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Sensory Development for Heavy Metal Detection: A Review on Translation from Conventional Analysis to Field-Portable Sensor

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Abstract:

Background

In recent decades, contaminations with heavy metals ions have adversely affected environment, food safety and human health. Heavy metals, leaching to water sources from the industrial effluents, are able to enter into the aquatic and food chains of humans and animals from a variety of anthropogenic sources.

Scope and Approach

Heavy metal detection has been an intensive area of research today. Both laboratory-based analytical instruments and innovative sensor devices like electronic nose, electronic tongue and bio/ chemical sensors have increasingly emerged to meet the demand for legislative actions on environmental pollution control and early warning. These evolving technology and developments particularly in the area of nanotechnology and sensors have become key contributing factors in heavy metal detection.

Key Findings and Conclusions

This endeavor aims at exploring this field in details to understand the key principles behind this flourishing science and summarize the recent development in heavy metal detection technologies. This article also gives a brief review of commercially available portable devices that has the potential to become the next gold standard instruments in heavy metal detection.

Keywords: Heavy metal; Analysis; Nanotechnology; Sensors; Portable devices; Data analytics;

1. Introduction

Water affects various aspects of the society, such as human/animal healthcare, food chain, tourism industry (Mikhailenko, Ruban, Ermolaev, & van Loon, 2020), etc., therefore improving the water quality can boost the economic growth of a nation, and contribute greatly in poverty reduction. Having access to clean and safe water for daily consumption *i.e.* drinking, cooking, personal hygiene and sanitation facilities is the fundamental and basic right of human (Samra, Crowley, & Fawzi, 2011). However, according to a report published by World Health Organization (WHO), there are 785 million people who are in lack of even basic drinking-water service, and 144 million people who are dependent on surface water (WHO, 2004d). Globally, at least 2 billion people use drinking water sources that are contaminated (WHO, 2019). Contaminated water can transmit diseases such as diarrhea, cholera, dysentery, typhoid, and polio (WHO, 2004d). In the last few decades, due to the growing increase in industrialization and urbanization, the presence of heavy metals poses a serious concern to human health. The focus on heavy metals and their detection has been much discussed because of the excessive leaching of these non-biodegradable metals. According to the recent report of the Central Water Commission (CWC), for the duration of May 2014 to April 2018, two-third of drinking water samples have been found contaminated and polluted by deadly heavy metals (Koshy, 2019). Iron (Fe), lead (Pb), nickel (Ni), chromium (Cr), cadmium (Cd) and copper (Cu) are registered as the major contaminants in the samples. Not only in water, heavy metal toxicity is also very common in food . This is mainly caused by irregular irrigation, sewage, unhygienic food processing and improper storage of the food. There are several instances where measurable amounts of heavy metals are found in various food products. Therefore, detection of heavy metals in food products is a serious issue that is being addressed by

researchers throughout the world. These toxic metals can be detected through conventional testing methods as well as with the help of modern innovative sensors.

Heavy metals are broadly defined as metals having high relative density ($>5 \text{ g cm}^{-3}$) with large atomic masses compared to water to cause serious toxicity when present in trace levels in biotic environment. The most toxic heavy metals are mercury (Hg), Cd, arsenic (As), Cr, thallium (Tl) and Pb, since they can cause adverse health effects even at the low level of concentrations. Although, less toxic heavy metals such as Fe, Cu, zinc (Zn), cobalt (Co) and manganese (Mn) which are found in our body and extensively used by various enzymes can only cause serious problems if they present above certain threshold levels.

Arsenic in water is mostly present in the more toxic inorganic form ($> 99\%$), and naturally exists at high levels in a number of countries' groundwater. Arsenic contaminated water used for drinking, food preparation and irrigation of food crops poses the greatest threat to public health.

In the 1980s, it was recognized that the As contaminated groundwater in the state of West Bengal in India caused illness and death, and threatened the health of millions of people (UNICEF, 2018; WHO, 2019). As the testing for arsenic was conducted in other countries, it became apparent that As contamination extended around the world including Taiwan, Hungary, Chile and Argentina.

Pb, on the other hand, is a cumulative toxicant affecting multiple body systems and is particularly harmful to young children. There is no level of exposure to Pb that is known to be without harmful effects. Another report published by United States Environmental Protection Agency (US EPA) states that Cd is highly persistent in water and has potential for bio-accumulation in biotic organisms (EPA, 2016). Cd enters the environment primarily through leaching from landfill and industrial effluents. Moreover, Cr as one of the major toxic heavy metals in water is also more

dangerous in its hexavalent state. Cr has two forms - trivalent and hexavalent, both of which needs to be considered for proper assessment of associated health risks in drinking water.

Until today, the conventional techniques remain the gold standard for quantification and monitoring of heavy metal ions. The main detection techniques include atomic absorption spectroscopy (AAS) (de Almeida Pereira, de Amorim, & da Silva, 2004), flame or furnace spectroscopy (Jianrong Chen & Teo, 2001), inductively coupled plasma mass spectrometry (ICP-MS) (N. Zhang, Suleiman, He, & Hu, 2008), energy dispersive X-ray fluorescence (EDXRF) spectrometry (Menéndez-Alonso, Hill, Foulkes, & Crighton, 1999), etc.. Unfortunately, these conventional analysis systems cannot meet the needs of fast detection (Kawamura & Miyata, 2016). Although conventional techniques are highly selective and sensitive to nanogram level of heavy metals, most of them lack field portability and require skilled workforce and time to operate (Luo, Wang, Wang, Huang, & Zhang, 2016). Moreover, their running costs are also high. With the dramatic elevation of heavy metal pollutions due to the industrial development and the fact that these heavy metals, if remain unmonitored properly in the environment, can bio-accumulate in the environment causing toxicity to existent life forms, there is a high demand for the development of a fast, rapid, portable and on-spot automated detection system.

In this endeavor, the toxicity limits and associated health risks of the most hazardous heavy metal ions have been discussed and different detection systems have been considered. Though there are a number of review papers focusing on the specific detection techniques or toxicity mechanisms, here, we aim to provide a comprehensive report covering wide ranges of techniques from conventional to newly-developed approaches for the fabrication of ideal devices. Finally, some commercialized field-portable instruments are mentioned and their pros and cons are discussed.

2. Heavy Metals: Toxicity limits and associated health benefactor/risks

In general, heavy metals are naturally occurring in the environment, and due to their increase in biotic flora and fauna in recent years, the regulatory authorities are to decide some essential standards for safe consumption of these heavy metals (Singh, Gautam, Mishra, & Gupta, 2011). Table 1 illustrates a list of different global and national regulatory authorities that determines and regulates these standards for safe consumption in drinking water. This list also highlights the difference in threshold limits due to the geographical variation and consumption limits of different population in drinking water.

77 **Table 1:** Maximum permissible limits of various heavy metals according to different regulatory authorities

Sl. No.	Heavy Metal	FSSAI (mg L ⁻¹)	WHO (mg L ⁻¹)	CODEX (mg L ⁻¹)	EU (mg L ⁻¹)	FDA (mg L ⁻¹)	Associated Health Risk	References
1.	Cadmium	0.003	0.003	0.003	0.005	0.005	<ul style="list-style-type: none"> • Nausea, Vomiting, Diarrhea • Muscle cramps • Salivation • Sensory disturbances • Liver injury • Convulsions • Shock and renal failure 	(ATSDR, 2012; CODEX; EPA, 2016; FSSAI; Jaishankar, Tseten, Anbalagan, Mathew, & Beeregowda, 2014; Khan, Khan, Qamar, & Waqas, 2015; Storelli, 2008; WHO, 2003a, 2003b, 2004a, 2004b, 2004c, 2004d, 2006, 2017, 2019)
2.	Arsenic	0.05	0.01	0.01	0.01	0.01	<ul style="list-style-type: none"> • Encephalopathy • Watery diarrhea that contains blood • Thickening of the skin • Darker skin, Abdominal pain • Diarrhea, Heart disease • Numbness, Cancer 	
3.	Lead	0.01	0.01	0.01	0.01	0.005	<ul style="list-style-type: none"> • Abdominal pain, Constipation, Headaches, Irritability, Memory problems • Inability to have children, • Tingling in the hands and feet • Intellectual disability • Behavioral problems • Anemia, Seizures • Coma 	
4.	Chromium	0.05	0.05	-	0.05	0.100	<ul style="list-style-type: none"> • Behavioral or psychiatric conditions • Depression 	

