EUROPEAN JOURNAL OF BIOMEDICAL
AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 5
Issue: 4
1036-1040
Year: 2018

A NEW HYDROXY-CYANO-BIPHENYL DERIVED CHEMOSENSOR FOR SELECTIVE DETECTION OF MERCURY

[1]Milind S. Thakare* and [2]Pravin M. Yeole

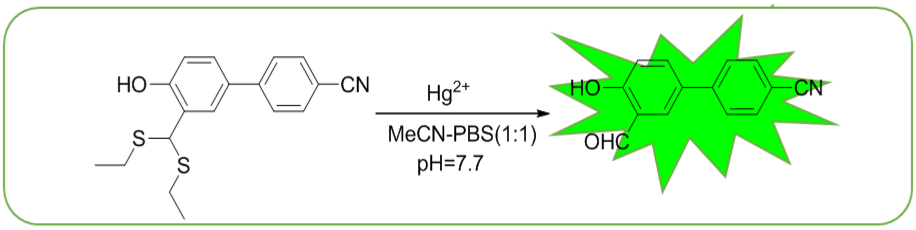
[1]Synthetic Organic Chemistry Lab, Pratap College, Amalner, PIN 425401 Maharashtra (India).
[2]Center for PG Research, R. L. College, Parola, PIN 425111 Maharashtra (India).

***Corresponding Author: Milind S. Thakare**
Synthetic Organic Chemistry Lab, Pratap College, Amalner, PIN 425401 Maharashtra (India).

Article Received on 20/02/2018 **Article Revised on 14/03/2018** **Article Accepted on 02/04/2018**

Abstract: A new fluorescence sensor based on condensation reaction of 3`-formyl-4`-hydroxy-4 biphenyl carbonitrile with 1,2-Ethanedithiol for the detection of mercury has been designed and developed. The probe proved to be highly selective, sensitive and responsive toward detection of mercury ions. We speculated that the sensing mechanism is based on mercury initiated desulphurization in aqueous medium leading to the formation of active fluorophore (Green Fluorescence) which also have been evidenced by the spectral analysis. Most remarkably, the response of the probe to the Hg^{2+} is very quick.

KEYWORDS: Mercury, Desulphurization, Fluorescent sensor, Cyanobiphenyl.



INTRODUCTION

The only metal exists in liquid form at room temperature is Mercury (Hg).[1] Mercury even in metallic state can easily evaporate and goes in atmosphere in the form of mercury vapor.[2-5] Mercury subsists in various forms which are divided into two general categories: Inorganic and Organic mercury compounds. Inorganic mercury compounds includes Hg (I) and Hg (II)[6-10] compounds while organo mercury compounds are chemicals in which mercury is covalently bonded to carbon, for example methyl mercury. Looking at the health perspective, substantial exposure to mercury vapor occurs via inhalation. Mercury vapor is readily absorbed through the lung tissues, maximum mercury absorption is through the lungs. Elemental mercury (in liquid form) is poorly absorbed from the gastrointestinal tract. Therefore, in toxicological point of view metallic mercury ingested is of not of any importance. Absorption through skin is low. Excessive internal mercury buildup will damage the cells, immune system, central nervous system, and can also lead to the impairment of the human organs, such as lungs kidney, stomach.[11-16] The United states based Environmental Protection Agency[17] has classified organic and inorganic mercury compounds as probable human carcinogens. Nephrotoxicity is a typical health effect of inorganic mercury compounds, while that of organomercury compounds is neurotoxicity i.e. impairment, and permanent damage to the central nervous system even in low concentration. It is also recognized that exposure at different stages of life causes different health effects. In the tragedies of Minamata Disease and Iraqs methyl mercury poisoning[18-22], infants born to mothers showed severe neurological impairment and delay in developmental process. Acute accidental exposure to high concentrations of mercury vapor causes erosive bronchitis and bronchiolitis with Hamman-Rich Syndrome. The patient may develop severe respiratory insufficiency. The US Environmental Protection Agency (EPA) has fixed a MCL i.e. maximum Hg^{2+} contaminant level in food and drinking water at 2ppb.[23-28] Therefore, Considering the threats associated with mercury toxicity, sensitive detection of mercury ions in the environment and biological systems has therefore become necessary[29-37], because these contaminants can cause serious health issues and environmental pollution problem. It becomes absolutely necessary to detect the presence of mercury in water and develop a simple yet environmentally friendly mercury sensor with high sensitivity and selectivity.

