

A Systematic Review of Biosensors Suitable for Environmental Biomonitoring of Heavy Metal Water Pollution

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Abstract: The heavy metal levels measured in several Philippine freshwater bodies exceed the limits set by the Department of Environment and Natural Resources. Current methods in testing heavy metals contamination in water bodies are usually costly and time consuming, thus, using environmental biosensors as an alternative in the biomonitoring of heavy metals is proposed. The systematic review used published articles in NCBI, PubMed, PLOS One, Science Direct, and Elsevier and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines in assessing the most suitable heavy metal biosensor in detecting common heavy metals (As^{3+} , Cu^{2+} , Cd^{2+} , Pb^{2+} , and Hg^{2+}) present in Philippine freshwater bodies. The Joanna Briggs Institute (JBI) appraisal checklist was used in assessing the quality of the 57 chosen journal articles for the study. The biosensors were categorized based on their transducer types, transduction methods, bioreceptors, and interfering ions. An elimination process was conducted wherein the biosensors were ranked based on the selection criteria set which is composed of the Limit of Detection (LOD) values that are converted into parts per million (ppm) and selectivity. The systematic review suggested optical biosensors as the most suitable biosensor type in detecting all of the five heavy metals. The results of the systematic review can serve as a foundation in developing suitable environmental biosensors in monitoring heavy metals in the bodies of water found in the Philippines.

Key Words: Biosensors; Environmental Biomonitoring; Heavy Metals; Water Pollution

1. INTRODUCTION

Heavy metal water pollution imposes both environmental and health risks (Zaynab et al., 2022) which may lead to heavy metal poisoning (Balali-Mood et al., 2021). In the Philippines, heavy metal pollutants usually originate from mine tailings (Ragasa et al., 2021). The Laguna Lake (Mercado et al., 2021) and Mangonbangon River (Decena et al., 2018) are some of the bodies of water in the Philippines identified to have high levels of heavy metal concentrations.

The Water Quality Monitoring Program (WQMP) of DENR consists of tests like atomic absorption spectrophotometry (AAS), Cold Vapor Technique, and Mercury Analyzer, and Silver diethyldithiocarbamate colorimetric test (Environmental Management Bureau, 2014), but it does not include the use of biosensors which are known for their advantages like high sensitivities,

selectivities (Tovar-Sanchez et al., 2019), and low response time (Castillo-Henriquez et al., 2020).

Hence, a systematic review of articles published in NCBI, PubMed, PLOS One, Science Direct, and Elsevier is conducted to propose a suitable environmental biosensor model for detecting the heavy metals, As^{3+} , Cu^{2+} , Cd^{2+} , Pb^{2+} , and Hg^{2+} in the polluted Philippine freshwater bodies. The LODs and selectivities were the basis of selecting the suitable biosensor model. The research aims to identify the different biosensor components like transducer types, transduction methods, and bioreceptor types utilized in designing the biosensor models that are specific to the five heavy metals present in the Philippine water bodies.

2. METHODOLOGY

2.1 Search Strategy

A literature search in the electronic databases, NCBI, PubMed, PLOS One, and ScienceDirect was conducted according to the PRISMA 2020 guidelines. The search keywords, “environmental biosensor”, “heavy metals”, “water pollution”, “mercury”, “Hg”, “lead”, “Pb”, “cadmium”, “Cd”, “copper”, “Cu”, “arsenic”, “As” and the Boolean search operator “AND” were utilized in the search process. Journal articles published between 2002 to 2020 and written in the English language were obtained. The chosen articles had undergone a title and abstract screening and were further assessed based on the exclusion and inclusion criteria.

2.2 Eligibility Criteria

The criteria in selecting the eligible articles were: (1) It must be a peer-reviewed journal; (2) Primary research article; (3) Written and published in the English language; (4) Discusses biosensors and environmental monitoring; (5) Talks about heavy metal water pollution (“water pollution”, “heavy metals”); (6) Includes data on the limit of detection and selectivity; (7) Includes biosensor information (transducers, transduction methods, bioreceptors).

