and DNA resulting in oxidative deterioration of biological macromolecules [1,2]. It is necessary to measure the heavy metals in consumable items accurately and precisely. Several adverse effects were seen in the human body due to heavy elements but among these is carcinogenesis which is more serious. Qualitative and quantitative analysis of metal ions performed by several instruments in a laboratory. Low-level detection is very important and it can be only possible through the advanced analytical instrument. The Instrument generally employed for the analysis are Atomic Absorption Spectrometry (AAS), Atomic Emission/Fluorescence Spectrometry (AES/AFS), Inductively Coupled Plasma Mass Spectrometry (ICP-MS), Inductively Coupled Plasma Optical Emission Spectrometry (ICP-OES), Neutron Activation Analysis (NAA), X-Ray Fluorescence (XRF) and Anodic Stripping Voltammetry (AVS) [3].

For example heavy metals arsenic is a cytotoxic element, it has been reported from the literature that exposure of this element to the human body can seriously risk for health. Generally, exposure to this element is from ingesting contaminated food and water, occupational exposure and environmental pollution. In pesticide industries, arsenic contact with people will cause several diseases. Contamination of arsenic in soil has the potential to enter the human food chain [4]. Arsenic is carcinogenic and has been detected in several malignant growths, from many research reports it had revealed that the development of cancer in the lung, bladder and skin is because of arsenic [5]. Mortality rates of cancer including colon, gastric, kidney, lung and nasopharyngeal is very high and lowlevel exposure to arsenic in the development of pancreatic cancer and non-Hodgkin's lymphoma [6,7]. The mechanisms of cancer caused by this heavy metal are the production of Reactive Oxygen Species (ROS), change in DNA function and epigenetic alterations. With arsenic the epigenetic changes like

Spectrometry

Spectrometry (FAAS).

(ETAAS)

techniques, occurrence of interference and difficulties, detection

alterations in DNA methylation, histones and miRNA that responsible for the malignant growth. This toxic element has a specific mechanism of action against the human lung epithelial cells, it alters the expression of the p53 protein that resulted in a decline in the expression of the p21 and another study reported that ability to reduce intracellular concentrations of glutathione, a heavy natural antioxidant [8]. The heavy metal lead is toxic and its exposure is a significant risk for health. The general source of this toxic metal is environmental pollution found in soil that can enter the human food cycle apart from this another source is aviation fuel mining [9]. In the human body, it has been observed that the exposure of lead maybe because of any cancer and is shown in research reports that it is not directly involved in cancer but it plays a supportive role, for example in glioma patients observed that along with cadmium, lead produce a highly toxic effect. Kidney cancer has a strong association with this toxic metal and also renal cancer [10]. Serious health complication has been reported in mercury toxic heavy metal, the source of mercury heavy metal is generally are in mineral form, a waste product of many industries. Mercury converts to vapor and enters the atmosphere or leech into soil or water systems, primary source of this toxic metal has been identified in populations that consuming in large quantities of seafood. From a research study, it was observed that increased mercury exposure is a strong cause of liver cancer and gastric cancer. A unique mechanism of this toxic metal is that it reduces the concentration of glutathione in the body [11].

Literature Review

In the twenty-first century, a large number of analytical techniques are available to perform the trace and ultra-trace analysis of elemental composition. The definition of the trace element is 100 ppm (parts per million) this concentration level is detected by the most widely used instrument that is Atomic Absorption Spectrometry (AAS) with flame atomization. For ultra-trace elements concentration level 1 ppm. Instruments with high sensitivity are required for the detection of such low levels. Common instruments like potentiometry, voltammetry, atomic spectrometry, X-ray and nuclear methods are used for the determination of trace elements.

An analytical technique like electrochemical methods is used for the estimation of free ions in solution (potentiometry) or free ions together with ions bound in labile complexes (voltammetry) and also gives the information of the oxidation state of some of the elements. For elemental analysis, the most common analytical technique used is Atomic Absorption Spectrometry (AAS) as it is very sensitive and can be determined the total element content within a sample. The sensitivity of AAS is affected by a matrix of the sample.