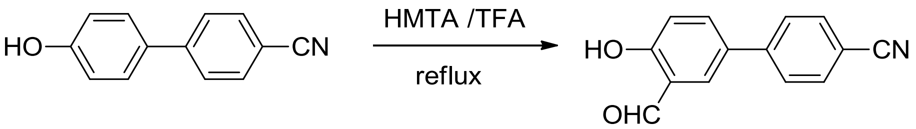
MATERIALS AND METHODS

All reagents and solvents (analytical grade) used herein were purchased from commercial suppliers and used without further purification. The water used throughout all experiments was doubly distilled. Spectral analysis i.e. proton NMR and 13C NMR were measured at Bruker AV, 200/400/500 MHz instruments in appropriate solvents using Tetramethyl silane (TMS, δ=0 ppm) as internal standard or the solvent signals are considered as secondary standards and the chemical shifts are shown in δ scales. The electrospray ionization (ESI) mass spectra were conducted with a Bruker ESQUIRE HPLC–MSAB 4000Q. Fluorescence spectra were performed with a Perkin–Elmer UV/Vis Spectrophotometer and a Photon Technology International, QuantaMaster 400 Spectrofluorometer, respectively, in degassed spectral grade solvents

Methods

1) Synthesis of Probe: The probe is synthesized in two steps as shown in scheme 1 and scheme 2
2) Sensing Study: Probe + Hg^{2+}

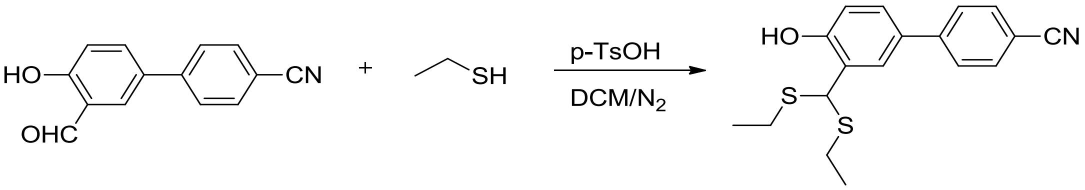
Synthesis of Probe



Scheme: 1 Synthesis of 3-formyl-4-Hydroxy-4-biphenylcarbonitrile.

Chemicals	Molecular Wt.	Quantity	Moles	density	Mole Ratio
HO-Biphenyl-CN	195.22	0.5	0.0025	-	1
HMTA	140.186	0.36	0.015	-	6
TFA	114.02	30ml	-	1.486	-

A solution of 4-Hydroxy-4-biphenylcarbonitrile (0.5 g) and hexamethylenetetramine (HMTA, 0.36 g) in trifluoroacetic acid (30 mL) was refluxed for 4 h. After completion, the reaction mixture was cooled to RT and diluted with 1.0 M HCl (60 mL). Resultant mixture was extracted with CH_2Cl_2 (60 mL). The organic layer was cleaned with water 3 times and once with saturated brine, and finally dried over magnesium sulfate. The solvents were removed on rotary evaporator afforded 3-formyl-4-Hydroxy-4-biphenylcarbonitrile (74%); as a white solid, mp 133–135^{0}C; FTIR: 3529, 2233, 1727, 1648, 1606, 1480, 1364, 1300,1263, 1224, 1169, 906, 824; δh(400 MHz DMSO-d6) 11.11 (1H, s),9.98 (1H, s), 7.76 (2H, d, J 10.52 Hz), 7.73 (2H, d, J 8.57 Hz), 7.64 (2H,d, J 8.56 Hz), 7.15 (1H, d, J 8.48 Hz); δC(100 MHz DMSO-d6, 25^{0}C,ppm): 191.44, 161.61, 143.79, 135.18, 133.30, 129.75, 127.75,127.26, 123.03, 119.34, 118.65, 109.95.

