RSC Advances

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/advances

RSC Advances

Review

Gold nanoparticle based nano systems for the colorimetric detection of Hg^{2+} ion contamination in the environment

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Velswamy Poornima[a],† Vincent Alexandar[b],† S. Iswariya[a], Paramasivan T Perumal[c *] and Tiruchirappalli Sivagnanam Uma[a *]

The review highlights the impact of heavy-metal contamination on the human population and the need for its detection. Minute amounts of mercury ions present in a soluble form in the water enter the life cycle of man and produces its impact to an extent that it can even affect the foetus inside the womb. All these issues necessitate the need for the detection of heavy-metal contamination in water sources. Here in the review proposes the development of simple gold nanoparticle based sensors for the visual detection of mercury. Gold nanoparticles that have been modified using various functional units are employed in the detection of Hg^{2+} contamination. Simple, colorimetric methods have been employed in the detection and the major advantage of these sensors is that they are not only simple yet are very effective. As the presence/absence can be detected using the naked eye, these sensors are furthermore user-friendly and above all very cheap when compared to the other methods that employ the use of highly sophisticated and costly instruments.

1. Introduction

The human environment is constantly being subjected to various pollutants that are hazardous to its flora and fauna. The majority of these pollutants are poisonous in nature and come from both natural and manmade sources. One such harmful material which is found to cause a major environmental threat is the heavy-metal contamination. Heavy-metals are high-density metals and are divided to two namely essential and nonessential metals. Nonessential heavy-metals are those that pose a serious toxic threat to the surroundings even at very low concentrations[1]. Major sources of heavy-metal contamination in the environment is broadly classified into the following six categories- Natural, Agricultural, Industrial, Domestic effluents, Atmospheric and other sources. Volcanic eruptions, marine aerosols, forest fire and wind-blown dust contribute to the natural sources of heavy-metal contamination. Agricultural sources include those from fertilizers, insecticides, and pesticides. Contaminants from mining operations, ore refining, sludge disposal, radioactive paint processing, untreated water, waste water passed over sewage, etc. contributes to the heavy-metal contamination from industrial and domestic sources[2]. Other sources include that from anthropogenic sources such as fly ash from soil, incinerations, material processing and paint alloys[3]. The major concern here is the mercury ion toxicity as they are found to be highly soluble in water and are the most toxic among all the nonessential heavy metals. Two-thirds of the mercury contamination occur naturally while the remaining one-third is contributed by mankind[4]. Mercury, present in all the four spheres of earth is a major area of concern as environmental pollution has blown on a global scale[5]. The current situation demands the need for the development of easier and faster methods for detection of mercury contamination. Gold nanoparticles, with their excellent tunable optical properties play a vital role in fulfilling this purpose. Modified gold nanoparticles are employed for the detection of mercury contamination by colorimetric methods that can be seen with the naked eye. It is by far the simplest and quickest among the various methods devised for the detection of mercury contamination.

2. Mercury Toxicity

2.1. Sources and Major Health Problems

Mercury toxicants are found in ground, rain- and sea water. Inorganic mercury present in the air settles down in the aquatic system where it gets converted into the lipophilic, organic MeHg which gets interlaced into the aquatic ecosystem. Alongside the damages incurred, MeHg gets accumulated into meat and vegetables. Mercury has an ease of access to mankind through various pathways such as air, water and food. It also finds its way through the vaccines[6]. The high solubility of mercury in water makes it easily available to mankind by finding its place in the food

[a] Bioproducts Lab, CSIR-Central Leather Research Institute (CLRI), Adyar, Chennai 600 020, Tamilnadu, India. E-mail: suma67@gmail.com; Tel: + 91 44 24420709; Fax: +91 44 24911589
[b] Faculty of Allied Health Sciences (FAHS), Chettinad Academy of Research and Education (CARE), Kelambakkam, Kanchipuram 603 103, Tamilnadu, India.
[c] Organic Chemistry Division, CSIR-Central Leather Research Institute (CLRI), Adyar, Chennai 600 020, Tamilnadu, India. Email: ptperumal@gmail.com; Fax: +91 44 24911539; Tel: + 91 44 24437223.
† Both the authors have contributed equally
Electronic Supplementary Information (ESI) available: details of tales, graphs and figures. See DOI: 10.1039/x0xx00000x

chain via fish and food, resulting in major medical complications to the human population. Mercury originating from volcanic eruptions enters the nearby water resource. Due to its high solubility, it remains dissolved in water thus entering into the aquatic ecosystem. Algal bodies and plants surrounding the water medium are found to accumulate dissolved mercury. This absorbed mercury interferes with plant metabolism thereby hindering photosynthesis and causing a decrease in the total chlorophyll content of the plant. It also inhibits algal growth. Mercury content present within the plant/algae is a direct function to the extent of contamination of the water body.

Fig 1. Graphical Representation of Methyl Mercury Poisoning in Humans

Methyl mercury obtained from the bacterial conversion of inorganic mercury is highly soluble in water and cannot be separated thus leading to bio-magnification. It gets accumulated in the fish and when ingested enters the human system and causes various medical complications, including the central nervous system damage to the foetus present inside the womb as shown in **Figure 1**. Development of the central nervous system takes place right from the embryo stage and continues until the embryo reaches adolescence. In such cases, exposure to even minute quantities of mercury toxicant might lead to a number of disorders such as motor dysfunction, nervous disorder and loss of verbal memory. It also causes neurological, nephrological, immunological, cardiac and reproductive disorders. Mercury being able to cross the blood-brain barrier due to it higher lipophilic nature may as well cause genetic disorders in an individual and is found to be one of the major factors leading to Alzheimer's, Parkinson's and Amyotrophic Lateral Sclerosis (ALS). Mercury contamination occurs via various means such as- by inhaling mercury vapors from the atmosphere, ingesting water and food contaminated with mercury and through atopic applications[7]. Consumption of methyl mercury-contaminated fish is the major source of mercury poisoning in humans. The harmful effects arising due to the consumption of heavy-metal lead to what is known as the "bio-toxic effect" which could be either of the three namely acute, chronic or sub-chronic[8]. Mercury penetrates the blood and gets accumulated in the erythrocytes and causes severe damage to various organ systems.

Different forms of mercury affect the human system variously as depicted in **Table 1**. Higher levels of MeHg in the cord blood as compared to that of the maternal blood is a proof that MeHg crosses the placental barrier[9]. Foetal methyl mercury poisoning affects the foetus resulting in brain damage, tremors and seizures to the developing foetus[7].