							<ul style="list-style-type: none"> • Anxiety, Schizophrenia • Kidney and liver diseases. 	
5.	Zinc	15	3.00	-	5.00	5.000	<ul style="list-style-type: none"> • Nausea • Vomiting • Cramps • Diarrhea 	
6.	Copper	1.5	2.00	-	2.00	1.000	<ul style="list-style-type: none"> • Vomiting, • Hematemesis (vomiting of blood) • Hypotension (low blood pressure) • Melena (black "tarry" feces) • Jaundice, Gastrointestinal distress. • Hemolytic anemia • Damage of the liver and kidneys. 	
7.	Iron	0.3	2.00	-	0.2	0.300	<ul style="list-style-type: none"> • Stomach pain, • Nausea and vomiting • Bloody vomiting may occur. • Metabolic acidosis, • Hypovolemic shock 	
8.	Mercury	0.001	0.006	0.001	-	-	<ul style="list-style-type: none"> • Harmful effects on central and peripheral nervous systems • Tremors • Insomnia and memory loss • Headaches and cognitive and motor dysfunction • Effects on the nervous, digestive and immune 	

							systems, lungs and kidneys, and may be fatal	
9.	Nickel	1.5	0.02	-	0.02	0.1	<ul style="list-style-type: none"> • Chronic bronchitis • Reduced lung function • Cancer of the lung and nasal sinus • Allergy • Cardiovascular and kidney diseases 	
10.	Manganese	-	0.4	-	0.3	0.05	<ul style="list-style-type: none"> • Fatness • Glucose intolerance • Blood clotting • Skin problems • Lowered cholesterol levels • Skeleton disorders • Birth defects • Neurological symptoms 	
11.	Antimony	-	0.02	0.005	0.005	0.006	<ul style="list-style-type: none"> • Irritation of the eyes, skin and lungs • Lungs disease • Vomiting • Diarrhea • Stomach ulcers 	
12.	Cobalt	-	0.05	-	-	-	<ul style="list-style-type: none"> • Vomiting and nausea • Vision problems • Heart problems • Thyroid damage • pneumonia 	

79 FSSAI: Food Safety and Standards Authority of India; WHO: World Health Organization; CODEX: Codex Alimentarius Commission
80 a body under Joint FAO/WHO Food Standards Programme in Rome; EU: European Union; USFDA: United State Food and Drug
81 Administration

3. Detection techniques

3.1. Conventional detection techniques

Some conventional detection techniques for common heavy metals quantification are discussed here. Cd can be conventionally detected by AAS and flame or furnace spectroscopy with detection limits of $5\mu\text{g L}^{-1}$ and $0.1\mu\text{g L}^{-1}$ (Dadfarnia, Assadollahi, & Shabani, 2007; WHO, 2004a). Shahlaei and Pourhossein used a bio-adsorbent of *A.niger* to pre-concentrate the analytes to achieve nanogram limit of detection (LOD) using electrothermal atomic absorption (ETAAS). Their experiment showed LOD value for As_2O_3 and As_2O_5 was 1ng L^{-1} and 5ng L^{-1} , respectively (Shahlaei & Pourhossein, 2014).

The most commonly used methods for Cr detection in water are laboratory-based methods, such as AAS and MS. Yuan et al. have used sodium diphenylamine sulfonate (DPH) reagents to detect Chromium through spectrophotometric techniques (Yuan, Fu, Wang, & Yuan, 2008). The pre concentration, separation and determination of Cr^{III} and Cr^{VI} have been achieved by Alonso et al. (Menéndez-Alonso, et al., 1999). They used a combination of ion exchange media and EDXRF spectrometry (Menéndez-Alonso, et al., 1999). Due to pre-concentration factor of 500, the LODs were obtained as 0.3 mg L^{-1} for Cr^{VI} and 0.4 mg L^{-1} for Cr^{III} . Luciano et al. also developed methodologies for chromium detection in drinking water by ETAAS using permanent modifiers. The best results obtained for chromium was with the use of rhodium permanent modifier. The detection limit was of $0.2\mu\text{g l}^{-1}$ for chromium (de Almeida Pereira, et al., 2004). Moreover, Zhang et al. have synthesized a new chromium(III)-imprinted 3-(2-aminoethylamino) propyl tri-methoxy silane (AAPTS)-functionalized silica gel sorbent with the help of a surface imprinting technique and employed the same as selective solid-phase extraction material for speciation analysis of

chromium in environmental water samples prior to its determination by ICP-MS. Under the optimized conditions, the detection limits were calculated to be 4.43 $\mu\text{g mL}^{-1}$ and 8.30 $\mu\text{g mL}^{-1}$ for the two Cr species (N. Zhang, et al., 2008). Moreover, Beere et al. have developed an ion chromatography system for the separation and determination of Cr (III) and Cr (VI) species in aqueous samples, and very high sensitivity was achieved using a chemiluminescence post-column reaction detector based on the catalytic oxidation of luminol. Detection limits were 0.05 and 0.1 $\mu\text{g L}^{-1}$ for Cr(III) and Cr(VI) respectively (Beere & Jones, 1994).

AAS is the most widely used method for the determination of Zn. The detection limit of the direct air–acetylene flame method is 50 $\mu\text{g L}^{-1}$ (Shabani, Dadfarnia, Moosavinejad, & Ahmadi, 2009). Low concentrations can be measured by chelating Zn with ammonium pyrrolidine dithiocarbamate and extracting it with methyl isobutyl ketone (detection limit 0.5 – 1 $\mu\text{g L}^{-1}$). Tony et al. has developed a rapid and sensitive flow injection analysis–atomic absorption spectrometric procedure for the determination of Zn based upon on-line pre-concentration on a micro-column packed with C_{18} material (Tony, Kartikeyan, Vijayalakshmy, Rao, & Iyer, 1999). Zn forms complexes with 5,7-dichlorooxine from weakly acidic or neutral solutions in the flow system and adsorbed on the column. The respective detection limit was 0.5 ppb. Matusiewicz et al. has also developed a simple method for the atomic absorption determination of Zn in river and estuarine water using two atom trapping techniques: a water-cooled dual silica tube and a commercially available double-slotted quartz tube mounted in an air-acetylene flame (Matusiewicz, Sturgeon, Luong, & Moffatt, 1991). The detection limit was 0.3 ng mL^{-1} for Zn using a 2 min in situ pre-concentration time with the dual silica tube atom trap, and 1.2 ng mL^{-1} for Zn using the double-slotted quartz tube. Cloud point extraction (CPE) has been used by Chen et al. for the simultaneous pre-concentration of Zn after the formation of a complex with 1-(2-thiazolylazo)-2-naphthol (TAN), and later analysis by flame

127 atomic absorption spectrometry (FAAS) using octyl-phenoxy-polyethoxy-ethanol (Triton X-114)
128 as surfactant (Jianrong Chen & Teo, 2001). The detection limit was 0.095 ng mL^{-1} for Zn.

129 The most important analytical methods for the detection of Cu in water are AAS with flame
130 detection, graphite furnace atomic absorption spectroscopy, inductively coupled plasma atomic
131 emission spectroscopy, inductively coupled plasma mass spectrometry (ICP-MS) and stabilized
132 temperature platform graphite furnace atomic absorption (ISO, 1986, 1996; ASTM, 1992, 1994;
133 US EPA, 1994). The ICP-MS technique has the lowest detection limit, and the AAS technique has
134 the highest. LOD for the other three techniques range from 0.7 to $3 \text{ } \mu\text{g L}^{-1}$ (WHO). Wen et
135 al. has proposed a new method based on dispersive liquid–liquid micro-extraction (DLLME) pre-
136 concentration using tetra-chloromethane (CCl_4) as extraction solvent for the spectrophotometric
137 determination of Cu in water and food samples. Under the optimal conditions, the limit of detection
138 for Cu was $0.5 \text{ } \mu\text{g L}^{-1}$ (Wen, Yang, Yan, & Deng, 2011). Cloud point extraction employing the
139 new reagent 6-[2'-(6'-methyl-benzothiazolylazo)]-1,2-dihydroxy-3,5-benzenedisulfonic acid as
140 complexing agent and Triton X-114 as the surfactant has been proposed by Lemos et al. for Cu
141 determination. Dilution of the surfactant-rich phase with acidified methanol was performed after
142 phase separation, and the Cu contents were measured by flame atomic absorption spectrometry
143 with a detection limit of $1.5 \text{ } \mu\text{g L}^{-1}$ (Lemos, Santos, dos Santos, Vieira, & Novaes, 2007). Rahil-
144 Khazen et al. has used inductively coupled plasma atomic emission spectrometry (ICP-AES) for
145 the determination of Cu in human serum (Rahil-Khazen, Henriksen, Bolann, & Ulvik, 2000).
146 Detection limits was $0.014 \pm 0.07 \text{ mmol L}^{-1}$ for Cu. Coale et al. has described the process of
147 detection of Cu in sea water using a flow-injection method with chemiluminescence (CL) detection
148 (Coale, Johnson, Stout, & Sakamoto, 1992). The determination was based on the formation of a
149 complex between Cu and 1,10-phenanthroline and the subsequent emission of light during the

150 oxidation of the complex by hydrogen peroxide. They constructed a flow-injection manifold which
151 provides for the separation of Cu from the sea water matrix with a column of immobilized 8-
152 hydroxyquinoline. An on-line flow injection solid-phase extraction procedure was developed by
153 Yu et al. for trace Cu separation and pre-concentration with detection by flame atomic
154 spectrometry (H.-M. Yu, Song, & Chen, 2011). A novel adsorbent-silica gel bound dithizone
155 (H₂Dz-SG) was prepared and used as solid-phase extraction of Cu from complex matrix. The
156 H₂Dz-SG quantitatively adsorbs Cu ions, and the retained Cu is afterwards collected by elution of
157 10% (v/v) nitric acid. The detection limit of Cu was 0.2 µg L⁻¹.