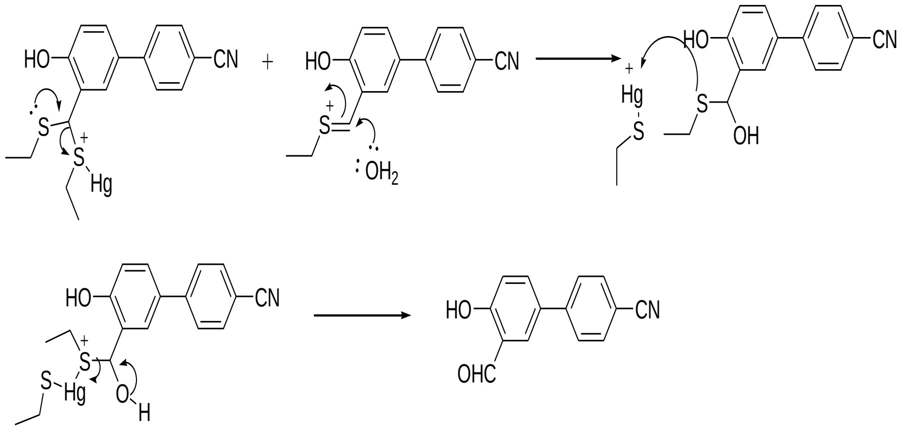


Scheme: 2 Synthesis of 3-(bis(ethylthio)methyl)-4-Hydroxy-4-biphenylcarbonitrile.

Chemicals	Molecular Wt.	Quantity	Moles	density	Mole Ratio
Formyl-HO-Biphenyl-CN	223.23	0.5	0.0022	-	1
SH-CH_2-CH_3	94.20	0.421	0.0044	1.123	2
TsOH	172.20	0.18	0.0011	-	0..5

3-formyl-4-Hydroxy-4-biphenylcarbonitrile (1 mmol), Ethane thiol 2 mmol) and p-toluenesulfonic acid (0.5 mmol) IN DCM were stirred for overnight under nitrogen. The solvent was removed under vacuume, The crude product was purified was purified by silica column using petroleum ether and DCM (20:1, v/v) as the eluent to afford probe. White solid, FTIR: 3530, 2229, 1607, 1475, 1370, 1299,1264, 1228, 1170, 905, 822; δh (400 MHz DMSO-d6) 11.10 (1H, s), 7.77 (2H, d, J 10.53 Hz), 7.73 (2H, d, J 8.57 Hz), 7.65 (2H,d, J 8.56 Hz), 7.11 (1H, d, J 8.48 Hz) 4.52 (s, 1H) 2.53-2.68 (m, 4H),1.26(t, J = 6 Hz, 6H), 13C (100 MHz DMSO-d6, 25^{0}C,ppm): 161.61, 143.79, 135.18, 133.30, 129.75, 127.75,127.26, 123.03, 119.34, 118.65, 109.95, 52.09, 26.37,14.33.