Two analytical techniques X-ray and nuclear employed for detections of very low quantity and matrix insensitivity and the result of the experiment of these instruments were used for comparison because their fundamental principles are different from those of other analytical techniques. The advantage or disadvantage of any analytical technique depends on several factors like the number of analytes, nature of analytes, use of limits and expenses [12]. Estimation of trace elements and contaminants in complex matrices by instrumental analysis required substantial sample preparation and/or extraction. Quantity of sample needs in large for the estimation of trace elements in food environmental, clinical and biological samples [13-16]. Elemental analysis is routinely carried out by Inductively Coupled Plasma Atomic Spectrometry (ICP-AES), Electrothermal Atomic Absorption

Flame

Atomic

Absorption

and

Presently, in the analytical field, several analytical techniques are available for the estimation of trace and ultra-trace elemental analysis. An analytical technique like atomic absorption spectrometry with flame atomization is used for the analysis of trace elements that are present in parts per million ranges. But in the case of ultra trace elements where concentration ranges are in parts per billion and below a lack of analytical technique in the laboratory due to the required analytical sensitivity. For any analytical technique, there is always an advantage and disadvantage and it depends upon the use of technique, the occurrence of interferences and difficulties, detection limits, the throughput of samples, and expenses. The classification of analytical technique in Figure 1.



Discussion

analysis.

Atomic absorption spectrometry

Flame Atomic Absorption Spectrometry (FAAS) is one of the conventional techniques for the quantification of trace metal ions. This technique compares to other techniques is very simple and inexpensive. The principle of the instrument is that the sample is introduced into a flame where it dissociated into constituent atoms. The flame is the source of electromagnetic radiation and is partially absorbed by the atoms. Based on Beer and Lambert's law quantification of trace elements was performed in various samples materials [17-19]. In many cases, the available analytical technique does not have desired sensitivity for the analysis of natural samples and suffers from matrix interferences. Before quantification, several procedures have required pre-concentration and separation of trace metals for the lower detection limits which improve the precision and accuracy of analytical results. General pre-concentration methods like solvent extraction, ion exchange, adsorption and co-precipitation are used in trace metals analysis [20-24].

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Inductively Coupled Plasma Atomic Emission Spectrometry (ICP-AES)

This analytical technique is also known as Inductively Coupled Plasma Optical Emission Spectrometry (ICP-OES) and it is one of the best techniques for the determination of trace elements with high sensitivity. The uniqueness of this technique is the use of plasma which provides very high temperatures (up to 8,000 K) for atomization of the analyte. The principle of this technique is that ICP is created by argon gas and it is ionized in the intense electromagnetic field and flows in a particular rationally symmetrical pattern toward the magnetic field of the radiofrequency coil. The collision between neutral argon and the charged particles developed stable plasma, as the sample is introduced to the plasma it collides with the electrons and charged ions and is broken down into charged ions. Detects many elements simultaneously in dynamic range. Before quantification, an effective pre-concentration step is required, the factors like sample volume, the concentration of the eluent, sample and eluent flow rates [25-27].

Inductively Coupled Plasma Mass Spectrometry (ICPMS)

The determination of trace and ultra-trace elements in liquid samples has different matrix compositions by this technique.

The detection level of analytes is sub- μ g/L even to sub-pg/L. Because of high sensitivity and low detection limits, isotopic determination and small sample volume made this technique applied in a wide range, in the area like industrial analysis, geological, environmental clinical and biological and food [28-32]. Principle, sample ionized in the same type of argon plasma as in the ICP-AES technique. The first liquid sample is nebulized with an effective nebulizer transforming it into a fine aerosol and then it is transported with argon to ICP torch. The process in the plasma involved is a nebulized water matrix and chemical compounds are evaporated, molecules dissociated into atomic constituents and then ionized into positively single charged ions. Further, the separated ions are detected by photomultiplier or faraday cup (Table 1 and Figure 2) [33,34].