2.2. Need for Detection of Mercury Contamination

Mercury contamination is found to be elevated among people consuming large amounts of food originating from the aqueous source. The general symptoms of mercury contamination in animals include weight loss, loss of appetite and laziness. Furthermore, mercury is known to cause a reduction in the reproductive rate among the contaminated fishes, thus leading to embryogenecity and teratogenecity[10]. High concentrations of mercury prevent mothers from getting conceived, even if they do so it results in a stillborn baby. Lower doses of mercury resulted in the birth of a live baby, but with serious neurological symptoms[11]. Prenatal exposure to organic mercury results in the extreme neurologic disorders such as autism among children. Autoimmune disorders are known to be caused by low dose contamination. Alongside acute dose of mercury, very low dose of the toxicant in water is in addition found to cause adverse health effects, which have created the need for the development of new methods to the detection of mercury contamination and to create a sense of environmental awareness among the public. Nanotechnology has led to the development of a novel method for the easier and simpler method for the detection of methyl mercury contamination in water.

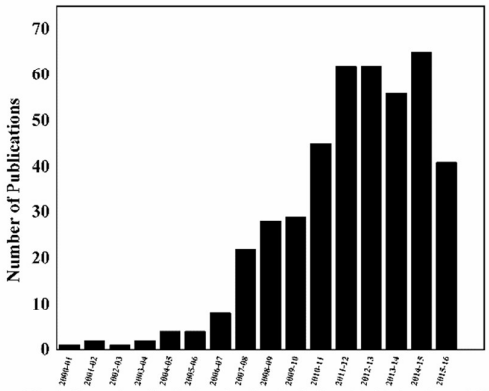

Fig 2. Yearwise Statistics for the Colorimetric Detection of Mercury Ions using AuNPs (2001-2016)

A literature search on ISI web of science using the keywords MERCURY and GOLD NANOPARTICLE and DETECTION in title search returned around 218 publications, which is the total number of scientific articles to this topic. **Figure 2** represents the number of publications on colorimetric detection of mercury using gold from the beginning to January 2016. The count is seen to be increasing every year indicating the need for mercury detection and adding a stress upon its importance.

2.3. Nano sensors for detection of mercury contamination

Drastic effects in the environment due to mercury pollution have created the demand for the development of highly sensitive and

selective methods in the detection of mercury[12]. Traditional coupled-plasma mass spectroscopy (ICPS) and fluorescence methods, such as atomic absorption spectroscopy[13], inductively

Mercury	Effect	References
	Acute Effects	
Elemental	**CNS effect:** tremors, irritability, insomnia, memory loss, neuromuscular changes, headaches, slowed sensory and motor nerve function, and reduction in cognitive function. **Kidney effects:** acute renal failure. **Gastrointestinal effects and respiratory effects**: such as chest pains, dyspnea, cough, pulmonary function impairment, and interstitial pneumonitis.	9,10
Inorganic	Acute oral exposure to inorganic mercury compounds include a metallic taste in the mouth, nausea, vomiting, and severe abdominal pain in humans.	9,10,11
Methyl mercury	CNS effects: including blindness, deafness, and impaired level of consciousness in humans.	9,10,11,12
	Chronic Effects	
Elemental	**CNS effects:** erethism (increased excitability), irritability, excessive shyness, insomnia, severe salivation, gingivitis, and tremors **Acrodynia syndrome**: severe leg cramps, irritability, paresthesia (a sensation of prickling on the skin), and painful pink fingers and peeling hands, feet, and nose.	9,10,13 9,10
Inorganic	**Kidney damage** **Mercury-induced autoimmune glomerulo nephritis** (induction of an immune response to the body's kidney tissue) in humans **Acrodynia syndrome**	9,10,11,13,14
Methyl mercury	**CNS effects:** paresthesia, blurred vision, and malaise. Effects at higher doses include deafness, speech difficulties, and constriction of the visual field. **Neurologic abnormalities** in human infants.	9,10,12 15
	Reproductive/Developmental Effects	
Elemental	Miscarriages, Spontaneous abortions, Birth defects	9, 13
Inorganic	Alterations in testicular tissue, Abnormalities of development.	913, 16
Methyl mercury	**CNS effect:** mental retardation, ataxia, and deafness, constriction of the visual field, blindness, and cerebral palsy. At lower methyl mercury concentrations, developmental delays and abnormal reflexes.	9,10,12
	Cancer Risk	
Elemental	**Cancer** in humans.	9,10,13
Inorganic	**Forestomach** and **thyroid tumors** in rats. An increased incidence of **renal tumors** in mice. **Carcinogenicity** in rats and mice.	16
Methyl mercury	**Carcinogenic effects** of methyl mercury in humans, and renal **tumors** in mice.	15

Table 1. Effect of elemental, inorganic and methyl mercury poisoning in the human population

spectroscopy[14] require complex sample preparation methods and are very expensive as they involve the use of highly sophisticated and bulky equipments[15]. Moreover, they lack in their sensitivity that led to the emergence of new analytical methods[16] based upon the use of molecular fluorophores, DNA, polymers, proteins[17], organic dyes and oligonecleotides[18]. All the aforesaid methods follow simple sample preparation procedures and do not involve the use of expensive equipments[19]. Though they have the convenience of being used for the analysis of water samples, they lack in sensitivity and selectivity owing to their poor solubility and cross sensitivity[20]. Though the fluorescence sensors are found to have a better selectivity, they present the problem of fluorescence quenching and also require organic solvent systems for the detection of heavy metals[21]. As an alternative, solution based optical probes were developed that could surpass the drawbacks of the traditional methods[22] for use in food analysis, environmental sciences and in biomedical assays[23]. These colorimetric sensors have an added advantage that they can be visualized with naked eye[24] and are found to possess the requirements of next-generation sensors with the advantage of being cost effective, simple and quicker with the possibility of infield detection[25]. Optical readouts are carried out in the solution phase and are helpful in overcoming the difficulties faced with the template based methods[26]. Among the various colorimetric tools available, metallic nanoparticles are found too very effective in biological sensing[27]. Metallic gold, especially in its nano form is found to be an efficient tool for the colorimetrical sensing of not only mercury but also other heavy metals[28].

3. Gold nanoparticles and Surface Plasmon Resonance

Among the various types of sensors available Surface Plasmon Resonance (SPR) based, optical sensors have their own benefits and are based on label-free detection[29]. SPR is defined as the collective oscillation of electrons, which is dependent on both the nature and size of the material[30]. The extreme sensitivity of SPR to slight changes in the refractive index than the medium surrounding the particle is exploited for highly sensitive detection and quantification of the analyte using absorption spectrometer[31]. Change in the mass concentration is also dependent on the molecular weight of the analyte[32]. As it is not advisable to present the metal surface directly to the analyte, surface functionalization is performed to facilitate the molecular reaction between the target and the sensor[33]. SPR mainly focuses upon the development of new methodologies in combination with various techniques for biomolecular interaction analysis[34]. Gold nanoparticles possess unique size and shape dependent properties, which are of high significance and are attributed to their localized Surface Plasmon Resonance (LSPR), a condition wherein their electrons exhibit a collective oscillation upon exposure to electromagnetic radiation[35]. This review deals with the different methods employed for the detection of mercury contamination and also the limits of detection for varying techniques. The highlight being that each of the techniques employed leads to the colorimetric detection of mercury with the naked eye.