Mechanistic Route



RESULT AND DISCUSSIONS

Conversion of 3-(bis(ethylthio)methyl)-4-Hydroxy-4-biphenylcarbonitrile confirmed by NMR spectral data (Fig: 4) to 3-formyl-4-Hydroxy-4-biphenylcarbonitrile (confirmed by NMR spectral data) upon addition of $HgCl_2$ this transformation of dithane derivative to aldehydes can be proceeded by mercury induced hydrolytic desulphurization process releasing the free fluorophore to generate the significant change of fluorescence. Reaction is verified by the mass spectra of the major product from the reaction of probe and Hg^{2+} were further investigated. There is a main peak at m/z 223.36 (Fig:3) which corresponded to the expected mass of the product of 3`-formyl-4`-hydroxy-4-biphenylcarbonitrile. The results clearly confirmed mercury triggered desulphurization of probe. The product of [Probe + $HgCl_2$] was isolated by a silica gel column and was then subjected to 1H NMR and mass analysis. The 1H NMR chemical shifts of Probe, and product of Probe + $HgCl_2$ are indicated in the spectral data provided, in which the disappearance of the dithioacetal **signal at 1.26 ppm, 2.53-2.68 ppm and 4.52 ppm of adjacent C-H bond,** while a new signal increased **at 9.99 ppm** corresponding to the proton **of aldehyde**. Furthermore, mass spectroscopy confirmed the formation of product of [Probe + $HgCl_2$] through the presence of an intense peak at m/z = 329.56. (Fig 3) The1H NMR and mass of the resulting product is exactly same to the reported compound in scheme 1. Selectivity study as shown in (Fig: 1) indicates that the probe is nonresponsive towards other metal ions. Other metal ions such as Ba^{++},Ni^{++},Co^{++},Ca^{++},Cd^{++},Mg^{++},Zn^{++},Pd^{++},Mn^{++} Fe^{++},K^{+},Na^{+},Li^{+},Al^{3+},Cu^{2+} were nearly nonresponsive, indicating that the selectivity for Hg^{2+}was relatively high, and also proving the selectivity of the deprotection reaction of thioacetal for the metal ions. Fig:2 indicates the emission intensity of probe system (λem. 525nm) gradually increased with continuing addition of Hg^{2+} with excitation wavelength at λexc. 420 nm

CONCLUSION

In summary, a cyanobiphenyl based fluorescent probe for detection of mercury ions was designed and synthesized. This probe displayed a fast and noteworthy fluorescence “turn-on” response to Hg^{2+} in PBS buffer solution (0.01 M, pH 7.4) with high, selectivity and sensitivity. The sensing mechanism was considered that the mercury initiated hydrolytic desulphurization of probe releasing the active aldehydic cyanobiphenyl fluorophore accompanied by strong green fluorescence emission, which also have been proved by spectral analysis. The electron-withdrawing feature of aldehyde group favors the ICT effect and induces the emission behavior.

ACKNOWLEDGEMENTS

Generous financial support by the UGC New Delhi, (Ref No.47-291/12(WRO) is gratefully acknowledged. MST and PMY are grateful to Principal, Pratap College, Amalner and Principal, R. L. College Parola for their timely support.

Selectivity study: of Probe with Hg^{2+} and other analytes.

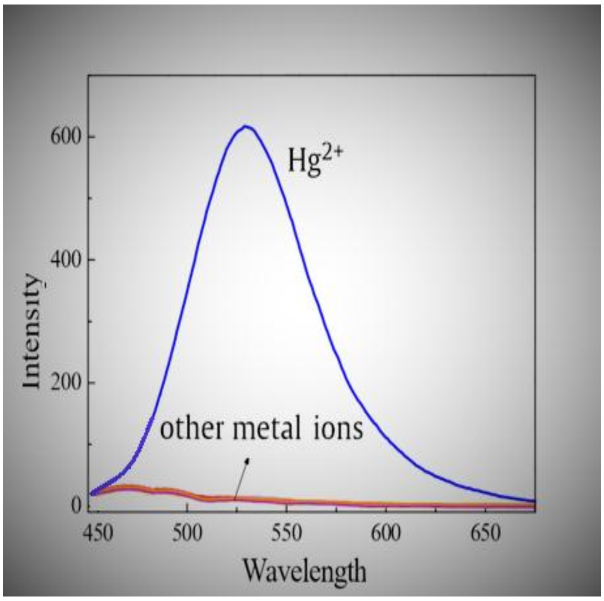


Fig.1 fluorescence spectra of probe (10 μM) in absence or presence of different cations in MeCN-PBS buffer solution (0.01 M,1:1 v/v, pH 7.4).