158 Fe in water can be determined by AAS (detection limit 1 µg L⁻¹) or by colorimetric methods
159 (detection limit 5 µg L⁻¹) (H.-M. Yu, et al., 2011). An automated shipboard analytical method for
160 determining Fe (III) in seawater has been developed by Obata et al. (Obata, Karatani, & Nakayama,
161 1993). The method was based on a combination of selective column extraction using chelating
162 resin and improved CL detection in a closed flow through system. In this method, Fe (III) in an
163 acidified sample solution was selectively collected on 8-quinolinol immobilized chelating resin
164 and then eluted with dilute hydrochloric acid. The resulting eluent was mixed with luminol
165 solution, aqueous ammonia, and hydrogen peroxide solution successively, and then the mixture
166 was introduced into the CL cell. The Fe concentration was obtained from the CL intensity. The
167 detection limit of Fe (III) was 0.05 nmol L⁻¹. A long liquid waveguide capillary flow cell has been
168 successfully adapted by Zhang et al., to a gas-segmented continuous flow auto-analyzer for trace
169 analysis of iron in water (J.-Z. Zhang, Kelble, & Millero, 2001). Utilization of the long flow cell
170 significantly enhances the sensitivity of automated colorimetric analysis of Fe by the ferrozine
171 method that allows the accurate determination of nanomolar concentrations of iron in natural
172 waters. The advantages of this technique were low detection limit (0.1 nM), small sample volume

(2 mL), high precision (1%), and automation for rapid analysis of a large number of samples. Sensitive visual and micro spectrophotometric methods have been developed by Kawakubo et al. for field determination of trace iron in fresh water samples (Kawakubo, Naito, Fujihara, & IWATSUKI, 2004). For the visual method, a water sample (0.45- μ m filtrate acidified to 0.1 M HCl) was placed in a glass vial and mixed with a reagent solution containing 1,10-phenanthroline, sodium thiocyanate and 0.1 M HCl. Fe was extracted as pink ferroin thiocyanate with 1 mL of 4-methy-2-pentanone. The sample up to 20 ml was added step-by-step, until the color of the extract was detected visually. Without any special instrument or color standard, iron down to 0.001 mg l⁻¹ (0.025 μ g) in a sample can be determined with an error of 20% in the field. Fernández et al. used a suppressor column for calcium removal in the determination of Fe in water samples by collision cell ICP-MS (Fernández, Alonso, & Sanz-Medel, 2004). Natural water samples may contain high levels of calcium, which interfere in Fe measurements by forming CaO⁺ and CaOH⁺ polyatomics that are not completely eliminated in the cell. In order to eliminate such calcium interferences on Fe, a conductivity suppressor column from a conventional ion chromatography system was connected between the pump and the ICP-MS nebulizer. Calcium removal by the suppressor column was higher than 99.99% for calcium concentrations up to 1000 ppm (sample pH between 2.5 and 7). In order to avoid the simultaneous removal of Fe, water samples were previously spiked with the chelating agent EDTA to form a negatively charged complex which is not destroyed in the suppressor column.

Stančić, Z. et al. (2016) has showed the detection of heavy metals in the food samples of Croatian city market, Varaždin through atomic absorption spectroscopic technique. Lettuce, carrot, red and white potato, onion, common bean, and cabbage were analyzed for the presence of heavy metals in them and the scientist had found 9 different heavy metals though analyzing the food samples

though AAS. Among the 9 heavy metals, Pb and Cd contamination was found to be mostly common in red potato, beans and carrots (Stančić, Vujević, Gomaz, Bogdan, & Vincek, 2016). Byers, H. L. et al. (2019) has also examined dried and wet consumable vegetable tissues for the presence of Pb and other heavy metals through WD-XRF and/or portable ED-XRF spectroscopy. They have analyzed both the dried and wet tissue samples of consumable vegetables and reported the presence of Pb in them. They also have found the measurable concentrations of the Pb found is relevant to the WHO standards (Byers, McHenry, & Grundl, 2019). Nisa, K. U. et al. (2020) has reported the presence of heavy metals in certain food samples like Cabbage, Cucumber, Cauliflower, Tomato and Lady finger, Banana, Water melon, Mango, peach, apple etc. through Flame atomic absorption spectroscopy (FAAS). Deuterium background hollow cathode lamps (double beam) was used for the detection of certain heavy metals like Pb, Cd, Fe, Cu, Co, Mn and Ni etc. They have found the level of Ni to be higher than the toxicity level in cucumber along with elevated level of Pb in several vegetables and fruits (Nisa & Khan, 2020). Erasmus, S. W. et al. (2020) has evaluated the percentage of Pb contamination in turmeric powder by Fourier transform-Raman (FT-Raman) spectroscopy. They analyzed the FT-Raman spectra by both univariate and multivariate statistics. Analyzing the Raman peak at 840 cm^{-1} and through a correlation study they have proposed a limit of detection (LOD) of 0.6% (Erasmus, van Hasselt, Ebbinge, & van Ruth, 2020). Graphite furnace atomic absorption spectrometry (GFAAS) has been used by GEORGESCU, I. M. et al. (2019) for Pb detection in non-animal food products. They have reported that wine, fruits, cereals, vegetables and mushrooms samples containing a weaker Pb contamination, while high contamination has been reported in fruit juice samples (GEORGESCU, et al.). Not only that, wheat and barley samples were analyzed for the presence of toxic heavy metals like Pb, Cd, As, Co, Hg, Ni etc. though ICP-MS/MS by Thabit, T. M. et al. (2020). The

219 samples were digested using microwave acid digestion prior to analysis via ICP-MS/MS. They
220 have reported that Pb and Cd as the most prevalent heavy metals were found in several samples
221 (Thabit, Shokr, Elgeddawy, & El-Naggar, 2020).

222

223

224 **Table 2:** Summary of conventional techniques for major heavy metal detection.

Heavy metal	Sample pretreatment	Methods of detection	Detection limit	References
As ³⁺	UV digestion and preconcentration using <i>Aspergillus niger</i> -activated charcoal as biosorbent	ETAAS	1 µg L ⁻¹	(Shahlaei & Pourhossein, 2014)
Cr ³⁺	pre-concentration using ion exchange media	EDXRFS	0.4 mg L ⁻¹	(Menéndez-Alonso, et al., 1999)
	Pyrolysis and atomization using rhodium permanent modifier	ETAAS	0.2 µg L ⁻¹	(de Almeida Pereira, et al., 2004)
	Solid-phase extraction	ICP-MS	4.43 ng L ⁻¹	(N. Zhang, et al., 2008)
	Separation on a Dionex AS4A anion exchange column	CL	0.05 µg L ⁻¹	(Beere & Jones, 1994)
Zn ²⁺	Preconcentration on a microcolumn of immobilized Alizarin Red S on alumina	FAAS	0.2 µg L ⁻¹	(Shabani, et al., 2009)
	Chelating with 5,7-dichlorooxine	AAS	0.5 µ L ⁻¹	(Tony, et al., 1999)
	In situ pre-concentration with the dual silica tube atom trap	AAS	0.3 µg L ⁻¹	(Matusiewicz, et al., 1991)
	CPE pre-concentration	FAAS	0.095 µg L ⁻¹	(Jianrong Chen & Teo, 2001)
Cu ²⁺	DLLME pre-concentration	Spectrophotometric	0.5 µg L ⁻¹	(Wen, et al., 2011)
	CPE pre-concentration	FAAS	1.5 µg L ⁻¹	(Lemos, et al., 2007)
		ICP-AES	0.014 mM	(Rahil-Khazen, et al., 2000)
	Chelating 1,10-phenanthroline	CL	0.4 nM	(Coale, et al., 1992)
	solid-phase extraction	FAAS	0.2 µg L ⁻¹	(H.-M. Yu, et al., 2011)
Fe ³⁺	selective column extraction	CL	0.05 nM	(Obata, et al., 1993)

3.2. Modified conventional techniques

Some conventional techniques are modified for the in-field sensing of heavy metals. They have similar sensitivity as conventional techniques, but have higher degree of portability and rapidness.

Kunimura et al. has developed a portable total reflection X-ray fluorescence spectrometer for the nano level detection of Cr (Kunimura & Kawai, 2007). The continuum X-rays emitted from the low-power X-ray tube was used without monochromatizing them. The MDL for Cr was a few nanograms or the level of 10^{13} atoms cm^{-2} . Kumar et al. has designed and developed a cost-effective, simple, sensitive and portable LED based fiber optic evanescent wave sensor for simultaneously detecting trace amounts of chromium (Kumar, Lee, Vallabhan, Nampoori, & Radhakrishnan, 2002).

A novel micro-cloud point extraction (MCPE) was developed by Ghasemi et al. as a fast, simple, and economical pre-concentration method for spectrophotometric determination of Zn in water samples (Ghasemi & Kaykhahi, 2017). In contrary to traditional cloud point extraction, this method does not need heating. To achieve the cloud point in room temperature, the MCPE procedure was carried out in brine. Triton X-114 was employed as a non-ionic surfactant and the analytes were chelated by 4-(2-pyridylazo) resorcinol prior to extraction. Under the optimized condition, calibration curve was found to be linear in the concentration range of 0.15-0.60 mgL^{-1} for Zn with a limit of detection of 51.7 $\mu\text{g L}^{-1}$. A high sensitive method of quantitative analysis for the determination of Zn in the nutrition supplements has been developed by Weng et al. using a novel water-soluble fluorescent sensor (Ghasemi & Kaykhahi, 2017). Under the optimized condition of 67 mM phosphate buffer, pH 7.4, and 5% (v/v) DMSO, the Zn concentration exhibited good linear relationship with fluorescence intensity in the range of 7.5×10^{-8} to 2.5×10^{-5} M with the

248 detection limit of 1.5×10^{-8} M. The sensor revealed high selectivity to **Zn** comparing with other
249 metal ions except for **Cd**.