S. No.	Objective	Method	Conclusion
1	Investigation of arsenic contaminant behavior in groundwater	Determination of arsenic speciation of oxyanions and thioanions is performed on the principle of comparing the pH of the sample with chromatographic elution pH.	The results of the experiment concluded that the presence of sulfide reacts with arsenite to form thioarsenite molecules S/As of 2:1 and 3:1. In the wide range of pH, the solid phase As_2S_3 dissolves into the sulfidic solution to form 3:1 thioarsenite with structural coordination
2	Phenyl arsenicals estimate in groundwater by an analytical technique	Determine the arsenic compounds like arsenite and arsenate and their degraded products like phenylarsonic acid, phenyl arsine oxide and diphenylarsinic acid by an analytical technique that is HPLC-ICP-MS	Low-level detection of degraded arsenic products is determined by an MS detector. Very accurately the quantity of diphenylarsinic acid (up to 2.1 mg/l) was determined in a water sample. An elevated concentration of inorganic arsenic up to 240 µg/l was founded. This method is suggested for the determination of arsenate and arsenite as well as phenylic arsenicals
3	Determination of arsenic speciation in the river and estuarine water	The analytical technique high- performance liquid chromatography-hydride generation-inductively coupled plasma-mass spectrometry (HPLC-HG-ICP-MS) used for the estimation of arsenic	Analysis of water sample, taken from river crosses a mining site where As (III) presence is high. The accurate and precise quantity is determined. A low quantity of arsenite was detected very accurately

Table 1: Estimation of heavy metals (arsenic, lead and phosphorus) by various analytical techniques.

		species like arsenite, arsenate, Monomethylarsonic (MMA) and Dimethyl arsenic (DMA) precisely	
4	Estimation of arsenite, arsenate, and its derivatives by analytical technique	Instrument HPLC-ICP-MS was used to determine the arsenite, arsenate, mono-methylarsinic acid, dimethyalarsinic acid and arsenobetaine in various water samples	The developed method is highly sensitive; detect the analyte at a very low-level 0.4 pg. For analysis sample taken surface and well waters where the major analyte reported are arsenite and arsenate, but also AsBet and DMAA were found which never been reported before
5	Capillary Zone Electrophoresis (CZE) analytical technique used for the determination of aqueous soil extract	The CZE analytical technique to determine the content of arsenic in the sample of soil compared with the total content measured by Inductively Coupled Plasma-Atomic Emission Spectroscopy (ICP- AES) is suited for the speciation of arsenic	The result of the analysis was indicated that the yield of phenyl arsenic compound derived from arsenic concentrations of the aqueous soil determined by ICP-AES after microwave digestion was founded 6%-32% of the total amount of arsenic content
6	Quantitative determination of arsenite As ⁺³ , As ⁺⁵ , Monomethylarsonate (MMA), Dimethyl Arsenate (DMA) and roxarsone	Analytical technique anion exchange chromatography to separate the arsenic species and inductively coupled plasma-mass spectrometry as an arsenic-specific detector	Analyzed more than 100 surface-water, groundwater and acid mine drainage samples and reference materials. Examine the total arsenic As ⁺³ , As ⁺⁵ , DMA and MMA. The quantity reported 13,000 μ g As ⁺³ L ⁻¹ and 3700 μ g As ⁺⁵ L ⁻¹
7	To understand the toxicity level of As ⁺³ , As ⁺⁵ , Dimethyalarsinate (DMA) and Monomethylarsonate (MMA) in environmental water	A sensitive and robust method developed by an analytical technique coupled plasma- mass spectrometer with MS/MS mode. The column used PRP- X100 and nitrate/phosphate mobile phase. The developed method was applied for the investigation of surface water and groundwater matrices	The result of the analysis found mean recoveries range 87.2% to 108.7% and the relative standard deviation of replicates of all analytes ranged from 1.1% to 9.0%
8	Determination of compounds Dimethyl Arsenate (DMA), Mono-Methyl Arsenate (MMA), As ⁺³ and As ⁺⁵ in drinking water	Analytical technique capillary electrophoresis coupled to electrospray mass spectrometry used to determine the organic and inorganic arsenic compounds in drinking water	By this analytical technique first, optimize the composition and nature of both electrophoretic separation mediums using Hexafluoro-2- propanol (HFIP) as an additive. Based on Dispersive Liquid- Liquid Micro-Extraction (DLLME) intended for rapid determination of the total content of inorganic arsenic in the water sample and second based on partial evaporation of the water sample, to detect the arsenic four species