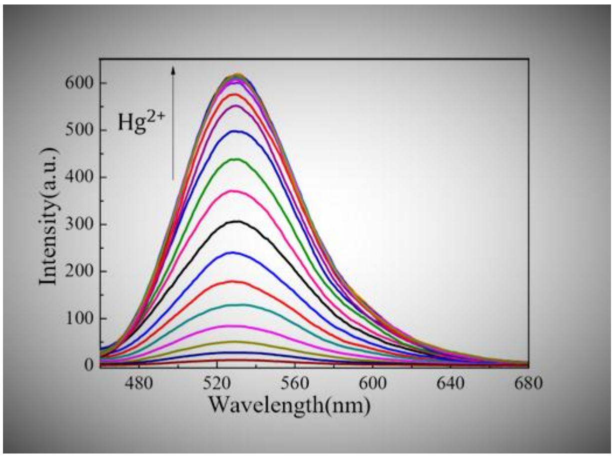


Fig.2 Concentration dependent changes in the emission spectra of probe (10 µM) upon the gradual addition of Hg2+ (from 0 to 10 equiv.) in MeCN-PBS buffer solution (0.01 M, 1:1 v/v, pH 7.4) at λex = 420 nm.

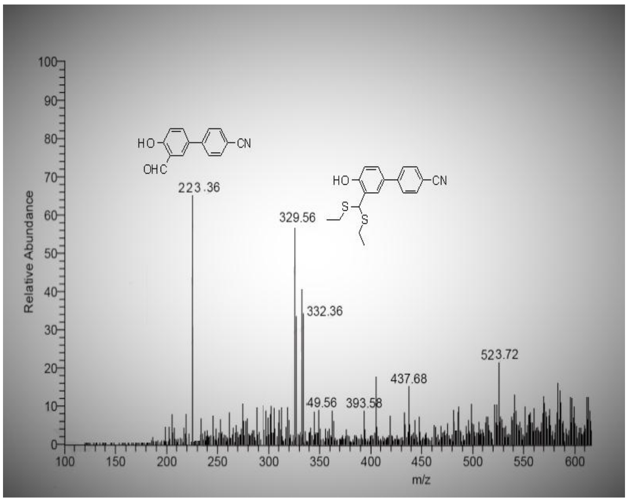


Fig 3: Masss spectrum of Probe after addition of Hg^{2+} clearly indicates formation of the expected fragments after mercury induced hydrolytic deslulphurization.

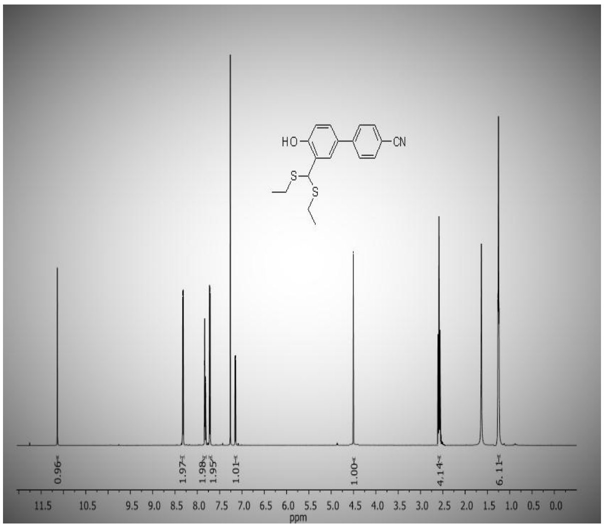


Fig 4: NMR spectrum of Probe 3-(bis(ethylthio) methyl)-4-Hydroxy-4-biphenylcarbonitrile.