3.1. Synthesis and Characterization of Gold nanoparticles

An acidic solution of 0. 01M tetrachord auric acid was prepared by dissolving HAuCl4 in dilute acetic acid. AuNPs with different capping agents were prepared by adding the different capping and reducing agents (NaBH4, Chitosan, and trisodium citrate) to 10mL of the gold chloride solution with under optimal temperature conditions. The reaction was carried out until the color of the gold solution turned wine red. **Table 2** provides the details about the temperature conditions maintained for the different reducing agents employed in the reduction of HAuCl4. The as-prepared gold nanoparticles were analyzed using UV-Vis spectroscopy. The obtained results confirmed the formation of gold nanoparticles with size <20 nm. These gold nanoparticles are modified variously for the detection mercury contamination. The increase of extinction with reaction time reveals the formation and increasing population of gold nanoparticles. The nanoscale electronic effect known as the SPR effect, causes metallic nanoparticles to absorb and scatter electromagnetic radiation of wavelengths considerably larger than the particles themselves. These effects are particularly noticeable in the visible part of the spectrum for gold. The optical absorbance spectrum of gold nanoparticles is a good indicator of size and shape36. In preliminary studies, no transparent or color variation occurred in the inter-mixture of gold solution mixed with a chitosan acidic solution. . At the same time, no distinct absorption peak of gold nanoparticles occurred on the UV–Vis spectra. According to the literature, the distinct absorption peak from the surface plasmon absorption of the gold nanoparticles is located between 510 and 530 nm. UV-Vis absorption peaks obtained were well within this range and indicate the formation of gold nanoparticles of in the size range <20 nm.

S.No.	Reducing Agent	Capping Agent	T (˚C)	Time (min)
1	$NaBH_4$	Uncapped	RT	60
2	$NaBH_4$	Chitosan	RT	30
3	Chitosan	Chitosan	Boiling	30
4	TSC	Uncapped	Boiling	30

Table 2 Synthesis of gold nanoparticles using different capping and reducing agents

Figure 3 represents the transmission electron microscopic images of the gold nanoparticles synthesized using different capping and reducing agents. **Figure 4** represents the UV-Vis spectroscopic images of gold nanoparticles. All the analysis confirmed that the size of the formed nanoparticles was less than 20 nmModification of gold nanoparticles for the detection of mercury.

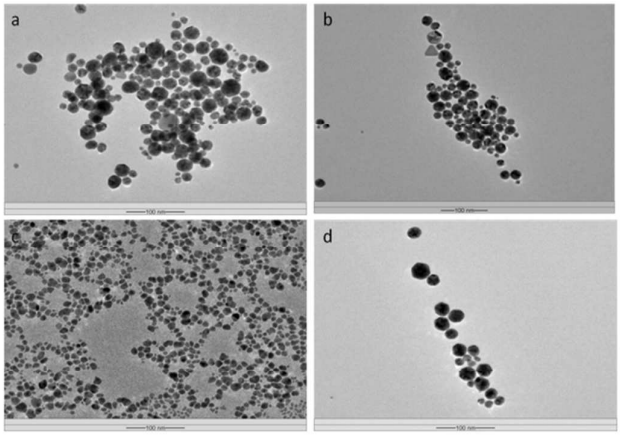

Figure 3 TEM images of a) TSC reduced b) $NaBH_4$ reduced c) $NaBH_4$ reduced Chitosan capped and d) Chitosan capped and reduced Gold nanoparticles

The as-prepared gold nanoparticles are modified/functionalized variously for the detection/quantification of methyl mercury. **Table 3 &4** represents the list of materials used in the functionalization of the gold nanoparticles, mechanism of functionalization and the limits of detection achieved. Figure 5 represents the various agents used in the detection, and the limits of detections achieved. All the detection methods followed the same mechanism of visual inspection for the detection. The limits of detection (LOD), achieved using different moieties varied from one to another and is discussed below in detail.

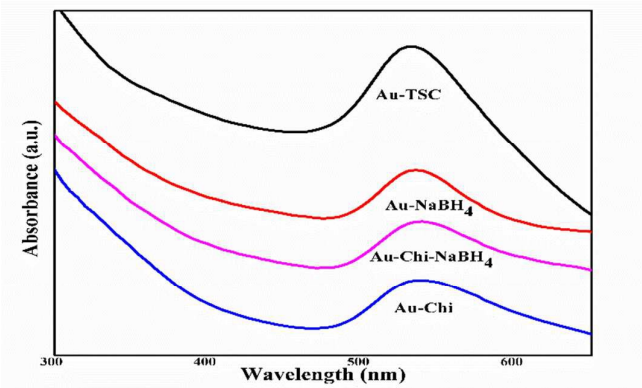

Fig 4 UV-Vis SPectroscopy of AuNPs Prepared using Different Reducing and Capping Agents

3.2. Modification of gold nanoparticles for the detection of mercury

The as prepared gold nanoparticles are modified/functionalized variously for the detection/quantification of methyl mercury. **Table 3** represents the list of materials used in the functionalization of the gold nanoparticles and the limits of detection achieved. **Figure 5** represents the various agents used for the detection and the limits of detections achieved. All the detection methods followed the same mechanism of visual inspection for the detection. The limits of detection (LOD), achieved using different moieties varied from one to another and is discussed below in detail.

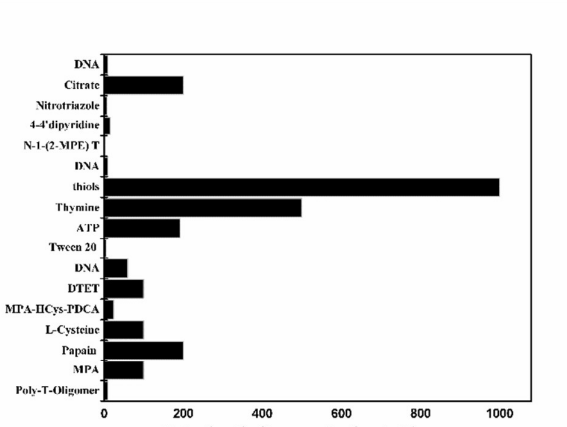

Fig 5. Different Functionalization units Vs. Detection Limit Concentration

3.3. Methods of modification of gold nanoparticles

A number of methods have been devised for the functionalization of gold nanoparticles. The method of functionalization depends on the end application of the as-prepared nanoparticles. For colorimetric detection of mercury, gold nanoparticles have been chosen as the appropriate nanomaterial as they possess SPR, which is an important attribute for these kinds of color changing reactions. Functional units have been designed such that they increase the reactivity between the AuNPs and Hg^{2+} ions when present at the solution. Single-stranded DNA with simple modifications is found to have an increased affinity to gold nanoparticles. DNA modification of AuNPs is achieved by a easy wet chemical method. A similar method is adapted for the amino acid functionalization. Esters, polythiols, nitrazole, carboxylic acids and other such groups are attached onto the surface of the gold nanoparticles that are synthesized using different capping and Reducing agents. Though simpler methods are adapted for the modification of gold nanoparticles, a few precautionary steps are to be considered while functionalizing the AuNPs such that it does not affect the integrity of the gold nanoparticle. These modifying units are found to enhance the sensitivity of the system they are employed in. Table 3 gives the different mechanisms that are involved in the functionalization of gold nanoparticles and the various functionalization units that are discussed during the review. One major point of concern while choosing the functionalization unit is to check that it does not disturb the dispersivity nature of the gold nanoparticle. In addition, it should be capable of inducing aggregation with the introduction of the analyte (Hg^{2+}), thereby bringing about a color change in the solution. Besides, there are methods that employ anti-aggregation of the gold nanoparticles, but the rule of thumb remains the same, i.e. the capacity to bring about color change, which makes the visual detection possible. The color change can be from red to blue (Red shift) or its reverse (Blue

Shift). Thus, a qualitative detection is achieved by naked eyes while quantitative detection can be achieved using a sophisticated instrument like UV-Vis spectrophotometer.