250 Quantitation technique of trace amounts of Cu (II) dissolved in natural water has been developed
251 by Gao et al. (Gao, et al., 2007). A novel detection approach named chromophore-decolorizing
252 with free radicals was developed for determination of trace heavy metal. Chen et al. has designed
253 a fluorescence resonance energy transfer (FRET)-mediated sensor, based on fluorescent polymeric
254 nanoparticles synthesized via a combination of a facile one-pot mini emulsion polymerization and
255 subsequently by surface modification technology. The nanoparticle-based dual-ion sensor can be
256 reversibly switched for multi-times by alternative addition of adequate Cu^{2+} or S^{2-} , and was also
257 applicable in a relatively wide pH range (pH 4 - 10), exhibiting excellent long-term photo-stability
258 for Cu^{2+} detection (Jian Chen, et al., 2015).

259 Microfluidic paper-based analytical devices (μ PADs) were used by Ogawa et al. to detect the iron
260 ion content in the water of a natural hot spring in order to assess the applicability of this process
261 to the environmental analysis of natural water (Ogawa & Kaneta, 2016). **The μ PADs were**
262 **fabricated using a wax printer after the addition of hydroxylamine into the detection reservoirs to**
263 **reduce Fe^{3+} to Fe^{2+} , 1,10-phenanthroline for the forming of a complex, and** poly(acrylic acid) for
264 ion-pair formation with an acetate buffer (pH 4.7). A novel colorimetric chemosensor containing
265 terpyridine was synthesized by Liang et al. that showed high selectivity and sensitivity for Fe(II)
266 and Fe(III) ions in neutral aqueous solution in the presence of other metal ions such as Cd^{2+} , Cr^{3+} ,
267 Zn^{2+} , Co^{2+} , Ni^{2+} , Cu^{2+} , Pb^{2+} , Na^{+} , Ca^{2+} , Mg^{2+} , K^{+} and Ag^{+} (Liang, et al., 2007). Upon the addition
268 of Fe^{2+} or Fe^{3+} , the sensor displayed a unique new peak around 567 nm in its absorption spectra,
269 and the color of the solution changed from light yellow to light magenta. Zhao et al. developed
270 Polyamine-functionalized carbon nanodots for the detection of Fe (II) (Lixia Zhao, et al., 2014).

Branched poly(ethylenimine)-functionalized carbon dots (BPEI-CDs) are used as a novel CL probe in alkaline solution for rapid detection of Fe (III) ions with high sensitivity and selectivity. A possible CL mechanism was studied by UV-Vis, fluorescence, CL, FTIR, XPS and EPR spectroscopy. An eco-friendly and simple fluorescent nitrogen-doped carbon quantum dot (N-CQD) biosensor was synthesized by Lv et al. via a hydrothermal method using ethylenediamine (EDA) and citric acid (CA) as precursors (Lv, et al., 2017). The surface functionalization of N-CQDs exhibited a bright blue emission under the excitation wavelength of 350 nm. As-prepared N-CQDs were further applied in Fe (III) detection. Spectroscopic data indicated that fluorescent carbon-based nanomaterials displayed a sensitive response to Fe^{3+} in the range of 0.5–1000 μM as a fluorescence sensor in real environmental samples. A novel rhodamine-based dual probe Rh-2 for trivalent ferric ions (Fe^{3+}) was successfully designed by Luo et al. and synthesized, which exhibited a highly sensitive and selective recognition towards Fe^{3+} with an enhanced fluorescence emission in methanol-water media ($v/v = 7/3$, $\text{pH} = 7.2$) (Luo, et al., 2016). The probe Rh-2 could be applied to the determination of Fe^{3+} with a linear range covering from 3.0×10^{-7} to 1.4×10^{-5} M and a detection limit of 1.24×10^{-8} M.

3.3. New age detection techniques

In the era of fast growing technology, rapid, high-throughput and field portable sensing instruments are much widely accepted due to their point-of-care application and low cost. To meet the high demands, the on-site portable sensors have been developed much rapidly. Though the technology yet lacks sensitivity and selectivity comparative to conventional methods, they have the potential to become primary point-of-care devices to accumulate data for sorting samples that need further attention.

Figure 1: Block diagram of a biosensor.

This section comprises of a brief review of the new advancement in methodologies for the detection of heavy metals with the use of chemical and biosensors. The transducer or the detector transform one signal into another one, and works in a physicochemical way - optical, piezoelectric, electrochemical, electro CL etc. signals resulting from the interaction of the analyte with the chemical or biological element, to easily measure and quantify the target analyte. Chemical or biosensory devices fulfill all the criteria that the conventional devices for heavy metal detection lack. Biosensors and chemical sensors are very much rapid, require minimum skill to operate, field portable, cost effective (Ronkainen, Halsall, & Heineman, 2010). On spot rapid detection of analyte is the main criterion that makes the biosensors and chemical sensors more preferable than the time consuming, costly conventional detection techniques.

There are various types of chemical and biosensors that are being applied to detect heavy metal contamination in water nowadays, which include ion imprinted sensors (Haupt & Mosbach, 2000), DNA aptamers (Patil, Rhodes, & Burgess, 2005), RNA-mediated biosensors (Velasco-Garcia & Missailidis, 2009), enzymatic biosensors (C. Chen, et al., 2013), protein-mediated biosensors (Bistolas, Wollenberger, Jung, & Scheller, 2005) etc.. Among them, use of ion imprinted electrochemical sensors, aptamer biosensors and enzymatic biosensors based on DNAzymes are more frequently seen (Y. Lu, 2002). A large variety of ion imprinted electrochemical sensors are available and can be easily modified to detect analytes with very low cost and minimum amount of time and labor (Yola, Eren, & Atar, 2015). Aptamers being single stranded DNA are to be handled more cautiously, but they are very much selective to the analyte like heavy metals and also modifiable with respect to the detection technique, i.e colorimetry or fluorimetry (Yola, et al., 2015). Moreover, enzymatic biosensors are used widely to detect heavy metals which preferentially use DNAzymes for specificity.

3.3.1. Enzyme-immobilized biosensors

Enzyme-based biosensors have been exploited for heavy metal ions detection extensively during last few decades. Biosensors use enzymes which are immobilized on the transducer surface and act as a bridge between the analyte and transducer. These type of sensors have an advantage of high sensitivity and selectivity for heavy metals detection. The enzymes are generally inhibited in the presence of heavy metals. This interaction is very specific for particular ions and hence has an enhanced signal generation. The enzyme is chosen based on their ability to transfer electrons.

According to Ilango et al., sol-gel-immobilized-urease conductometric biosensor on a thick film interdigitated electrode was developed (Ilango, Daniel, Krastanov, Zachariah, &

Elizabeth, 2006). The biosensor can be used for heavy metal ions determination in liquid samples. The biosensor exhibited good response to changes in urea concentration within the range of 1 mM to 15 mM. After standardizing the sensor for Urea, the biosensor has been used to determine the heavy metal ions of different concentrations. The heavy metals ranging from 0.1 mM to 10 mM could be detected. Among the three metals used, the amount of inhibition is found to be more in Cd, followed by Cu and Pb. The sensitivity was 1 mM in the spectrophotometric technique and 5 mM in the electrical method. Moyo used horseradish peroxidase (HRP) biosensor to detect Zn ions in aqueous solutions (Moyo, 2014). Maize tassel-multiwalled carbon nanotube (MT-MWCNT) composite has been used as a matrix for physical adsorption of HRP onto the surface of a glassy carbon electrode through electrostatic interactions. The HRP/MT-MWCNT biosensor was applied for the detection of Zn²⁺ in aqueous solution. The biosensor designed was able to determine Zn²⁺ in the range of 0.35 - 12 mg L⁻¹ with a detection limit of 7.5 µg L⁻¹. The inhibition was found to be reversible and uncompetitive when data was modeled using the Dixon and Cornish-Bowden plots. The biosensor was found to have good repeatability, reproducibility and high selectivity. The developed biosensor can be used to detect other HRP inhibiting trace metal ions.

Recent advances in this field suggest the use of DNAzyme based technology. DNAzyme based sensing can be applied as fluorometric, colorimetric and conductometric sensitivity. In Lu's work, nanoparticles were firstly coated with DNAzymes which have specific binding site for heavy metals and also tagged with quencher, then incubated with substrate DNA strands tagged with specific fluorophore (Y. Lu, et al., 2003). The quencher being in close proximity of the fluorophore quenched the fluorescence, but when incubated with heavy metals, the DNAzyme efficiently cleaves the substrate DNA, making the fluorophore free from the quencher, giving measurable fluorescence that is described in Figure 2.

Figure 2: Schematic pathway for DNAzyme based optical detection of heavy metal ions.

A novel fluorescence biosensor based on DNAzyme for rapid, simple, sensitive and selective detection of **Pb** ions was reported by Li and Lu (J. L. a. Y. Lu, 2000). It was reported that the quantifiable detection range was from 10 nM to 4 μ M and the selectivity was greater than 80-fold for **Pb** divalent ions over other metal ions. Enzyme immobilized biosensors are sensitive and selective but takes more time than aptamer based sensing or ion imprinted polymer based sensing. Some other enzymatic sensors used for detection of heavy metals are listed in Table 3.

358 **Table 3:** Enzymatic sensors for detection of heavy metals.