9	By analytical techniques, IEC/ SEC-HPLC/ICP-DRC-MS and ESI-MS/MS performed the study of As, Cr and Sb in bottled flavored drinking water samples	Extended the developed analytical procedure for AsIII, AsV, CrVI, SbIII, and SbV analysis and arsenic speciation procedure for AsB, AsIII, DMA, MMA and AsV quantification by using analytical HPLC/ICP-DRC-MS and ESI-MS/MS to get a better result and it is called bespoke speciation analysis	A developed method by an individual analytical technique that is HPLC/ICP-DRC-MS and ESI-MS/MS gives a better result like the precision value range from 2.5% to 5.5% and from 3.6% to 7.2%, respectively and recoveries value ranged 97% to 106% and from 99% to 106%. These results indicate that the developed method was robust and use for the analysis of the sample
10	Advanced hyphenated technique HPLC/ICP-DRC-MS used for the analysis of multi- elemental speciation analysis having five toxic species: As (III), As (V), Cr (VI), Sb (III), and Sb (V) in drinking water	Chromatographic separation and quantification of As (III), As (V), Cr (VI), Sb (III) and Sb (V) in drinking water with hyphenated technique HPLC/ ICP-DRC-MS used Dynamic Reaction Cell (DRC) with oxygen as a reaction gas was involved in the experiments	The result of the analysis confirmed the lack of interference influence on analytical signals as their values were in the range of 91%-110%. The developed method was tested on drinking water samples characterized by mineralization up to 650 mg L-1
11	Micro determination of lead in drinking water by Atomic Absorption Spectrophotometer (AAS)	A simple, rapid, precise and reliable analytical method. Incorporates co-precipitation of lead on zirconium hydroxide followed by instrument Atomic Absorption Spectrophotometer (AAS) using 283.3 nm wavelength	First, by co-precipitation technique separate the trace metal ions. Easily trace metal ions separated then performed filtering, centrifuging and washing of the precipitate. Estimation of lead in water was performed by instrument flame atomic absorption spectrometry with a combination of 2- mercaptobenzo-thiazole as a chelating reagent and copper as a co-precipitate carrier
12	Analytical technique flotation- spectrophotometric used for the determination of trace amounts of lead	The principle of this method is flotation of a complex of Pb ⁺² ions and Alizarin yellow between aqueous and n- hexane interface at pH=6. It is a very simple and highly selective method for separation, pre- concentration and determines extremely low concentrations of lead	The advantage of this method is it very simple and easily performed. The quantification of Pb (II) in the range of 8 ngmL ⁻¹ -170 ngmL ⁻¹ in various environmental samples
13	Analytical technique Atomic Absorption Spectrometry (AAS) with dithizone extraction to determine lead in drinking water	First extractions performed, take 10 ml of water sample and adjusted to alkaline pH extracted with 5 ml of 0.01% dithizone in chloroform. Washed the chloroform phase and evaporated to dryness. Dithizone chelated lead is reextracted into 2 ml of 5% HNO ₃ the analyzed in instrument Perkin Elmer Atomic Absorption Spectrometer (AAS) for its quantification	For quantitative analysis first prepared calibration of the curve in range 0 µg/L to 40 µg/L, then determine lead in spiked water samples and recovery founded 97%