S.No.	Type of AuNP	Modifying Unit	Mechanism of Modification	References
1	Turkevich method	**Probe A**- Au-3'S-ATGCTCAACTCT5', **Probe B**- Au-5'S-CGCATTCAGGAT3' **Probe C**-Oligonucleotide linker	Simple wet chemical synthesis at room temperature by means of coordination chemistry	12
2	Reduction by $NaBH_4$	Thymine acetamidoethanethiol	Thymine-1-ylacetic acid with cysteamine	13
3	Nanogold aptamer	Single stranded DNA (ssDNA)	Self-assembly of the aptamer by catalytic reaction	16
4	Gold Chromophore	Thiourea	Desulfarization reaction of thiourea with AuNP	18
5	AA stabilized AuNP	Glycine	Photochemical synthesis by Irgacure 2959	35
6	DTET-AuNPs	Dithioerythritol	Ligand exchange interaction	14
7	Thiol group	Thiol	Fixing AuNP onto amine functionalized glass slides	17
8	NTA-AuNP	3-Nitro-1-H-1,2,4-triazole	Triazole ring of NTA interacts with AuNP surface	15
9	Green synthesis	Chitosan	By means of core/shell formation	28
10	Quantum Dot	Mercury Sulfide (HgS) quantum dots	Formation of HgS QD shell onto AuNP surface	23
11	Buffer stabilized	Tween 20	Ion Redox modulated surface chemistry	47
12	Anti-aggregation	L-Cysteine	Wet chemical synthesis	19
13	DNA-AuNP	Mercury specific DNA	Incubation in HEPES at room temperature	37
14	T-SH-AuNP	N-1-(2-Mercaptoethyl) thymine	Ligand Exchange interaction	41
15	Anti-Aggregation	4,4'-Dipiridyl (DPy)	Coordination chemistry between AuNP and DPy	22
16	Protein-AuNP	Pappain	Obtained by incubating papain solution to PBS	29
17	Peptide AuNP	NH_2 –Leu-Aib-Tyr-Ome	In situ reduction by the carboxylated peptide	27
18	Acid stabilized AuNP	3-Mercaptopropionic Acid	Coordination Chemistry	43
19	DNA-AuNP	**Probe A**: 5'HS-C10-A10-T-A103' **Probe** B: 5'HS-C10-T10-T-T10 3'	Through the thiol group present in DNA	24
20	Amino Acid	L-Cysteine	Through the S- atom present in L-Cys	42
21	Optically modified	MPA-H-Cys-PDCA	Incubating AuNP with MPA-HCys-PDCA	21
22	Acid Modified	3-MPA and AMP	Electrostatic interaction	45
23	Naphthol	1,8-Naphtholimide	Aqueous phase synthesis	48
24	Quaternary Ammoniun	Hydrophilic (11-Mercapto Undecyl)-trimethyl ammonium (MTA)	Ligand exchange interaction	44
25	DNA functionalized	Poly thymine (T_{33}) oligo in Mn^{2+}	Mn^{2+} groups on AuNP binds to backbone of DNA	38

Table 3 Different modifying units and the methods of modification of gold nanoparticle

4. Methods of detection of Mercury

4.1. DNA

DNA oligonucleotide-functionalized gold nanoparticles upon addition to a solution of methyl mercury showed a sharp bathochromic shift from 520 nm to 556 nm with a change in the colour of the solution from wine red to dark purple due to the conversion of MeHg to Hg^{2+} and due to the aggregation of the gold

nanoparticle. The change in colour was visible to the naked eye, and the aggregation was confirmed using transmission electron microscopy[12]. Mercury specific DNA modified AuNPs colorimetric probe brought about a detection of mercury of concentration 60 nM in edible fish, which was very much lower than the toxicity level determined by the U. S. environmental protection agency (EPA)[36]. Itamar *et.al*, devised an oligonucleotide-based method for the colorimetric detection of Hg. The method was based upon the formation of hairpin bend wherein the spatially separated T residues are linked to Hg^{2+} leading towards the formation of a stiff structure resulting in the aggregation of gold nanoparticles. LOD of this method was found to be 10 nM[37]. Polythimine oligonucleotide functionalized citrate-capped AuNPs brought about the detection of Hg^{2+} (10 nM) in the presence of Mn^{2+} ions. When the number of thymine residues was >33, the aggregation was found to take place within 6 minutes[38]. The LOD achieved by this method was 100 nM[24]. Single strand DNA modified nanogold probe with its unique optical and electrical properties is considered to be one of the best nanoparticles for nanoanalytical chemistry. Nanogold ssDNA (NGssDNA) probe is employed for the detection of Hg^{2+} based on the change in the resonant scattering spectra brought about by the aggregation of NGssDNA upon the addition of mercuric ions. The method was based upon the detection of change in the solution color owing to DNA-AuNP aggregation. The major advantage to this method is that it enables the assay to be carried out in aqueous media without the need for other organic co-solvents.

The fundamental principle to the detection of other heavy-metal ions using DNA is achieved by imparting slight modifications in the system and quantification is also achieved by studying the change in DNA melting temperature (Tm). A 15-mer-thrombin binding sensing element modified gold nanoparticles was developed for the salt-induced gold nanoparticle aggregation. The aptamer molecule consisted of six thymidine and nine guanosine units that interact in a specific manner to form a hairpin-like or a quadruplex structure. In addition to Hg^{2+} sensing these AuNP reporting probes can also be used to characterize conformational changes in an oligonucleotide[39]. Presence of thiol modification of the surface of gold nanoparticle enhanced the adherence of Hg^{2+} ions on its surface. Hence, thymidine-modified AuNPs were effective for the detection of Hg^{2+}.