S. No	Sensor configuration	Transduction principal	Metals detected	Range of detection	LOD	References
1	GOx entrapped on novel ultra-thin poly(brilliant green) (PBG) films electrodeposited in ethaline DES on multiwalled carbon nanotube (MWCNT) modified glassy carbon electrodes (GCE)	Amperometric	Hg ²⁺ , Cd ²⁺ , Pb ²⁺ , and Cr (VI)	Hg ²⁺ (2.5-100 nM), Cd ²⁺ (10 - 100 nM), Pb ²⁺ (10 -120 nM), Cr (VI) (2.5-60 nM)	Hg ²⁺ (2.30nM), Cd ²⁺ (1.75 nM), Pb ²⁺ (2.70 nM), Cr (VI) (2.44 nM)	(da Silva, Ghica, & Brett, 2020)
2	Mg ²⁺ -dependent DNAzyme subunits, azide or alkaline modified, immobilized on magnetic beads	Fluorimetry	Cu ²⁺	10 nM to 10μM	2 nM	(W. Wu, Yu, Chen, & Yang, 2019)
3	Pb ²⁺ -specific DNAzyme immobilized on magnetic beads, coupled to rolling circle amplification (RCA)	pH metry	Pb ²⁺	1.0–100 nM	0.91 nM	(Tang, Xia, Tang, Zhang, & Zhou, 2019)

4	8–17 DNAzyme (the recognition element) immobilized on carboxyl-functionalized graphene modified electrode	Electrochemical	Pb ²⁺	10 ⁻¹³ to 10 ⁻⁷ mol·L ⁻¹	1.74 × 10 ⁻¹⁴ mol·L ⁻¹	(Z. Yu, et al., 2019)
5	Pb ²⁺ -specific DNAzyme containing the capture probe (NH ₂ -CP) immobilized on Au nanoparticles (AuNPs)-loaded Fe ₃ O ₄ nanocomposites modified electrodes	Electrochemical	Pb ²⁺	1 pM – 500 nM	0.32 pM	(J. Zhao, Zheng, Gao, & Xu, 2018)
6	Peroxidase-mimicking DNAzyme	Chemiluminescence	Hg(II)	12 - 600 nM	12 nM	(Gribas & Sakharov, 2018)
7	GR-5 DNAzyme based Pb ion strip biosensor	Colorimetric	Pb ²⁺	0.01 to 100 μM	0.05 nM (S/N = 3) and 1 nM (with naked eyes)	(H.-B. Wang, Ma, Fang, Zhao, & Hu, 2018)
8	Mg ²⁺ -specific DNAzyme (Mg ²⁺ -DNAzyme) for target cycling and hybridization chain reaction (HCR) assembled DNA hydrogel for signal amplification	Impedance biosensor	Hg(II)	0.1 pM - 10 nM	0.042 pM	(Cai, Xie, Zhang, Tang, & Tang, 2017)

9	fluorescent Cu ²⁺ sensor (PL-Cu 1.0) based on the relationship between glutathione/Cu ²⁺ and catalytic activity of Pistol-like DNAzyme (PLDz)	Fluorimetry	Cu ²⁺	80 nM to 30 µM	21.1 nM	(S. Wang, et al., 2017)
10	Cu ²⁺ -dependent DNA ligation DNAzyme	Detection through personalized glucose meter	Cu ²⁺	10 nM to 10 µM	1 nM	(Ming, Fan, Jiang, Wang, & Lv, 2017)
11	Cu ²⁺ -specific RNA-cleaving DNAzymes (PSCu10)	Fluorimetry	Cu ²⁺	5 nM to 200 nM	1.6 nM	(Huang & Liu, 2016)
12	Pb ²⁺ sensor based on DNAzyme and molecular beacon (MB)	Colorimetry	Pb ²⁺	0.05 to 5 nM	20 pM	(Yun, et al., 2016)
13	Urease and Glucose Oxidase based biosensor	Photoluminescence	Cu ²⁺ , Pb ²⁺ , Cd ²⁺	10 nM to 1 mM	10 nM	(Syshchyk, Skryshevsky, Soldatkin, & Soldatkin, 2015)
14	Specifically modified <i>Saccharomyces cerevisiae</i> strain immobilized in alginate beads	Colorimetry	Cu ²⁺	1 - 100 µM	1 µM	(Vopálenská, Váchová, & Palková, 2015)

15	Ultrathin polypyrrole–glucose oxidase (PPy–GOx) potentiometric biosensor	Potentiometry	Cu^{2+} , Hg^{2+} , Cd^{2+} and Pb^{2+}	Cu^{2+} (0.079–16 μM), Hg^{2+} (0.025–5 μM), Pb^{2+} (0.10–15 μM) and Cd^{2+} (0.04–62 μM)	0.079 μM for Cu^{2+} , 0.025 μM for Hg^{2+} , 0.024 μM for Pb^{2+} and 0.044 μM for Cd^{2+}	(Ayenimo & Adeloju, 2015)
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3.3.2. Aptamers-based biosensors

Aptamers are classified as short chain nucleotides or oligos which are synthesized based on the binding capability of the heavy metals. These oligos are generally synthesized by systematic evolution of ligands by exponential enrichment (SELEX) methodology sequentially. The general principle behind aptamer based sensing can be of either two types: one through the immobilization of aptamer on the **electrochemical** electrode surface for enhanced sensitivity, and the other through aptamer-based **substrate such as** gold nanoparticles (AuNP) reactions **to generate colorimetric response** (Y. Wu, Liu, Zhan, Wang, & Zhou, 2012) (Figure 3).

Figure 3: Schematic representation of aptamer-based AuNP for heavy metal detection.

Both of which can be applied to determine the specific metals present in a sample. Their sensitivity and LOD are generally not as low as the conventional techniques, but are quite efficient and high through output in detection of contaminated samples. Their rapid and portable nature gives them an advantage of being field portable technology. According to Wang and Si, they have used a novel aptamer biosensor based on multi-walled carbon nanotube (MWCNT) which allows for fluorescent energy transfer on binding with heavy metal such as Pb^{+2} ions and helps in their rapid detection (Si, 2013). The LOD has been reported to be 20 nM for Pb detection. Similarly, aptamer based technology has also been applied for the detection of cadmium divalent ions. Wu et al. showed that Cd specific aptamer[Cd -4] could be used for the detection of Cd divalent ions by a colorimetric reaction (Y. Wu, Zhan, Wang, & Zhou, 2014). The functionalized AuNP were hybridized with poly (diallyldimethylammonium chloride) (PDDA) resulting in a duplex complex. In presence of Cd divalent ions, the wine red solution of AuNP changed to blue due to no duplex formation and hence no aggregation of AuNPs. The LOD for this was reported to be 4.6 nmol/L. Lastly, electrochemical based aptasensors such as developed by Zhu et al. which is a sensitive electrochemical aptasensor based on the carboxylic acid functionalized multi-walled carbon nanotubes (MWNTs-COOH) and the direct electrodeposited AuNPs was developed for Pb^{2+} detection in water samples (Zhu, 2017). Methylene blue (MB) was selected as the G4-binding indicator and redox probe. The sensor could detect Pb divalent ions in a range from 0.01 to 50 pmol L^{-1} with a detection of 4.3 fmol L^{-1} .

Moreover, Zhou et al. has reported a method for the detection of Cu^{2+} ions by azide-and terminal alkyne-functionalized gold nanoparticles in aqueous solutions using click chemistry (Y. Zhou, Wang, Zhang, & Jiang, 2008). The catalyst, Cu (I), was conveniently derived from the reduction of Cu(II) in the presence of sodium ascorbate. This method allows the naked eye, without the aid

of any advanced instrument, to visualize the presence of Cu^{2+} ions by the aggregation of AuNPs as a result of the Cu (I)-catalyzed conjugation between the two functional groups. This method for the detection of Cu^{2+} ions relies on the Cu (I)-catalyzed 1,3-dipolar cyclo-addition of alkynes and azides on the surface of functionalized AuNPs, that results in the aggregation of AuNPs. A simple, rapid, sensitive and field-portable colorimetric technique for the determination of Cr(III) in aqueous solution based on an aggregation-induced color transition (wine-red to blue, discernible by the naked eye, easily measurable in the extinction spectrum of the particles) of dithiocarbamate-modified N-benzyl-4-(pyridin-4-ylmethyl) aniline ligand (BP-DTC) functionalized gold nanoparticles (AuNPs) has been developed (Liang Zhao, Jin, Yan, Liu, & Zhu, 2012). The method could be used to determine Cr (III) with a detection limit of 31 ppb and also applied in the indirect determination of Cr(VI) in waste water. Some other aptamer based detections of heavy metals are listed in Table 4.

406 **Table 4:** Aptamer-based detection of heavy metals.