REFERENCES

1. Lars J. Norrby, Why is mercury liquid? Or, why do relativistic effects not get into chemistry textbooks? *J. Chem. Educ.*, 1991; *68*(2): 110.
2. A.H. Stern, A review of the studies of the cardiovascular health effects of methylmercury with consideration of their suitability for risk assessment. Environ. Res., 2005; 98: 133–142.
3. T.W. Clarkson, L. Magos and G. J. Myers, The toxicology of Mercury–current exposures and clinical manifestations. N. Engl. J. Med., 2003; 349: 1731–1737.
4. M.F. Wolfe, S. Schwarzbach, R.A. Sulaiman, Effects of mercury on wildlife: a comprehensive review, Environ. Toxicol. Chem., 1998; 17: 146–160.
5. Renzoni A, Zino F, Franchi E, Mercury levels along the food chain and risk for exposed populations. Environ Res., 1998; 77: 68–72.
6. Von Burg R, Greenwood M.R, Metals and their compounds in the environment. VCH, Weinheim, 1991; 1045–1088.
7. Boening D W Ecological effects, transport, and fate of mercury: a general review. Chemosphere, 2000; 40: 1335–1351.
8. Richardson SD, Temes T A, Water analysis: emerging contaminants and current issues. Anal Chem., 2005; 77: 3807–3838
9. Xuefang Wang Dr., Lester Andrews Prof. Dr., Sebastian Riedel Dr., Martin Kaupp Prof. Dr. Mercury Is a Transition Metal: The First Experimental Evidence for HgF4, Angew. Chem. Int. Ed., 2007; 46: 8371–8375.
10. P.B. Tchounwou, W.K. Ayensu, N. Ninashviliand D. Sutton, Environmental exposure to mercury and its toxico pathologic implications for public health Environ. Toxicol, 2003; 18: 149–155.
11. C. N. Glover, D. Zheng, S. Jayashankar, G. D. Sales, C. Hogstrand and A.-K. Lundebye, Methylmercury speciation influences brain gene expression and behavior in gestationally-exposed mice pups Toxicol. Sci., 2009; 110: 389–400.
12. M. Korbas, S. R. Blechinger, P. H. Krone, I. J. Pickering and G. N. George, Localizing organomercury uptake and accumulation in zebrafish larvae at the tissue and cellular level Proc. Natl. Acad. Sci. U. S. A., 2008; 105: 12108–12112.
13. Carvalho CML, Chew EH, Hashemy SI, Lu J, Holmgren A Inhibition of the human thioredoxin system-a molecular mechanism of mercury toxicity. J Biol Chem., 2008; 283: 11913–11923.
14. Clarkson TW, Magos L, Myers GJ (The toxicology of mercury-current exposures and clinical manifestations. New Eng J Med., 2003; 349: 1731–1737.
15. Atchison, W. D.; Hare, M. F. FASEB J., 1994; 8: 622–629. Mechanisms of methylmercury-induced neurotoxicity
16. Tchounwou, P. B.; Ayensu, W. K.; Ninashvili, N.; Sutton, D, Environ Toxicol Environmental exposure

to mercury and its toxico pathologic implications for public health. Environ. Toxicol, 2003; 18: 149–175.