4.2. Amino Acids

Amino acid modified gold nanoparticles are found to be highly sensitive in the detection of mercury. Owing to the cheap availability of amino acids, thymine-based derivatives are used for the detection of Hg^{2+} ions. Thymine acetamido ethanethiol (T-SH) is designed as a recognition unit for the detection of Hg^{2+}. The combined presence of T-SH and Hg^{2+} brought about the aggregation of gold nanoparticles producing a shift in the absorption spectrum from 520 nm to 660 nm with the limit of detection being 50 nM[13]. Mercaptoethyl modified thymine functionalized gold nanoparticle probe had a detection limit of 2.8 nM[40].

L-Cysteine modified AuNPs had a LOD of 100 nM[41]. Water dispersible, glycine capped gold nanoparticles, which are unique in the determination of mercury. The presence of mercury is confirmed by the color change as the solution which is brought about by the aggregation of glycine capped gold nanoparticles in the presence of metal. The anionic stabilized gold nanoparticle could achieve a sensitivity of 10 μM[35]. The presence of a thiol moiety in cysteine enables the facile binding of gold nanoparticle to the amino acid via gold-thiol bonding. The major advantage in the Sulphur group is the worry-free binding of Hg^{2+} to the Sulphur group. The presence of mercury brings about the aggregation of gold nanoparticle through the inter particle cross linking. Zhang et. al., could achieve a detection limit of 50 nM[19]. Gold nanoparticles modified using carboxylated peptides brought about the detection limits to as low as 200 pM wherein the N-terminus amino group is anchored to the AuNP and C-Terminus carboxyl group is left available for binding with Hg^{2+}. The major advantage with this method is that the detection time is only 5 minutes. As compared with the other methods of detection peptides are highly biocompatible and hence can be used for other biotechnological applications.

4.3. Acids, Esters and Polythiols

The thiophilic nature of Hg^{2+} has attracted scientists to explore the use of thiol groups for the detection of mercury. Based upon this fact dithioerythritol (DTET) functionalized gold nanoparticles have been employed for the detection of mercury. The basic mechanism upon which this system works is through the sulphur-Hg^{2+}-sulphur interaction between the DTET- modified gold nanoparticles. The major principle underlying the system is based on Mie Theory, which states that when the inter-particle distance between two nanoparticles becomes less than the sum of their radii.

S. No.	Size (nm)	Functionalization	pH	Medium	Detection time (min)	LOD	Detection Mechanism	References
1.	11.7	Carboxylated peptide	2.0	Water (RT)	10	200 pM	Dipole-dipole interaction	**26**
2.	13.1	Polythymine oligonucleotide	7.4	PBS (RT)	5	10 nM	Salt induced aggregation	**39**
3.	13.3 ±	Mercaptopropioc	9	Tris borate	60	100 nM	Metal induced aggregation	**43**

	0.5	acid		buffer (RT)				
4.	42	Papain	6	Water (RT)	no	200 nM	Metal induced aggregation	**28**
5.	no	DNA	no	no	no	100 nM	Thymidine–Hg^{2+}–Thymidine coordination chemistry	**24**
6.	16	L-Cysteine	no	Water (RT)	10 -30	100 nM	UV radiation	**42**
7.	4	MPA-HCys-PDCA	no	Water (RT)	10	5ppb	Non linear optical Properties	**21**
8.	16.0± 1.9	Dithioerythritol	6.6	PBS (RT)	10	100 nM	Sulfur-Hg^{2+}- sulfur interaction	**14**
9.	100	Chemodosimeter	no	Water (no)	10	10 µM	Scatteing property	**47**
10.	50	1,6-hexanedithiol	no	No	no	1- 10 nM	Single-nanoparticle-based metal ion sensing	**17**
11.	13.1	3-MPA-AMP, R6G/MPA/AMP	7.4	PBS (RT)	30	50-500 nM	Metal induced aggregation	**43**
12.	13 ± 1	Tween 20	7.9	Drinking water and Seawater (RT)	5	0.001 nM	Citrate induced aggregation	**20**
13.	13.1 ± 0.5	DNA	No	Water (RT)	10	60 nM	T-Hg-T complex induced aggregation	**37**
14.	13	Tween 20 (1)	7.2	Water (RT)	30	5 nM	Aggregation	**46**
15.	12.2	Cysteine	5.0	Drinking water (RT)	no	50 nM	Au S bond - Hg-cys complex induced aggregation	**19**
16.	5±2	Glycine	7.5	Water (RT)	no	10 µM	Heavy metal induced aggregation	**35**
17.	13	Adenosine Triphosphate	7.4	Sodium borate buffer (RT)	3	193 nM	Thiourea induced aggregation	**18**
18.	13	Thymine	9.0	Sodium borate buffer (45-50 ° C)	10	500 nM	T-Hg-T complex induced aggregation	**13**
19.	13	Quaternary ammonium		No	no	1000 nM	T-Hg-T mismatch	**44**
20.	14 – 30	DNA	7	PBS (RT)	5	10 nM	T-Hg-T coordination chemistry	**12**
21.	no	N-1-(2-MPET)	7.4	PBS (RT)	5	2.8 nM	T-Hg-T complex formation	**41**
22.	13	4-4'dipyridine	7.0	Tris HCL and Tap water (RT)	no	15 nM	Anti-aggregation	**22**
23.	10	sDNA	No	Water (60° C)	15	1.7 pM	T-Hg-T mismatch	**48, 55**
24.	no	HgS	3.57	Water (RT)	90	0.5 nM	SPR	**23**
25.	no	Chitosan	7	No (RT)	no	5 pM	SPR	**27**
26.	~ 13	Nitrotriazole	8.0	Tris buffer (RT)	60	7 nM	Salt induced anti aggregation	**15**
27.	13.1± 4	Citrate	No	Lake water	no	200 nM	Salt induced anti aggregation	**40**
28.	13	DNA	No	Tris-acetate	20	10 nM	Hg^{2+}-bis-thymine complex	**38**

29.	13	Poly thymine DNA	No	50 mM NaCl)	no	10 fM	T–Hg^{2+}–T coordination	**56**
30.	13	DNA	7.4	Tris-HCl buffer	no	1 Nm	Hg^{2+}-DNA complex	**57**

Table 4 Summary of the variously modified gold nanoparticles, their working pH, medium, size, LOD and mode of action of Hg^{2+}