The articles were considered ineligible for the systematic review if: (1) It is also a systematic review and meta-analysis; (2) There is duplication of data; (3) It discusses biosensors not used in environmental monitoring and water pollution; (4) Talks about water pollution, but not heavy metal detection; (5) Talks about antibody-based biosensors used for health-related or disease detection; (6) It has incomplete information (transducer types, transduction methods, bioreceptor types, the limit of detection and selectivity values); (7) The study did not test the biosensors in real water samples (8) Did not meet all of the inclusion criteria mentioned above.

2.3 Data Extraction

The authors collected information from the studies based on the eligibility criteria set. The data taken from the articles included the following information: (1) Details about the journal article (Title, author, publication year); (2) Detailed information about the biosensors (such as the transducer type, transduction method, bioreceptor type); (3) How the biosensors were developed or used and how they operate; (4) Limit of detection values; (5) Selectivity performance based on interfering ions.

2.4 Quality Assessment

For the critical appraisal of the studies, there were checklists accessible for the reviewers to use. The checklists consisted of questions or criteria that evaluate the quality of study through its aspects, such as the

methodology and analysis. The JBI provides different checklists that reviewers can choose from, depending on the design of their study. The JBI appraisal checklist for non-randomized control trials was used in assessing the articles to avoid publication bias. The methodological quality of the chosen studies was evaluated using the checklist which consisted of nine (9) questions. These questions were answered with – “yes”, “no”, “unclear”, or “not applicable”. After answering the checklist, the study was given an overall appraisal by the reviewers of either: include, exclude, or seek further information.

2.5 Sample and Data Collection

A total of 57 articles were chosen for the systematic review. The researchers gathered the following information about the biosensors: transducer types (electrochemical and optical), transduction methods, bioreceptor types (nucleic acid, chemical, microorganism, and enzyme), LOD, and interfering ions utilized in the biosensor selectivity tests.

2.6 Data Analysis

The data collected were organized in Microsoft Excel. Article information (author and year of publication), biosensor details (transducer type, transduction method, and bioreceptor), LOD values, and interfering ions were the categories used in sorting the biosensor information. The LODs were converted into ppm. The biosensor models were evaluated based on the LOD in comparison to the heavy metal concentration in the heavy metal polluted freshwaters in the Philippines and selectivity performance (interfering ions).

3. RESULTS AND DISCUSSION

The summary of the search analysis results is presented in Fig. 1.

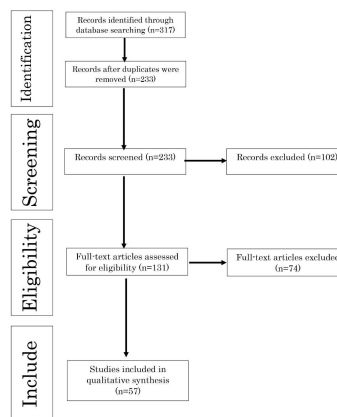


Fig. 1. PRISMA Flow Diagram of the step-by-step process in the selection of journal articles for the systematic review.

All 57 journal articles passed the quality assessment of the JBI checklist. The evaluation of the suitable biosensors for the contaminated water sources included the following: the sensitivity with the use of the limit of detection values, the number of contaminated locations of freshwater bodies reported in the Philippines, and the selectivity performance by the interfering ions present. The assessment of the interfering ions was based on the 12 frequent heavy metal contaminants in the various bodies of water in the Philippines which are lead (Pb^{2+}), copper (Cu^{2+}), nickel (Ni^{2+}), cadmium (Cd^{2+}), chromium (Cr^{3+}), zinc (Zn^{2+}), manganese (Mn^{2+}), titanium (Ti^{2+}), aluminum (Al^{3+}), iron (Fe^{2+}), mercury (Hg^{2+}), and arsenic (As^{3+}) (Perelonia et al., 2017; Magalona et al., 2019; Olivares et al., 2019).

Table 1. Summary of results for lead detection of biosensors.

Criterion	Type of biosensor	Author/s
Sensitivity	Optical	Du et al. (2018)
Selectivity	Optical	Fu et al. (2012)
No. of Applicable Water Sources	Optical	Du et al. (2018), He et al. (2020), Gao et al. (2013)
	Electrochemical	Zhang et al. (2019)
Overall Assessment	Optical	He et al. (2020)

The optical biosensor developed by Du et al. (2018) had the highest sensitivity for lead detection, while the optical biosensor developed by Fu et al. (2012) showed the highest selectivity as it detected lead ions present in a solution that also contains nine (9) interfering ions. For the number of bodies of water wherein the biosensor can detect lead, there were three optical biosensors (Gao et al., 2013; Du et al., 2018, He et al., 2020), and an electrochemical biosensor (Zhang et al. 2019). In the overall assessment, it was found that the optical biosensor by He et al. (2020) was the suitable biosensor model for lead detection.