14	Determination of lead in water samples by graphite furnace atomic absorption spectrometry after cloud point extraction	Lead formed a complex with 2- (5-Bromo-2-pyridylazo)-5 (diethylamino)-phenol (5-Br- PADAP) then require a Cloud Point Extraction (CPE) for the preconcentration after this step estimation performed by instrument Graphite Furnace Atomic Absorption Spectrometry (GFAAS) using octylphenoxypolyethoxy ethanol (TritonX-114) as surfactant	Separation of the two phases was accomplished by centrifugation for 15 min at 4000 rpm. Under the optimum conditions <i>i.e.</i> , pH 8.0, cloud point temperature 40°C, [5-Br- PADAP]=2.5 × 10 ⁻⁵ mmol l ⁻¹ , [Triton X-114]=0.05%, added methanol volume=0.15 ml, pre- concentration of only 10 ml sample permitted an enhancement factor of 50-fold
15	Determinations lead in wastewater by flame atomic absorption spectrometer	The principle for this analysis is determining lead in wastewater and effluent by flame atomic absorption spectrometry after preconcentration of lead by the rapid co-precipitation technique with gallium phosphate	The determination of lead in the sample does not affect by gallium phosphate in flame atomic absorption spectrometry at 250.0 nm in final concentration. Used co- precipitation technique, which does not require the complete collection of the precipitate
16	By the flame atomic absorption spectrometry determine trace lead in water and milk tea powder samples with organic co-precipitation	The method applied for the determination of trace lead with flame atomic absorption spectrometry after pre- concentration of lead by rapid co-precipitation technique with PAR-Fe (III) at pH 6.0. Examined the other analytical parameters such as pH, amount of reagent, the standing time of the precipitate	Performed analysis of lake water and the milk tea powder samples. The Detection Limits (DL) were founded 18.7 microg x L-1 for Pb (II). RSD's and the standard addition recovery of this method were in the ranges of 1.03%-2.24% and 94.2%-98.3% respectively
17	Precipitate sulfate by improved precipitation technique and the used chelatometric titration with HEDTA for the determination of lead	Estimation of lead by selective titrimetric analysis performed, prior have done modified method of precipitation	Back titration method adopted, precipitate collected and transferred more than HEDTA solution, the excess of the sample back titrated with Zn (II) at pH 5.0-5.5. Used catechol violet and xylenol orange as a mixed indicator give a sharper end-point. This method was successfully used to estimate Pb in non-ferrous alloys
18	Analytical technique atomic- absorption spectrophotometry with electro-thermal atomization used for the estimation of lead in drinking water	The use of electro-thermal atomization to determine concentrations of lead in water, although sensitive, generally suffers from suppressive interference effects that can produce large and variable negative bias	The pre-treatment technique can be either impregnation of the furnace tube with lanthanum or the addition of lanthanum (as lanthanum chloride) to each sample
19	Quantification of lead in Industrial samples using 1,3- Benzenediamine N, N'-bis (2- furanylmethylene) in presence of surfactant by direct spectrophotometric method	For spectrophotometric analysis, Schiff's base is one of the excellent chelating agents for the determination of metal ions. Lead (II) with 1,3- Benzenediamine, N, N'-bis (2-	The colored complex of lead has a maximum absorbance at 620 nm in presence of Sodium Lauryl Sulfate (SLS) as a surfactant with molar absorptivity 10.16×10^3 L