It brings about a red shift in the spectrum along with peak broadening and a decrease in the intensity. DTET-AuNP can be used in the detection of Hg^{2+} with concentrations >100 nM[14]. Mercaptopropionic acid modified gold nanoparticles aid in the highly sensitive detection of Hg^{2+} ions in the presence of 2,6-pyridine carboxylic acid (PDCA). The Ionic strength of the solution used plays a crucial role for the detection of heavy-metal ions. The pH of the solution can be tuned by varying the buffer composition and henceforth the surface charge density can also be controlled. MPA ligand density on MPA-AuNP, cooperativity of PDCA and the buffer composite aid for the selectivity and sensitivity of the system. This low-cost system has a limit of 100 nM and is believed to lay the foundation to the development of nanosensors which could be employed for the detection of Hg^{2+} in both biological and environmental samples[42]. For the better assessment of human health and environmental safety, efforts have been made to improve the detection of mercury from water and other resources. 1,6-hexane thiol modified gold nanoparticle system for the detection of Hg^{2+} is based upon the shift in the localized surface plasmon resonance (LSPR) of the individual gold nanoparticle owing to the binding of analyte to the gold nanoparticle. The shift across the wavelength spectrum of an individual nanoparticle was tracked with the help of LSPR induced scattering spectrum using a dark field microspectroscopy (DFMS) system. Using this method it was possible to reach the sensitivity levels as low as 100 pM[17]. A cost-effective system based on the second-order nonlinear optics (NLO) property of the gold nanoparticle has been designed in order to achieve a gold nanoparticle based colorimetric detection of mercuric ions, which does not involve the complex tagging and labelling of AuNPs which in turn prove to be very costly. The precision of the system based on NLO is found to be around 5 ppb. Hyper-Rayleigh scattering (HRS) technique has been employed in the monitoring of NLO properties. As the system does not involve the application of electrostatic field and phase matching, it can be used for a wide range of systems. Herein gold nanoparticles modified using MPA, homocysteine (HCys) and PDCA are subjected to the detection of Hg^{2+} and other heavy-metal ions. The major advantage to this method is that it is completely labeled free and HRS assay does not involve the use of any fluorescent probe. Alongside it is highly selective, and it takes a maximum of only 7 minutes for the detection of mercury contamination[21].

Adenosine monophosphate (AMP) and MPA modified AuNPs are capable of detecting Hg^{2+} ions against the concentration as low as 500 nM. High negative charge density on the surface of MPA/AMP modified gold nanoparticle enables the complete dissolution in a high salt solution. Aggregation of nanoparticles in the presence of mercury is by the coordination between the carboxyl group of MPA and Hg^{2+}, which also renders it highly selective in a salt solution. Another major reason for the aggregation of these particles is due to the reduced electrostatic repulsion between the particles that arises due to a decreased zeta potential on each AuNP. It is found that the sensitivity of the system depends on the concentration of AMP and the optimal molar concentration of AMP to MPA is 1:500. This molar ratio of AMP and MPA used during the synthesis of AuNP, brings about the visual color change from red to purple upon exposure to Hg^{2+}. The sensitivity of the system was further improved to 50 nM by the addition of a fluorescent tag rhodamine 6G (R6G) to this MPA/AMP-capped AuNP[43]. Quaternary ammonium group terminated thiol-capped AuNPs (QA-AuNP) are used in the solar irradiation assisted detection of Hg^{2+} in aqueous media at room temperature. This method does not make use of any masking agents and possesses a dynamic detection range from 30 nM to 0.01M The principle behind this system is the abstraction of Hg^{2+} that brings about the aggregation of AuNPs. It is a well-known fact the Hg^{2+} possesses a greater affinity towards the thiol groups. Thus, the thiolate groups attached onto the surface of Qa-AuNP are removed by the affinity of mercury thereby bringing about a destabilization of the solution finally resulting in an aggregation[44].

Herein, hydrophilic (11-mercapto-undecyl)-trimethyl ammonium is used as the QA terminated thiol. The high positive charge at the surface of the QA ions renders them highly stable in acidic solution due to the electrostatic force of repulsion between the cations and the positive charge of H^+ ions. Whereas there occurs a strong interaction between these cations and the OH- ions in basic solution resulting in an aggregation. In the presence of Hg^{2+}, the greater affinity of mercury to thiol groups displaces the H^+ ions and brings about the chemisorption of Hg^{2+} onto the thiol groups. Thereby producing a change in the absorption spectra bringing about red to purple colour change. This method of detection could be used as a better platform for the lab on chip development and the minimum detection concentration using this method was analyzed as 30 nM. The major advantage in this method is that it does not require any sophisticated instrumentation. Adenosine triphosphate (ATP) modified gold nanoparticles (sAuNP) have been found to be stable over various pH ranges and results in an immediate aggregation when presented in a Hg^{2+} environment. Concentrations as low as 193 nM could be detected using sAuNP based chemo sensor[18].

4.4. Nitro group

Nitrogen atoms are found to have a significant affinity towards gold atoms. Nitrotriazole groups are used for the detection of mercury. 3-nitro-1H-1,2,4-triazole (NTA) functionalized gold nanoparticles are used in the detection of mercury with the sensitivity levels being as low as 7 nM. Capping of AuNPs with NTA is achieved by the strong affinity of nitrogen atoms in the triazole ring to the gold nanoparticle surface. Coordination chemistry between the NTA moieties and Hg^{2+} ions had enabled the development of NTA capped AuNPs as a suitable probe for the detection of heavy-metal

contamination. As described previously, the sensing modality is primarily through the colorimetric changes and is envisioned through the release of NTA from the AuNPs in the presence of Hg^{2+} ions and its binding to the same leading to the aggregation of AuNPs, thus enabling the detection of mercury. Dynamic ranges for the detection can be achieved by modifying the amounts of NTA in NTA-AuNP probe. The assay was also used for the detection of other heavy metals in environmental samples[15].

4.5. Quantum Dots

Mercuric sulphide quantum dots are used in the detection of mercury. The HgS quantum dots are made to form in situ Au@HgS core-shell nanostructure. Sulphide atom present in the core-shell structure acts as a mono dentate ligand establishing a strong link between the gold and the sulphide group. Thus, upon the addition of mercury, there existed a red shift with the increase of absorption intensity. This was aided by the core-shell structure that enhanced the availability of free electrons enhancing the Surface Plasmon Resonance oscillation. The probe which is used for both qualitative and quantitative analysis is capable of detecting mercury levels as low as 0.486 nM[23].

4.6. Polymers

The major advantage of using polymers over the other materials is their increased biocompatibility. Chitosan, being a heteropolymer is nontoxic in nature and possesses biocompatibility, biodegradability, and antibacterial property. The presence of reactive amino groups in chitosan enables the aggregation of metal ions in solution. Chitosan capped gold nanoparticles (CH-AuNP) showed a blue shift in the localized surface plasmon resonance (LSPR) with the addition of Hg^{2+} ions. The interesting fact about CH-AuNP is that it showed a blue shift in the plasmon absorption peak while all the other methods of detection showed a red shift upon the addition of Hg^{2+}. The sensitivity of this method was found to be as low as 5 pM, which is the least number achieved using the colorimetric method of Hg^{2+} detection[27].

4.7. Aromatic Compound

Though a large number of compounds have been used in the gold nanoparticle based colorimetric detection of mercury, the use of aromatic compound 4,4'-dipyridyl (DPy) follows a different mechanism of action for detection. While the other methods of detection are based upon the aggregation of the gold nanoparticles upon the addition of Hg^{2+}, this method follows the detection based on anti-aggregation of gold nanoparticles. Three major steps upon which this probes functions rely on the size of the AuNP, aggregation reagent DPy and upon the anti-aggregation process. Higher sensitivity and selectivity of the probe rely mainly upon the affinity of DPy to Hg^{2+}. This method of sensing has been able to achieve detection limits of about 15 nM and is suitable for both on-site and real-time analysis. Dynamic ranges can be achieved by modifying the amounts of anti-aggregation reagent used[16].