S. N.	Sensor configuration	Transduction principal	Metals detected	Range of detection	LOD	References
1	Pb(II)-aptamer(Apt)	Fluorimetry	Pb ²⁺	0.0005 - 0.46 $\mu\text{mol L}^{-1}$	0.25 nmol L ⁻¹	(D. Li, Yuan, Li, Luo, & Jiang, 2020)
2	Hg ²⁺ specific aptamer with rolling circle amplification	Colorimetry	Hg ²⁺	2.5 to 100 nM	1.6 nM	(Shijia Wu, Yu, He, & Duan, 2020)
3	Aptamer-functionalized gold nanoparticles (AuNPs)	Colorimetry	Cd ²⁺	2–20 $\mu\text{g L}^{-1}$	1.12 $\mu\text{g L}^{-1}$	(Gan, et al., 2020)
4	DNA-based specific aptamer probes labeled with ferrocene (or methylene blue) and thiol groups at their 5' and 3' termini, respectively	Electrochemical	Hg ²⁺ and Pb ²⁺	0.1 to 1000 ng mL ⁻¹	0.1 ng mL ⁻¹	(Abu-Ali, Nabok, & Smith, 2019)
5	G-quadruplex DNA aptamer and an electrochemically reduced graphene oxide (ERGO) electrode	Electrochemical	Pb ²⁺	10 ⁻¹⁵ M to 10 ⁻⁹ M	0.51 fM	(S. H. Yu, Lee, & Kim, 2019)
6	DNA aptamer-programmed self-assembly of CdTe quantum dots	Fluorimetry	Hg ²⁺	0-100 nM	3.33 nM	(H. Guo, et al., 2019)
7	A mercury ion aptamer electrochemical biosensor based on a Thymine-Hg ²⁺ -Thymine (T-Hg ²⁺ -T) structure	Electrochemical	Hg ²⁺	0.01 to 500 nM	0.005 nM	(Liu, et al., 2018)

8	Triple-helix molecular switch with 2-amino-5,6,7-trimethyl-1,8-naphthyridine as the signal indicator	Fluorimetry	As ³⁺	10 ng L ⁻¹ to 10 mg L ⁻¹	5 ng L ⁻¹	(Pan, Li, Zhou, & Chen, 2018)
9	Aptamer-based fluorescence biosensor	Fluorimetry	Hg ²⁺	2 to 160 nM	0.2 nM	(Sun, et al., 2018)
10	Ultrasensitive aptamer electrochemical biosensor based on glass carbon electrode (GCE) modified with chitosan (CS), gold nanoparticles (AuNPs)	Electrochemical	Cd ²⁺	0.001 nM to 100 nM	0.04995 pM	(Liu, et al., 2017)
11	Hg ²⁺ specific aptamer	Fluorimetry	Hg ²⁺	0.13 ng mL ⁻¹ to 4 ng mL ⁻¹	0.13 ng mL ⁻¹	(Z. Wu, et al., 2017)
12	Hg ²⁺ specific aptamer	Colorimetry	Hg ²⁺	1 ng mL ⁻¹ to 32 ng mL ⁻¹	0.28 ng mL ⁻¹	(Xiao, et al., 2016)
13	Hairpin structure of complementary strand of aptamer, thionine, AuNPs	Electrochemical	Pb ²⁺	0.6-50 nM	312 pM	(Taghdisi, Danesh, Lavaee, Ramezani, & Abnous, 2016)
14	Hg ²⁺ specific aptamer	Electrochemical	Hg ²⁺	1x10 ⁻¹⁴ mol L ⁻¹ to 2x10 ⁻¹² mol L ⁻¹	5.0x10 ⁻¹⁵ mol L ⁻¹	(J. Li, Sun, Wei, Zhang, & Zhang, 2015)
15	G-quadruplex aptamer specific to Pb ²⁺	Fluorimetry	Pb ²⁺	0 to 400.0 nM	0.6 nM	(Qian, Shan, Chai, Chen, & Feng, 2015)

3.3.3. Ion Imprinted Sensors

Ion imprinted polymers contains specific cavities towards specific ions. Usually, the polymers are synthesized by polymerization of monomer in presence of ions. The ions are sequentially extracted from the polymer producing complementary cavities on the polymer matrix (Biju, Gladis, & Rao, 2003). Binding of specific ions in the cavities formed on the polymer matrix gives signals that can be captured and analysed for further study. These ion imprinted polymers can easily be polymerized on to the electrodes for electrochemical detection of analyte molecules. Recently ion imprinted polymers are widely used in various applications like chemical separations (Dam & Kim, 2008), catalysis (Wulff, 2002), or molecular sensors (Takeuchi & Haginaka, 1999) etc. Such process of ion imprinted polymer based detection is illustrated in Figure 4.

Figure 4: Schematic representation of ion imprinted based sensing.

420 The transduction principle may be based on differential pulse voltammetry (DPV), square wave
421 voltammetry (SWV) or impedance spectroscopy, etc.. Owing to the attractive properties like
422 sensitivity, accuracy and selectivity including cost reduction, ion imprinting approach for heavy
423 metal ion detection has become promising alternative of conventional techniques (Sebastian &
424 Mathew, 2018).

425 Poly(diphenylamine-co-2-aminobenzonitrile) (p(DPA-co-2ABN)), a polyaniline derivative, was
426 electrodeposited on the surface of electrode and applied for detection of Cd^{2+} ions using DPV
427 (Philips, Gopalan, & Lee, 2012). p(DPA-co-2ABN) contains a cyano group which pre-
428 concentrates the **Cd** divalent ions to form a cyano chelation complex. This pre-concentration helps
429 in electrochemical detection of **Cd** divalent ions effectively with a LOD of 0.255 mg L^{-1} . The
430 technique uses the principle of simple oxidation of metals due to applied voltage and simultaneous
431 increase in current due to increased electron flow which is proportional to the amount of metal
432 oxidized. This increase in current is seen as distinct peaks in between a constant potential range.

433 Hosseini et al. reported a highly selective and sensitive **Zn** ion-selective membrane electrode based
434 on N,N'-phenylenebis (salicylideaminato) as a new carrier (Hosseini, Abkenar, Ganjali, &
435 Faridbod, 2011). The membrane is composed of poly (vinyl chloride) (PVC), *o*-nitrophenyl octyl
436 ether (NPOE) as plasticizer, potassium tetrakis(*p*-chlorophenyl) borate (KTPClPB) as lipophilic
437 ionic additive, and N,N'-phenylenebis (salicylideaminato) as sensing material. The electrode
438 displays a Nernstian response to Zn^{2+} ions over a wide concentration range of 5.0×10^{-7} –
439 $1.0 \times 10^{-1} \text{ M}$ with the slope of $29.4 \pm 0.2 \text{ mV per decade}$ and a detection limit of $2.6 \times 10^{-7} \text{ M}$.
440 The sensor has a fast response time of $< 10 \text{ s}$ and it can be used in the pH range of 3.0–7.0 for at
441 least 2 months without any significant **divergence** in potential.

Gooding et al. has shown an electrochemical sensor for the detection of Cu ions that has a LOD below 1 pM (Gooding, Shein, & Lai, 2009). This extraordinarily low limit of detection is achieved in two ways. The first is to use SAM modified electrodes to give low background current where electron transfer to the underlying polycrystalline electrode is achieved through gold nanoparticles attached to the terminus of the SAM. The gold nanoparticles are modified with cysteine to allow Cu accumulation. In the second way, the low LOD are achieved by the addition of cysteine-modified nanoparticles to the sample solution, as well as the SAM modified electrode. The complexation of Cu with the nanoparticles in solution causes them to aggregate with these aggregates accumulating on the electrode. Thus a higher percentage of Cu in the solution is collected at the electrode, giving the enhanced detection limits. Though this technique has yet to be modified to achieve LOD values comparable to the conventional detection methods and near the standard toxicity limits, the advantage of this technique is its high through output nature, cost effectiveness and rapid screening of samples which can be further developed to make it portable in nature. Some other ion imprinted sensors for detection of heavy metals are listed in Table 5.

457 **Table 5:** Ion imprinted sensors for detection of heavy metals.

S. N.	Sensor configuration	Transduction principal	Metals detected	Range of detection	LOD	References
1	Magnetic ion-imprinted polymer (Fe ₃ O ₄ @SiO ₂ @IIP)	Electrochemical	Pb ²⁺	0.1–80 ng mL ⁻¹	0.05 ng mL ⁻¹	(Dahaghin, Kilmartin, & Mousavi, 2020)
2	Fluorescent ZnSe quantum dots (QDs) with ion imprinting technology	Fluorimetry	Cd ²⁺ and Pb ²⁺	for Cd ²⁺ : 1 to 70 µg L ⁻¹ and for Pb ²⁺ : 1 to 60 µg L ⁻¹	for Cd ²⁺ : 0.245 µg L ⁻¹ and for Pb ²⁺ =0.335 µg L ⁻¹	(J. Zhou, et al., 2020)
3	Boronic acid functionalized MoS ₂ quantum dot	Fluorimetry	Hg ²⁺	0.005 to 41 µmol L ⁻¹	1.8 nmol L ⁻¹	(X. Guo, Huang, Wei, Zeng, & Wang, 2020)
4	Blue and red dual channel dual emission carbon dots (DDCDs) as ion imprinted fluorescence polymers	Fluorimetry	Cr ³⁺ and Pb ²⁺	for Cr ³⁺ = 0.1 to 6.0 µM and for Pb ²⁺ =0.1 to 5.0 µM	for Cr ³⁺ : 27 nM and for Pb ²⁺ :34 nM	(H. Lu, Xu, & Liu, 2019)
5	Nanoparticles of the Hg(II)-imprinted polymers	Electrochemical	Hg(II)	0.06 to 25.0 nM	18 pM	(Ganjali, Rahmani, Shokoohi, Farmany, & Khazaei, 2019)
6	Ion imprinted polymers nanoparticles (nanoIIPs) immobilised on the surface of gold screen printed electrodes (SPAUE)	Electrochemical	Cu ²⁺	1.9 and 61 nM	74 pM	(Di Masi, et al., 2019)