17. United States Environmental Protection Agency, Clean air mercury rule, 40 CFR Parts 60, 63, 72, and 75, 2005.
18. Takeuchi T, Morikawa N, Matsumoto H, Shiraishi Y A pathological study of Minamata disease in Japan. Acta Neuropathol, 1962; 2: 40–57.
19. Minamata disease: methylmercury poisoning in Japan caused by environmental pollution.Harada, M. Crit. Rev. Toxicol, 1995; 25: 1–24.
20. Why Methylmercury Remains a Conundrum 50 Years after Minamata, Weiss, B. Toxicol. Sci., 2007; 97: 223–225.
21. Amin Zaki, L.; Elhassani, S.; Majeed, M.A.; Clarkson, T.W.; Doherty, R.A.; Greenwood, M.Intra-uterine methylmercury poisoning in Iraq Pediatrics, 1974; 54: 587–595.
22. Bakir, F.; Damluji, S. F.; Amin-Zaki, L.; Murtadha, M.; Khalidi, A.; Al-Rawi, N. Y.; Tikriti, S.; Dhahir, H. I.; Clarkson, T. W.; Smith, J. C.; Doherty, R. A. Methylmercury poisoning in Iraq. Science, 1973; 181: 230–241.
23. United States Environmental Protection Agency. Available online: https://www.epa.gov/ground-waterand-drinking-water/table-regulated-drinking-water-contaminants (accessed on 27 September 2016).
24. World Health Organization. Available online: http://www.who.int/water_sanitation_health/dwq/chemicals/mercuryfinal.pdf (accessed on 27 September 2016).
25. C. Song, B. Yang, Y. Zhu, Y. Yang, L. Wang, Ultrasensitive sliver nanorods array sensor for mercury ions, Biosens. Bioelectron, 2017; 87: 59–65.
26. W. Crowe, P.J. Allsopp, G.E. Watson, P.J. Magee, J.J. Strain, D.J. Armstrong, E. Ball, E.M. McSorley, Mercury as an environmental stimulus in the development of autoimmunity-A systematic review, Auto immun. Rev., 2017; 16: 72–80.
27. J. Vas, M. Monestier, Immunology of mercury, Ann. N.Y. Acad. Sci., 2008; 1143: 240–267.
28. A. Masih, A. Taneja, R. Singhvi, Exposure profiles of mercury in human hair ataterai belt of North India, Environ. Geochem. Health, 2016; 38: 145–156.
29. E.M. Martinis, P. Berton, R.A. Olsina, J.C. Altamirano, R.G. Wuilloud, Trace mercury determination in drinking and natural water samples by room temperature ionic liquid based-preconcentration and flow injection-cold vapor atomic absorption spectrometry, J. Hazard. Mater, 2009; 167: 475-481.
30. H. Bagheri, M. Naderi, Immersed single-drop micro extraction-electrothermal vaporization atomic absorption spectroscopy for the trace determination of mercury in water samples, J. Hazard. Mater, 2009; 165: 353-358.
31. X.P. Zhu, S.D. Alexandratos, Determination of trace levels of mercury in aqueous solutions by inductively coupled plasma atomic emission spectrometry: Elimination of the ‘memory effect’, Microchem. J., 2007; 86: 37-41.
32. Q. Li, Z. Zhang, Z. Wang, Determination of Hg2+ by on-line separation and pre-concentration with atmospheric-pressure solution-cathode glow discharge atomic emission spectrometry, Anal. Chim. Acta, 2014; 845: 7-14.
33. P. She, Y.X. Chu, C.W. Liu, X. Gao, K. Zhao, J.G. Li, H.J. Du, X. Zhang, H. Wang, A.P. Deng, A competitive immunoassay for ultrasensitive detection of Hg2+ in water, human serum and urine samples using immunochromatographic test based on surface-enhanced raman scattering, Anal. Chim. Acta, 2016; 906: 139-147.
34. Y. Zhu, X.X. Jiang, H.Y. Wang, S.Y. Wang, H. Wang, B. Sun, Y.Y. Su, Y. He, A polyadenine-mediated assembly strategy for designing surface-enhanced resonance raman scattering substrates in controllable manners, Anal. Chem., 2015; 87: 6031-6038.
35. Y.H. Ma, Z.A. Zhang, M. Ma, B. Chen, L. Wei, L.H. Xiao, A bright carbon-dot-based fluorescent probe for selective and sensitive detection of mercury ions, Talanta, 2016; 161: 476-481.
36. D. Li, C.Y. Li, Y.F. Li, Z. Li, F. Xu, Rhodamine-based chemodosimeter for fluorescent determination of Hg2+ in 100% aqueous solution and in living cells, Anal. Chim. Acta, 2016; 934: 218-225.
37. Q.S. Zhang, Y.H. Li, H.J. Zuo, C.Y. Wang, Y.J. Shen, A new colorimetric and ratiometric chemodosimeter for mercury（Ⅱ）based on triphenylamine and benzothiadiazolenovel, J. Photoch. Photobio. A., 2017; 332: 293-298.