		furanylmethylene) (BDFM) formed a colored complex	mol ⁻¹ cm ⁻¹ the complex was stable at room temperature and for a long time
20	A Flow Injection Analysis (FIA) system with on-line pre- concentration and spectrophotometric detection for the determination of lead in aqueous samples	Developed a method for the analysis by FIA system followed spectrophotometric detection. FIA systems based on the reaction of lead (II) with 4-(2- pyridylazo) resorcinol (PAR) in buffer pH 9 with an adsorption maximum at 523 nm	The detection limit of this developed method 11 μ g L ⁻¹ from aqueous lead solution at a sampling rate of 12 h ⁻¹ . Linear detection range is 0.10 to 0.90 mg L ⁻¹ . Evaluated precision and accuracy with a standard synthetic solution and a real sample and the result indicated 2.4% RSD and 90%-117% recovery
21	Determination of phosphorus by the spectrophotometric method by using bismuth- phosphomolybdate complex	Based on the formation of the blue Bismuth- Phosphomolybdate complex (BiPMo), estimated phosphorus for the P-PO4-3 ion natural waters by spectrophotometric analysis which is very simple, easy and sensitive	This method is very simple and easily performed. The developed method is the sensitive, quick and simple determination of trace amounts of phosphorus as orthophosphate in natural waters even in laboratories equipped with simple instruments
22	Based on the reaction of vanadomolybdophosphate with malachite green determine phosphorus in river water by spectrophotometric	The development of an ion- associate between vanadomolydophosphate and malachite green in aqueous acidic solution (0.5 M sulphuric acid); determine $0-1 \times 10^{-5}$ M of phosphate	The developed complex was stabilized by adding polyvinyl alcohol and estimated at 620 nm with molar absorptivity 1.05×10^5 I mol ⁻¹ cm ⁻¹ . The other ions like silicate and arsenate do not interfere in the analysis, interference of arsenate is avoided by reduction with thiosulfate
23	Estimation of trace amounts of phosphate in water and soil by spectrophotometric analysis	The principle of this method is the formation of phosphomolybdate by reaction between ammonium molybdate and hydrazine by a reduction in acidic medium produce blue of uncertain composition	System followed the Lambert-Beer's law at 830 nm in concentration range 0.5 μ g/mL-5 μ g/mL of phosphate, complex showing blue colour with maximum absorption and have Relative Standard Deviation (RSD) of 0.1% and correlation coefficient of 0.99 and at this wavelength molar absorptivity 2.9 × 10 ⁴ L mol ⁻¹ cm ⁻¹
24	Spectrophotometric simultaneous estimation of phosphate and silicate ions in river water by using ion- exchange chromatography separation and post-column derivatization	Phosphate and silicate ions were separated by the ion- exclusion column packed with a polymethacrylate-based weakly acidic cation-exchange resin in the H+ form (TSKgel Super IC- A/C) by using ultrapure water as eluent	Examine the effects of sulphuric acid, sodium molybdate and ascorbic acid concentration and reaction coil length, which form the reduced complexity of molybdate and ions. The detector response of phosphate and silicate ions was examined. The concentration under the optimized condition color- forming reactant 50 mM sulfuric