4.8. Proteins

Protein functionalized gold nanoparticles are also employed for the detection of heavy-metal contamination. The detection system based on the protein probe depends mainly upon the pH of the system. Papain, an enzyme with seven cysteine residues is rich in thiol group and is used in the detection of mercury. It is capable of adhering directly onto the surface of gold nanoparticle. Papain, in the presence of mercury, is found to bring about a modulation of fluorescence. Thus, a system of detection using papain has been designed wherein it brings about a shift in the color from red to blue that could be envisioned with the naked eye. The system was found to have utmost sensitivity at pH 6 as the system was found to be very stable at pH ≥ 6. P-AuNPs were highly stable with no significant aggregation at increased pH whereas when the pH level reached 6, presence of mercury brought about the aggregation of P-AuNPs of heavy metal. The system was found suitable for real time analysis of heavy-metal contamination[28].

4.9. Surfactants

A novel "blue-to-red" colorimetric strategy for the detection of Hg^{2+} based on the ion redox-modulated chemistry of AuNPs. The minimum detectable concentration through this method was found to be 5 nM. This method was based upon the shift in the wavelength from blue to red in contrast with the other methods that relied upon the change in colour from red to purple. Three major advantages to this method are that it relies on the blue to red shift which could be detected with a greater sensitivity than with the red to purplish transition. Secondly, it does not involve the need for the selection of ion chelating moieties and the complicated modification techniques and finally, as mentioned above it has a very high sensitivity which is evident to its LOD[45]. Tween 20 modified citrate stabilized AuNPs are employed for the detection of Hg^{2+} and also other metal ions. It is found that citrate groups are present at the surface of the gold nanoparticles, and the presence of Tween-20 prevents them from getting aggregated. Removal of Tween-20 resulted in the aggregation of gold nanoparticles. When Hg^{2+} ions are presented as a solution containing Tween-20 modified citrate-capped AuNP, mercury due to its greater affinity towards AuNPs brings about the desorption of tween-20 and its adsorption onto AuNP surfaces thus bringing about an aggregation and henceforth a colour change. It is to be noted that addition of Tween-20 to citrate stabilized AuNP does not bring about any displacements, and remains dispersed throughout the solution. Studies carried out based on the extinction spectra show that the sensitivity and selectivity of the method depend upon the nanoparticle concentration, surfactant chain length and also upon the ionic strength of the solution. Increased concentration of the surfactant brought about a decrease in the nanoparticle aggregation whereas increasing nanoparticle concentration caused an increase in the aggregation of NPs. At the same time, it was found that in a solution with high ionic strength, the slight

electrostatic force of repulsion between the Tween-20 moieties provided a barrier for the metal ion induced aggregation. With a fixed reaction time of 5 minutes, the limit of detection using this sensor was 100 nM for sea water and 200 nM for drinking water, which is very much in compliance with the minimum levels of Hg^{2+} in drinking water as given by WHO. It was also examined that a proper choice of masking agent would enable the detection of various other metal ions with improved sensitivity[20].

4.10. Chemodosimeter

A mercury specific chemo dosimeter (CHD) based on the mercury-induced intramolecular guanylation of thiourea attached to the 1, 8-naphthalimide immobilized onto the surface of gold nanoparticle was developed. CHD with a benzoyl thiourea component was capable of detecting mercury ions with utmost specificity, but the drawback lied in its unstable nature in aqueous media. In order to overcome this hurdle, a new CHD with phenylthiourea substituted in place of benzoyl thiourea was developed. Surfactant-induced modification of the chemo sensor without any modification of the basic chemical structure within the sensor molecule was found to have high efficiency and increased dispersivity in aqueous media. Furthermore, the naphthalimide signaling moiety and thiourea moiety enable the selective detection of Hg^{2+}. CHD based system of detection has an LOD of 10 μM and it can be used for both qualitative and quantitative detection of not only mercury but also other metals that might be present in environmental samples. Improvements in the design of the chemo dosimeter with the proper choice of nanomaterial and suitable surfactant would lead toward the development of new systems for detection with greater accuracy[46].

5. Conclusion

In conclusion, it may be summarized that gold nanoparticles are used as well sensing elements in both modified and unmodified form[47]. The major advantage of a gold nanoparticle based detection system over the other conventional methods such as atomic absorption spectroscopy, atomic emission spectroscopy, inductive coupled mass spectroscopy (ICP-MS), ICP-OES, and fluorescence spectroscopy are that it can be detected with a naked eye. AuNP based colorimetric system does not involve the use of expensive instruments. Furthermore, AuNP based system does not require complicated sample preparations. Moreover, it is evident that modification of the gold nanoparticles does not involve any difficult methodology and allows the easy detection of moieties, which is visible to the naked eyes. Gold nanoparticles are highly biocompatible and can, therefore, be used in the detection in biological environments. Among the various functionalization units studied, each unit is found to be efficient in the detection of not only mercury but also other heavy-metal contamination in both biological and environmental samples. Thus, gold nanoparticle based sensors can be used for highly sensitivity and selectivity. The easily tunable optical property of gold nanoparticles enables not only the detection but also the quantification of Hg^{2+} in the sample which is impossible with the other systems. Another positive aspect of AuNP based system is that it possesses very high levels of sensitivity and selectivity, which are not an attribute of the other systems. AuNP based colorimetric systems do not have the problem of poor solubility or cross sensitivity, which is a major drawback of the other instrument based methods. In a nut shell; gold nanoparticle based colorimetric sensing of heavy-metal ions would prove a prominent tool for detection of environmental contamination. Further modifications of the available system would serve a significant environmental tool without requiring any complex instrumentation. Also, other noble metall silver in its nano form possesses similar tunable optical properties and are employed in the detection heavy metal contamination[48]. Under certain conditions the sensor system based on metallic nanoparticles are posed with stability issues and also get aggregated in due course of time. Silica capped gold nanoparticles are also used in the stabilisation of the system and are sensitive for low doses of mercury[49]. A number of colorimetric sensors have been developed for the detection of heavy metal contamination in water and other sources. And gold nanoparticles prove to be very effective tool in serving the purpose as the synthesis methods are simple and easy functionalization is achieved[50]. Tunable optical properties add to the increased sensitivity of the system.

Acknowledgements

The author would like to acknowledge the support from Department of science and technology (DST), Ministry of India for providing financial assistance in the form of woman scientist scheme-A under the grant SR/WOS-A/LS-1211/2014.