7	Ion-imprinted chitosan-graphene nanocomposites (IIP-S)	Electrochemical	Cr (VI)	1.0×10^{-9} to 1.0×10^{-5} mol/L	6.4×10^{-10} mol/L	(Shuping Wu, Dai, Cheng, & Li, 2018)
8	Cadmium (II) imprinted polymer nanoparticles (IIP-NPs) immobilized cadmium(II)-selective electrode	Electrochemical	Cd ²⁺	0.008 to 0.05 μ M and in the ranges from 0.05 to 0.80 μ M	1×10^{-4} μ M	(Dahaghin, Kilmartin, & Mousavi, 2018)
9	Acrylic acid as monomer and N,N methylene bisacrylamide as crosslinker	Electrochemical	Zn (II)	1 to 5 ppm	1.32x10-4 μ M	(Sebastian & Mathew, 2018)
10	Itaconic acid-Pb ²⁺ complex and ethylene glycol dimethacrylate produced nano-structured ion imprinted polymer	Electrochemical	Pb ²⁺	1.0×10^{-11} – 8.0×10^{-8} mol L ⁻¹	3.8 pmol L ⁻¹	(Alizadeh, Hamidi, Ganjali, & Rafiei, 2017)
11	Cadmium (II) IIP particles in 2-nitrophenyloctyl ether as a plasticizer and embedded in a polyvinylchloride polymeric matrix	Electrochemical	Cd ²⁺	2.0×10^{-7} – 1.0×10^{-2} mol L ⁻¹	1.0×10^{-7}	(Ivari, Darroudi, Zavar, Zohuri, & Ashraf, 2017)
12	Ion-imprinted polymer (IIP) on the surface of reduced graphene oxide (RGO)	Electrochemical	Hg ²⁺	0.07 to 80 μ g L ⁻¹	0.02 μ g L ⁻¹	(Ghanei-Motlagh, Taher, Heydari, Ghanei-Motlagh, & Gupta, 2016)

13	Ion imprinted polymer (IIP) with Pb (II) as a template, methacrylic acid as a monomer, 8-hydroxyquinoline as a ligand, ethylene glycol dimethacrylate (EGDMA) as a crosslinker, and azobisisobutyronitrile as initiator.	Electrochemical	Pb ²⁺	0.05 – 60 µM	0.01 µM	(Hu, Xiong, Huang, & Lai, 2016)
14	Carbon ionic liquid paste electrode (CILE) impregnated with novel Hg ²⁺ ion imprinted polymeric nanobeads (IIP) based on dithizone	Electrochemical	Hg ²⁺	0.5 nM–10 nM and 0.08 µM–2 µM	0.1 nM	(Bahrami, Besharati-Seidani, Abbaspour, & Shamsipur, 2015)
15	Glassy carbon electrode (GCE) modified with zinc ion-imprinted polymers (GC/IIP)	Electrochemical	Zn (II)	5×10^{-10} to 1×10^{-8} M	0.5 nM	(Behnia, Asgari, & Feizbakhsh, 2015)

3.3.4 Other types of Sensors

Presence of heavy metals in water can be detected through several chemical and electrical sensors that include, electrochemical, impedimetric, electronic tongue (e-tongue), electronic nose (e-nose) mediated detection. This section describes some of the prominent detection evidences of several heavy metals in portable water through the mention techniques.

Noble metal based electrodes were used by Wei, J. et al (2015) to detect heavy metals like Cr(IV) in water through voltammetric technique. They used electrochemical impedance spectroscopy to detect trace amount of chromium in drinking water. The strategy was such that the crown ethers bind to HCrO_4^- specifically to form sandwich complexes. This complex formation inhibits the access of redox probes to the Au electrode. This in turn increases the electron transfer resistance that can be measured. The scientist have reported the range of detection as 1 to 100 ppb and the LOD as 0.0014 ppb at pH 5 (Wei, et al., 2015). Similarly, Canhoto, O. F., & Magan, N. (2003) had showed an indirect measurement of heavy metal concentration in water through e-nose using bacterial culture as an assisted signal transducer. They have shown that the presence of 0.5 ppm concentration of heavy metals can change the volatile production patterns by modifying the activity of microorganisms. Different microbial species like *Escherichia coli*, *Enterobacter aerogenes*, *Pseudomonas aeruginosa* was used to detect low concentrations of different heavy metals Cd, As, Pb and Zn using an electronic nose (Canhoto & Magan, 2003). Teodoro, K. B et al. (2019) has reported a modified electronic tongue based heavy metals detection in water where cellulose nanowhiskers (CNW), nanocomposites based on electrospun nanofibers and silver nanoparticles is used as the sensor material. The mentioned materials are combined to form 6 different sensing materials that are used to fabricate an impedimetric e-tongue. They have shown that the sensor array can efficiently detect Pb^{2+} at concentrations as low as of 10 nmol L^{-1} in

drinking water (Teodoro, Shimizu, Scagion, & Correa, 2019). Similarly, an automated electronic tongue was developed by Mimendia et al (2010) for the detection of mixture of heavy metals like Pb^{2+} , Cd^{2+} and Cu^{2+} in water. They have used the sequential injection technique to get the best output. They have formed a sensor array that contains four Ion Selective Electrode (ISE) sensors. Among the four sensors, two were based on Cd and Cu while the rest were Pb and Zn sensors. Fast Fourier Transform (FFT) and Artificial Neural Networking (ANN) was implemented to get best results from the sensor array (Mimendia, Legin, Merkoçi, & del Valle, 2010). Electronic tongue based redox water quality sensors were explored by Kuhlman, G. M. et al. (2004) for the detection of heavy metals in water. They have used nine planar electrochemical cells along with a conductivity sensor. Detection of heavy metals was performed by anodic stripping voltammetry (ASV). They have reported a linear calibration curve for Pb, Cu, Zn and Mn cations (Kuhlman, Keymeulen, Buehler, & Kounaves, 2004). A novel electronic tongue coupled with stripping voltammetry was used for environmental contamination detection by Men, H. et al (2005). They have used multiple light-addressable potentiometric sensor (MLAPS) along with two groups of electrochemical sensors for the efficient detection of Cr(VI) and Fe(III) ions. Anodic and cathodic stripping voltammetry was used to detect low concentrations of heavy metals in water along with a prototype development of a field portable handheld electronic tongue (Men, et al., 2005). Moreover, Wilson, D. et al. (2012) has reported an automated flow injection potentiometric system with electronic tongue for the efficient detection of heavy metals in water. The electronic tongue was an array of 5-sensors that includes Cu^{2+} and Ca^{2+} -selective electrodes. With this sensor array real time monitoring of the heavy metals is possible. They used ANN for better output generation from the sensor array as well (Wilson, Del Valle, Alegret, Valderrama, & Florido, 2012).

Besides these various modern sensor based detection techniques, scientists also explored nanomaterials to detect trace amount of heavy metals in food. Wenqin Wu, et al., has proposed the use of Fe₃O₄ nanoparticle coupled multiwall carbon nano tubes and its fluorinated versions towards the detection of Cd²⁺, Pb²⁺, Cu²⁺, and Hg²⁺ in food. They have reported the LODs of the Fe₃O₄/F-MWCNTs electrochemical sensor were 0.08, 0.02, 0.05 and 0.05 nM for Pb²⁺, Cu²⁺, Hg²⁺, Cd²⁺ respectively (Wenqin Wu, et al., 2019). Similarly, Pungjunun, K. et al. (2020) has mentioned the use of bismuth nanoparticle modified graphene screen printed electrode for the electrochemical detection of Sn(II) and Pb(II) in canned food samples. They used square-wave anodic stripping voltammetry technique in presence of CTAB and oxalic acid to reduce the interferences. Under optimal conditions, both metals showed a good linear range of 10–250 ng mL⁻¹, and their LODs were calculated as 0.26 ng mL⁻¹ and 0.44 ng mL⁻¹ for Sn (II) and Pb(II), respectively (Pungjunun, et al., 2020). A FET based ion selective sensor was developed by Tatavarthi, S. S. et al. (2020) to detect Arsenite (As(III)) in food and water. The developed sensor showed a high sensitivity towards arsenite with a dynamic range of detection of 10⁻¹⁰ M to 10⁻⁴ M. They have reported the LOD of the sensor as 10⁻¹⁰ M that is comparable to the conventional detection through ICP-MS (Tatavarthi, Wang, Wang, & Chen, 2020). Similarly, a fluorinated graphene/gold nanocage nanocomposite was developed by Tan, Z. et al. (2020) towards the detection of heavy metals in agricultural food. The scientists used the developed fluorinated graphene/gold nanocage (FGP/AuNC) electrode for the simultaneous detection of heavy metals like Cd²⁺, Zn²⁺, Cu²⁺, Pb²⁺ and Hg²⁺ through anodic stripping voltammetry in real samples like tea, peanut, ripe bolt etc. They have reported that the results were highly consistent and very much relatable with the conventional detection techniques like ICP-MS or AAS (Tan, Wu, Feng, Wu, & Zhang, 2020). Moreover, Zhang, W. et al (2020) has reported the use of gold nanoparticles modified electrode based smart

device towards the detection of heavy metals in cow milk, orange juice and apple juice etc.. They have also developed a solid stage microwave digestion device for the proper digestion of the sample. The electrochemical analysis showed good sensitivity towards detection and a stability up to 72 hours (W. Zhang, et al., 2020). Palisoc et al. (2019) has also reported the use of a graphite based electrode extracted from a Zn battery towards the detection of Cd and Pb in trace amounts in herbal food supplements. The electrodes were modified with bismuth nanoparticles and used in anodic stripping voltammetric technique for trace metal detection. The linear range was found to be 5 ppb to 1000 ppb with LODs of 1.06 ppb for Cd^{2+} and 0.72 ppb for Pb^{2+} (Palisoc, Vitto, & Natividad, 2019).