			acid, 10 mM sodium molybdate reducing agent, 50 mM ascorbic acid and length of 6 m. The linearity of the calibration curves of phosphate and silicate ions were 50 microg L ⁻¹ -2000 microg L ⁻¹ and 250 microg L ⁻¹ -10,000 microg L ⁻¹ respectively
25	Environmental water containing silicate and phosphate determined by analytical technique pre-column derivatization ion-pair liquid chromatography	By this analytical technique estimate, the soluble silicates and phosphate in an environmental sample of waters preceded by the formation of their yellow alpha- heteropolymolybdates	The pre-column coloring reactions at moderate-pH were reproducible for both silicate and phosphate in all quantification ranges with RSD less than 2% and 5% respectively. The linear calibration lines between concentrations mg-SiO ₂ /L and mg-PO4/L and peak area intensities were obtained for silicate and phosphate both with acceptable determination coefficients r (2) of 0.9999. The limits of determination for both analytes were 0.007 mg-SiO ₂ /L and 0.003 mg-PO ₄ /L, which were calculated theoretically using 10 sigma/ slope
26	Determination of phosphate in water sample by a simple spectrophotometric method	Formation of phosphomolybdate complex followed by its reduction with thiourea in an aqueous sulphuric acid medium	The result of the analysis is based on Beer's Law at 840 nm in linearity range 0.5 μ g/ml-10.0 μ g/ml. Molar absorptivity, correlation coefficient, and Sandell's sensitivity values are found to be 1.712 mol ⁻¹ cm ⁻¹ , 0.9769 μ g cm ⁻² and 0.0555 μ g cm ⁻² respectively
27	Determination of phosphate in a water sample by a simple spectrophotometric method	Determine phosphorus as its ion associate with a quaternary ammonium salt and molybdoantimonophosphoric acid immobilized on silica gel in the concentration range 1.9 µg P/L -124 µg P/L	The developed method was tested in the determination of various phosphorus forms in natural waters
28	Factorial design for multivariate optimization of the pre- concentration system for spectrophotometric phosphorus determination	Extraction of phosphorus as phosphomolybdenum blue was performed on to Ambulate XAD-4 polymeric adsorbent. Quantification performed in ultraviolet-visible spectrophotometer based on the formation phosphomolybdate and reduction to molybdenum blue	By using two-level full factorial design optimized the method taking three variables (resin amount, sample volume, flow rate). At 0.08 microg mL ⁻¹ the relative standard deviation was 2% and limit of detection was 2.23 microg L ⁻¹ (N=15)
29	Estimation of phosphate in sugarcane juices, water and detergent samples by simple	The principle of this method is the formation of phosphomolybdate with added	Developed a calibration curve at 715 nm based on Lambert- Beer's law in the concentration

spectrophotometric analytica technique	molybdate followed by its reduction with sodium sulfide in aqueous sulphuric acid molar absorptivity, correla coefficient and Sand sensitivity 6.1 x 3 mol ⁻¹ co 0.999 µg cm ⁻² and 0.0156 cm ⁻² respectively	. The were lation dell's cm ⁻¹ , 6 μg
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Arsenic

Molecular mechanism of arsenic-induced cancer: The power of carcinogenic capacity of this toxic metal is usually linked with its biotransformation. The arsenic metal in drinking water is easily absorbed by the gastrointestinal tract. As this toxic metal is ingested its oxidation state is a pentavalent form (As⁺⁵) and enters the cells through the membrane transporter-like Inorganic Phosphate Transporters (PiT) and aquaporins. Inside the cell, it reduces to more toxic that is in trivalent form (As^{+3}) in glutathione-dependent reaction that а proceeds bv polynucleotide phosphorylase and mitochondrial ATP synthase. Further for the detoxification process As⁺³ and its methylated conjugates are transferred to hepatocytes into bile as glutathione conjugates. In the liver, the availability of mono- and dimethylated As⁺³ species are highly reactive and it induces to damage different organs including the lungs. The damage of different organs occurs primarily because of the generation of Reactive Oxygen Species (ROS).

Arsenic biotransformation as a toxicity activation mechanism: During the metabolism of arsenic a series of redox reactions happened, pentavalent convert to trivalent species. Oxidative methylation gives methylated tri- and pentavalent metabolites. Apart from the detoxification methylation can activate the toxic and carcinogenic potential of arsenic. Research reported that the mono/dimethylated arsenical species can change the gene transcription and are more potent enzyme inhibitors and cytotoxins than nonmethylated species [65,66]. S-Adenosylmethionine (SAM) functioned as a methyl group donor; the cellular processes can interfere with the arsenic metal ion that altered epigenetic mechanism that participates in-induced carcinogenesis [67,68]. Purine nucleoside phosphorylase reduced As⁺⁵ to As⁺³, with SAM a methyl group donor As⁺³ is methylated via an As⁺³ methyltransferase producing mono and © Copyright iMedPub

dimethylated trivalent species. As⁺³ could be carcinogenic for the skin. The toxicity of arsenic metal results from its ability to interact with proteins sulfhydryl functional groups and substitute phosphorous in a variety of biochemical reactions. *In vitro* studies reported the inactivation of enzymes through sulfhydryl groups like dihydrolipoyl dehydrogenase and thiolase [69].