References

1 L. C. Rai, J. P. Gaur and H. D. Kumar, *Biol. Rev.*, 1981, **56**, 99–151.
2 S. Shribman, A. Davis, N. Vella and G. Giovannoni, *J. Neurol. Neurosurg. Psychiatry*, 2013, **84**, e2–e2.
3 P. C. Nagajyoti, K. D. Lee and T. V. M. Sreekanth, *Environ. Chem. Lett.*, 2010, **8**, 199–216.
4 M. Patra and A. Sharma, *Bot. Rev.*, 2000, **66**, 379–422.
5 Z. S. Zhou, S. J. Wang and Z. M. Yang, *Chemosphere*, 2008, **70**, 1500–1509.
6 F. Zahir, S. J. Rizwi, S. K. Haq and R. H. Khan, *Environ. Toxicol. Pharmacol.*, 2005, **20**, 351–360.
7 K. a. Graeme and C. V. Pollack, *J. Emerg. Med.*, 1998, **16**, 45–56.
8 J. O. Duruibe, M. O. C. Ogwuegbu and J. N. Egwurugwu, *Int. J. Phys. Sci.*, 2007, **2**, 112–118.
9 G. Guzzi and C. A. M. La Porta, *Toxicology*, 2008, **244**, 1–12.
10 a Léonard, P. Jacquet and R. R. Lauwerys, *Mutat. Res.*, 1983, **114**, 1–18.
11 S. Nabi, *Bull. Env. Pharmacol. Life Sci*, 2014, **3**, 272–285.
12 X. Xue, F. Wang and X. Liu, *J. Am. Chem. Soc.*, 2008, **130**, 3244–3245.
13 X. Liu, X. Cheng, T. Bing, C. Fang and D. Shangguan, *Anal. Sci.*, 2010, **26**, 1169–72.
14 Y.-R. Kim, R. K. Mahajan, J. S. Kim and H. Kim, *ACS Appl.*

Mater. Interfaces, 2010, **2**, 292–5.
15 X. Chen, Y. Zu, H. Xie, A. M. Kemas and Z. Gao, *Analyst*, 2011, **136**, 1690–6.
16 Z. Jiang, G. Wen, Y. Fan, C. Jiang, Q. Liu, Z. Huang and A. Liang, *Talanta*, 2010, **80**, 1287–91.
17 H. D. Song, I. Choi, Y. I. Yang, S. Hong, S. Lee, T. Kang and J. Yi, *Nanotechnology*, 2010, **21**, 145501.
18 S. Kim, N. H. Lee, S. H. Seo, M. S. Eom, S. Ahn and M. S. Han, *Chem. - An Asian J.*, 2010, **5**, 2463–2466.
19 N. Ding, H. Zhao, W. Peng, Y. He, Y. Zhou, L. Yuan and Y. Zhang, *Colloids Surfaces A Physicochem. Eng. Asp.*, 2012, **395**, 161–167.
20 C. Y. Lin, C. J. Yu, Y. H. Lin and W. L. Tseng, *Anal. Chem.*, 2010, **82**, 6830–6837.
21 G. K. Darbha, a K. Singh, U. S. Rai, E. Yu, H. T. Yu and P. C. Ray, *J. Am. Chem. Soc.*, 2008, **130**, 8038–8043.
22 Y. Li, P. Wu, H. Xu, Z. Zhang and X. Zhong, *Talanta*, 2011, **84**, 508–12.
23 F. Zhang, L. Zeng, C. Yang, J. Xin, H. Wang and A. Wu, *Analyst*, 2011, **136**, 2825–2830.
24 J. S. Lee, M. S. Han and C. a. Mirkin, *Angew. Chemie - Int. Ed.*, 2007, **46**, 4093–4096.
25 M. R. Knecht and M. Sethi, *Anal. Bioanal. Chem.*, 2009, **394**, 33–46.
26 S. Si, A. Kotal and T. K. Mandal, *J. Phys. Chem. C*, 2007, **111**, 1248–1255.
27 C. Radhakumary and K. Sreenivasan, *Analyst*, 2011, **136**, 2959–2962.
28 Y. Guo, Z. Wang, W. Qu, H. Shao and X. Jiang, *Biosens. Bioelectron.*, 2011, **26**, 4064–4069.
29 H. N. Daghestani and B. W. Day, *Sensors*, 2010, **10**, 9630–9646.
30 Y. Cho, S. S. Lee and J. H. Jung, *Analyst*, 2010, **135**, 1551–5.
31 J. M. Walker, *Biosensors and Biodetection*, 2009, vol. 504.
32 X. Ma, Z. Sheng and L. Jiang, *Analyst*, 2014, **139**, 3365–8.
33 T. Senapati, D. Senapati, A. K. Singh, Z. Fan, R. Kanchanapally and P. C. Ray, *Chem. Commun. (Camb).*, 2011, **47**, 10326–10328.
34 K. S. Phillips and Q. Cheng, *Anal. Bioanal. Chem.*, 2007, **387**, 1831–1840.
35 K. Hamaguchi, H. Kawasaki and R. Arakawa, *Colloids Surfaces A …*, 2010, **367**, 167–173.
36 J. Wu, L. Li, D. Zhu, P. He, Y. Fang and G. Cheng, *Anal. Chim. Acta*, 2011, **694**, 115–119.
37 D. Li, A. Wieckowska and I. Willner, *Angew. Chemie*, 2008, **120**, 3991–3995.
38 C.-J. Yu, T.-L. Cheng and W.-L. Tseng, *Biosens. Bioelectron.*, 2009, **25**, 204–10.
39 Y. Wang, F. Yang and X. Yang, *Biosens. Bioelectron.*, 2010, **25**, 1994–8.
40 L. Chen, T. Lou, C. Yu, Q. Kang and L. Chen, *Analyst*, 2011, **136**, 4770–3.
41 F. Chai, C. Wang, T. Wang, Z. Ma and Z. Su, *Nanotechnology*, 2010, **21**, 025501.
42 C.-C. Huang and H.-T. Chang, *Chem. Commun. (Camb).*, 2007, 1215–1217.
43 C. Yu and W. Tseng, *Langmuir*, 2008, 12717–12722.
44 D. Liu, W. Qu, W. Chen, W. Zhang, Z. Wang and X. Jiang, *Anal. Chem.*, 2010, **82**, 9606–9610.
45 T. Lou, Z. Chen, Y. Wang and L. Chen, *ACS Appl. Mater. Interfaces*, 2011, **3**, 1568–1573.
46 B. Leng, L. Zou, J. Jiang and H. Tian, *Sensors Actuators, B Chem.*, 2009, **140**, 162–169.
47 L. Chen, J. Li and L. Chen, *ACS Appl. Mater. Interfaces*, 2014, **6**, 15897–904.
48 L. Chen, L. Chen, X. Fu and W. Lu, *ACS Appl. Mater. Interfaces*, 2013, **5**, 284–290.
49 G. Wang, Z. Chen, W. Wang, B. Yan and L. Chen, *Analyst*, 2011, **136**, 174–8.
50 X. Han, Y. Liu and Y. Yin, *Nano Lett.*, 2014, **14**, 2466–2470.

Fig 1. Graphical Representation of Methyl Mercury Poisoning in Humans

73x30mm (300 x 300 DPI)