Both sensors and biosensors have their own pros and cons. Attributed to the use of bioreceptors, biosensors possess high specificity and affinity. On the other hand, they are expensive and inherently unstable due to the biological origins. The bioreceptors greatly increase the production cost of biosensor devices. Preserving their activity is another big challenge, as their functions are easily affected by the complex immobilization procedures and harsh environmental conditions, resulting in short shelf-lives. Compared to the enzymes and aptamers, the biomimetic ion imprinted polymers could be a good option to address the cost and stability issues. We envision that the high robustness and stability under a wide range of conditions, easy design of recognition sites for analytes, and low production cost would make ion imprinted polymers more popular in future biosensors for heavy metal detection. Another inherent limitation of biosensors is the low multiplexing capability. Most biosensors are dedicated to specific analytes, therefore not transferable between applications. For multi-analyte analysis, parallel biosensors are needed, which significantly increases the technical expenditure. On the contrary, chemical/physical sensors can easily be adapted for multiplex detection, whereas lack of specific recognition elements makes

them prone to interferences in the complex sample matrix. Therefore, the selection of appropriate sensing methods is highly depending on the water sample types, the operational environments, the affordability, as well as the requirements on sensitivity, selectivity and the throughput.

4. Field-portable commercialized instruments

This section explicitly gives a brief review of the market available portable instruments which are widely used and distributed. Integration of different units of target recognition, signal generation, signal transduction or amplification, signal reception and signal processing element result in a production-worthy heavy metal ions detection system to replace traditional signal detectors and workstations. Various materials and devices have been explored towards miniaturization of such units (Mehrotra, 2016). Analogue to digital conversions has been applied to demonstrate quantitative analysis of heavy metal ions. The goal of miniaturization has become more real owing to high-end computation like Big Data, cloud computing and neural network with the help of intelligent processors (Dash, Shakyawar, Sharma, & Kaushik, 2019). Introduction of light-emitting diodes (LEDs), complementary metal oxide semiconductor (CMOS) or charge-coupled device (CCD) based camera and smart phones and miniaturized electronic components (two, three or four layer PCB) enable the designing of portable sensor devices towards processing optical or electrochemical signals. This generates a new strategy to replace classical bulky and expensive components by combining the smartphone or camera or imaging system to realize a portable, rapid, and cost-effective quantitative detection. Table 6 lists some market available devices for detection of heavy metals.

As shown in the table, majority of the commercial devices are based on either electrochemical detection or optical detection. Both of them are powerful and convenient analytical tools for the

rapid and on-site detection of heavy metals. However, compared to the laboratory-based instruments, the analytical parameters of these portable devices are inevitably comprised due to the miniaturization. Therefore, the design and development of new sensors and biosensors with improved characteristics are required to overcome these limitations. One promising strategy is to combine the advanced nanomaterials with the sensors and biosensors to enhance their performance. For optical sensors and biosensors, colorimetric and fluorescence assays are the most popular signal transduction methods. New types of nanomaterial-based optical labels, such as quantum dots, upconversion nanoparticles provide lower background and sharper emission bandwidths, thereby leading to higher sensitivity. For electrochemical sensors and biosensors, the efficiency is largely dependent on the appropriate selection of the transducer surface. Modification of electrodes with different nanomaterials such as carbon nanostructures or metal/polymer nanomaterials can offer higher conductivity and catalytic activity to accelerate signal transduction, resulting in increased signals. We believe more excellent platforms that harness the synergistic effects of nanomaterials and sensors/biosensors will appear on market for heavy metal detection.

587 **Table 6:** Market available devices for detection of heavy metals

S.N.	Handheld Device	Targeted Heavy Metals	Principle of Detection	Image	Specifications	Reference
1.	uMED	Cadmium, Zinc, Lead	Square wave anodic stripping voltammetry		LOD = 4 µg/L <ul style="list-style-type: none"> • Rapid Detection and screening • Best for analysis in resource limited condition. 	(Nemiroski, et al., 2014)
2.	ANDalyze	Lead, Copper, Zinc, Cadmium	Fluorescence based sensing		LOD = 2 µg/L(Pb), 0.6 µg/L(Cu), 1 µg/L(Zn), 0.1 µg/L(Cd) <ul style="list-style-type: none"> • User friendly detection procedure without any user training • Rapid detection (Less than 2 minutes) • Highly sensitive and selective • Computer based result monitoring • re-sampling time is minute • No harmful reagents, environmentally friendly. 	(ANDalyze)

3.	DEP-Chip	Cadmium, Lead, Arsenic, Copper, Zinc	Differential pulse voltammetry		<p>LOD = 2.6 $\mu\text{g/L}$ (Cd), 4.0 $\mu\text{g/L}$ (Pb), 5.0 $\mu\text{g/L}$ (As), 15.5 $\mu\text{g/L}$ (Cu), 14.4 $\mu\text{g/L}$ (Zn).</p> <ul style="list-style-type: none"> • Disposable electrode printed (DEP)-On-Go 	(Biyani, et al., 2017)
4.	AppliTrace	Cadmium, Lead, Copper, Arsenic, Zinc, Iron	Anodic stripping voltammetry		<p>LOD = 1 $\mu\text{g/L}$</p> <ul style="list-style-type: none"> • Hot acid Digestion. (decompose organic matters to reduce noise) • Pre concentration methods for better detection. 	(AppliTrace)

5.	Portable heavy metal ion detector INE-SJB-801	Cadmium in rice and heavy metals (as zinc, cadmium, arsenic, mercury, etc.) analysis in drinking water.	Anodic stripping voltammetry		<ul style="list-style-type: none"> • Cost: Low cost than atomic absorption spectrophotometry. • With glassy carbon electrode system, this is accurate, low detection limit, suitable for precise measurement. • With screen-printed electrode test system, plug and play, suitable for rapid detection on the spot 	(MRC)
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5. Pros and cons of current devices

Over the recent years, advances in system integration and automation have accompanied with the fabrication of many analytical instruments for the detection of heavy metal ions. Most of the reported methods have presented the privileges of high accuracy and design simplicity, nevertheless, there are some deficiencies regarding the development of an ideal sensing device for heavy metal detection.

Reproducibility and signal stability is still a big challenge in the development of sensors when operating within low concentrations of analytes. Although advances in nanotechnology and integration with sensors/biosensors have enabled fabrication of highly sensitive platforms, yet to overcome the issue due to the difficulties in controlling the size distribution and homogeneity of nanostructures in large scales. Another challenge would be the multiplexing and selectivity of current devices. The commercialized systems mainly lack the bio-recognition elements to make them less selective and hamper their multiple quantification ability. Onsite monitoring of water pollutants is also another issue, as there is a dramatic variation between the water quality and pH in different sampling areas to make it difficult to use the same device in e.g. Asia and Europe and expect to observe similar results. In addition, there is still a high demand for the fabrication of an affordable and fully-automated field-portable device for the real-time monitoring of various heavy metal ions on a single platform.

6. Conclusion

This endeavor states about various conventional development along with recent trends like sensor based development towards field portability. The conventional systems will always be sensitive approach. In parallel to the conventional analysis, field-portable sensors are very much promising

612 wherein rapid screening is concern. Previously, the column sensitivity in conventional systems
613 was the concern for the scientists. Thus, researchers developed new column materials which could
614 be able to reach at the limits set by various regulatory authorities. In later stage, it has been found
615 that these conventional detection systems are lagging for rapid screening and field-portability.
616 Sensors or biosensors are integrated with receptors and decision support system (DSS) which
617 enable the features like pace and portability. These sensory systems come with receptors,
618 transducers and DSS along with digital display as a package. New age receptors like aptamers
619 (synthetic receptors) and ion-imprinted receptors have been exhibited the forte in the
620 transformation from classical receptors like enzymes, antibodies etc. to smart receptors. A
621 significant numbers of studies have been based on developing stable receptors, immobilization of
622 receptors and resulted in a solid background and experience in this field. Earlier, receptors were
623 mainly used for the detection of trace heavy metals in various types of water bodies, because the
624 principal condition for conducting a signal (either optical or electrochemical) was the presence of
625 a label marker. Thus, it was difficult to extract heavy metal ions from soil, plants, or other solid
626 objects. The recent progress on the efficient extraction of heavy metal ions from solid media allows
627 working on fruits, vegetables and soils etc. However, numbers of other ions, orientation of
628 receptors are the areas where a considerable attention should be waged to reduce interference and
629 noise. In view of work done towards development of field-portable sensory for heavy metal
630 detection, optical and electrochemical based sensors are evolving as cheaper and simpler approach
631 than some other methods. However, there are need in terms of increased reproducibility and anti-
632 interference ability among these sensor devices. Therefore, future research on optical and
633 electrochemical fields may build upon these aspects.

634 **Declaration of competing interest**

635 The authors declare that they have no known competing financial interests or personal
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