Table 2. Summary of results for mercury detection of biosensors.

Criterion	Type of biosensor	Author/s
Sensitivity	Electrochemical	Tang et al. (2017)

Selectivity	Optical	Han et al. (2016), Chen et al. (2014), Deng et al. (2011), Huang et al. (2013)
No. of Applicable Water Sources	Optical	Han et al. (2016), Lin and Tseng (2010), Guo et al. (2015), Cheng et al. (2017), Zhou et al. (2012), He et al. (2011), Zhu et al. (2015), Li et al. (2020)
	Electrochemical	Tang et al. (2017), Singh and Mittal (2012), Zhang et al. (2015), Tortolini et al. (2015)
Overall Assessment	Optical	Han et al. (2016)

The electrochemical mercury biosensor designed by Tang et al. (2017) had the best sensitivity. A combination of optical and electrochemical biosensors was recommended based on the number of applicable water sources as seen in Table 2. In the selectivity performance evaluation, four (4) optical biosensors were suggested as they were able to detect mercury in solutions containing nine (9) interfering ions. Based on the assessment of the three criteria (sensitivity, selectivity, and the number of applicable water sources), the optical biosensor developed by Han et al. (2016) was considered to be the most suitable type for mercury detection.

Table 3. Summary of results for arsenic detection of biosensors.

Criterion	Type of biosensor	Author/s
Sensitivity	Electrochemical	Yadav et al. (2019)
Selectivity	Optical	Pan et al. (2018)
No. of Applicable Water Sources	Optical	Pan et al. (2018), Dieudonné et al. (2020)
	Electrochemical	Yadav et al. (2019), Zhu et al. (2020)
Overall Assessment	Optical	Pan et al. (2018)

The electrochemical biosensor that was developed by Yadav et al. (2019) had the highest sensitivity for arsenic. Along with this, an electrochemical biosensor and two optical biosensors were able to detect arsenic in all of the reported water sources. The optical

biosensor designed by Pan et al. (2018) was also recommended based on its selectivity performance wherein it was able to identify arsenic among seven (7) other interfering ions. In the overall evaluation, it was the optical biosensor by Pan et al. (2018) that was deemed to be most suitable for the detection of arsenic in various bodies of water.

Table 4. Summary of results for copper detection of biosensors.

Criterion	Type of biosensor	Author/s
Sensitivity	Optical	Kaur and Verma (2018)
Selectivity	Optical	Zong et al. (2016)
No. of Applicable Water Sources	Optical	Kaur and Verma (2018), Ren et al. (2018), Xu et al. (2018)
Overall Assessment	Optical	Ren et al. (2018)

The optical biosensors developed by Kaur and Verma (2018), Ren et al. (2018), and Xu et al. (2018) were found suitable for all of the reported copper-contaminated bodies of water. It was the biosensor by Kaur and Verma (2018) that had the highest sensitivity. For the selectivity criterion, the optical biosensor by Zong et al. (2016) was suggested as it was able to detect the presence of copper among nine (9) interfering ions. Overall, it was the optical biosensor developed by Ren et al. (2018) that was deemed to best fit for the detection of copper because of its LOD value and selectivity performance, where it detected copper among eight (8) other interfering ions.

Table 5. Summary of results for cadmium detection of biosensors.

Criterion	Type of biosensor	Author/s
Sensitivity	Electrochemical	Ebrahimi et al. (2017)
Selectivity	Optical	Elcin and Oktem (2020)
No. of Applicable Water Sources	Optical	Luan et al. (2016)
	Electrochemical	Ebrahimi et al. (2017), Wei et al. (2012), Li et al. (2019)
Overall Assessment	Optical	Zhou et al. (2012), Zhu et al. (2017)

The electrochemical biosensor developed by Ebrahimi et al. (2017) showed to have the highest sensitivity as it had the lowest LOD value. It also fits the criteria of having the most applicable water sources, along with an optical biosensor and other electrochemical biosensors. Based on the selectivity, it was the optical biosensor of Elcin and Oktem (2020) that had the best performance. In the overall assessment, it was found that the optical biosensors developed by Zhou et al. (2012) and Zhu et al. (2017) were the most suitable based on their LOD values and selectivity performance.