Lead

The heavy metal leads toxicity induced cancer by damaging and disrupting the DNA along with the repair system of cellular tumor regulatory genes through the generation of ROS. Several research studies have been reported that the generation of ROS by lead change the structure and sequence of chromosome and alter the transcription processes by replacing zinc in certain regulatory proteins [70]. Excessive exposure to lead causes toxicity and it is called lead poisoning, the effects of poisoning are generally related to the gastrointestinal tract and central nervous system disorder. In the human body, lead poisoning might be acute or chronic. Diseases because of acute exposure such as loss of appetite, abdominal pain, fatigue, sleeplessness, renal dysfunction, hypertension, arthritis, hallucinations and due to chronic exposure mental retardation, birth defects, autism, psychosis, allergies, paralysis, weight loss, dyslexia, muscular weakness, kidney damage, coma and may even cause of death. The acute and chronic condition is preventable but the diseases that happened due to lead toxicity are very dangerous as it can affect most of the body organs [71]. A condition of edema has been found in excess levels of lead in the body in which the plasma membrane of the blood-brain barrier moves into the interstitial spaces and also alters the function of the central nervous system by disrupting the intracellular second messenger systems [72].

Lead is a divalent element and it can easily substitute the divalent metal cations and such substitutions have been seen in cellular function, the substitution of an essential element with divalent lead inhibits the cellular functions by binding with various proteins and in some cases, it has been observed that lead can change the functional activity of metal-chelating proteins by substituting the normal metal cation. The synthesis of heme is also inhibited by deactivating the d-aminolevulinic acid dehydrase zinc-containing enzyme. The disorder in the nervous system is generally due to interference of lead with calcium-dependent processes related to neuronal signaling and intracellular signal transduction [73]. In many *in vitro* and *in vivo* studies found that lead compounds cause genetic damage through many indirect mechanisms which include inhibition of

DNA synthesis and repair, oxidative damage and interaction with DNA-binding proteins and tumor suppressor proteins.

Phosphorus

Drinking water inorganic phosphate is a source of phosphorus, for cellular function an optimum concentration of its required as the concentration increases in an intracellular fluid becomes toxic. The toxic level of phosphorus causes cancer in the body. Inorganic phosphate is incorporated into the cells which regulate cellular function. This element is present in nucleic acid, Adenosine Triphosphate (ATP) and other metabolites. Many biochemical pathways alter as the concentration reach in toxic level, membrane transport of minerals disturb and some damage the membrane of some cells. Thyroid, breast and lung cancer are because of the high concentration of NaPi2b in normal tissue [74]. A high concentration of phosphate enhanced the expression of the gene in forkhead box protein C2 (FOXC2), osteopontin and vascular endothelial growth factor in dosedependent manners that alter the synthesis of nucleic acid, a wrong formation of the nucleic acid cause of cancer [75]. High concentrations of phosphate directly damage the mitochondrial membrane, produce Reactive Oxygen Species (ROS), reduce nitric oxide production and induce apoptosis and also, activate the PKC pathway these events are responsible for the cause of cancer [76]. High phosphate level in serum indicates the stage of cancer and can predict the survival of patients. The researcher reported that a high level of phosphate in cells stimulates tumorigenesis it is due to exerting mitogenic effects on tumor cells, enhancing angiogenesis, inducing chromosome instability and finally metastasis [77,78].

Conclusion

This review article concludes that drinking water with heavy metals like arsenic, lead, and phosphorus is present in the toxic level cause of several diseases. Cancer disease due to the toxic level of heavy metals in the human body induces the generation of free radicals which interfere in the nucleic acid synthesis and finally damage the DNA. Providing safe drinking water in a population is very necessary and it can be possible if the estimation of heavy metals has been performed with advanced analytical techniques. In the human body, the requirement of heavy metals is very low as it crosses the level of concentration it starts to accumulate in the body. That's it is necessary to know the metal ions concentration in the drinking water before use.

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Conflict of Interest

The authors declare no conflicting interest.

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