In all of the proposed optical biosensors, they were designed to be analyte-specific wherein the heavy metal ions attach to the specific bioreceptors, which results in high sensitivity of the biosensor (Peña-Bahamonde et al. 2018). The capability of the biosensor model to identify the designed analyte in the presence of other pollutants was assessed in the selectivity performance. All of the five (5) biosensors recommended showed high performance in sensitivity and selectivity. With this, it is also indicated that a multianalyte biosensor for the detection of these heavy metals may be beneficial and economical, especially for places where intensive monitoring of contamination in water bodies is much needed.

4. CONCLUSION

The sensitivity of optical biosensors showed to be suitable for copper and lead detection, while electrochemical biosensors are recommended for their sensitivity for arsenic, cadmium, and mercury detection. Optical biosensors are suitable for all five (5) heavy metals based on their selectivity performance. For the overall assessment, it was found that an optical biosensor model is the most recommended for lead, mercury, arsenic, copper, and cadmium contamination. The systematic review conducted was beneficial as it can serve as a foundation for future research on the application of biosensors for environmental monitoring, particularly heavy metal water pollution, in the Philippines. An extensive list had also been compiled with information on different bodies of water in the country where the appropriate biosensor may be used. Based on the information inferred, it was further recommended to possibly construct a multianalyte optical biosensor for the detection of more than one heavy metal analyte especially to detect the concentration range of heavy metal pollution reported in the Philippines. The different components of the biosensors, such as the transducer type, transduction method, and bioreceptor type, must also be considered for this.

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6. REFERENCES

- Balali-Mood, M., Naseri, K., Tahergorabi, Z., Khazdair, M. R., & Sadeghi, M. (2021). Toxic Mechanisms of Five Heavy Metals: Mercury, Lead, Chromium, Cadmium, and Arsenic. *Frontiers in Pharmacology*, 12. <https://doi.org/10.3389/fphar.2021.643972>
- Castillo-Henrriquez, L., Brenes-Acuña, M., Castro-Rojas, A., Cordero-Salmerón, R., Lopretti-Correa, M., & Vega-Baudrit, J. R. (2020). Biosensors for the Detection of Bacterial and Viral Clinical Pathogens. *Sensors*, 20(23), 6926. <https://doi.org/10.3390/s20236926>
- Chen, J., Zhou, S., Wen, J. (2014). Disposable Strip Biosensor for Visual Detection of Hg²⁺ Based on Hg²⁺-Triggered Toehold Binding and Exonuclease III-Assisted Signal Amplification. *Analytical Chemistry*, 86, 3108–3114.
- Cheng, L., Wei, B., He, L.L., Mao, L., Zhang, J., Ceng, J., Kong, D., Chen, C., Cui, H., Hong, N. (2017). “Off-On”switching electrochemiluminescence biosensor for mercury(II) detection based on molecular recognition technology. *Analytical Biochemistry*, 518, 46–52.
- Deng, L., Zhou, Z., Li, J., Li, T., Dong, S. (2011). Fluorescent silver nanoclusters in hybridized DNA duplexes for the turn-on detection of Hg²⁺ ions. *Chemical Communications*, 47, 11065.
- Decena, S. C., Arguilles, M., & Robel, L. (2018). Assessing Heavy Metal Contamination in Surface Sediments in an Urban River in the Philippines. *Polish Journal of Environmental Studies*, 27(5), 1983–1995. <https://doi.org/10.15244/pjoes/75204>
- Dieudonné, A., Prévéral, S., Pignol, D. (2020). A Sensitive Magnetic Arsenite-Specific Biosensor Hosted in Magnetotactic Bacteria. *Stams AJM*, editor. *Applied and Environmental Microbiology*, 86.
- Du, X.L., Kang, T.F., Lu, L.P., Cheng, S-Y. (2018). An electrochemiluminescence sensor based on CdSe@CdS functionalized MoS₂ and hemin/G-quadruplex-based DNzyme biocatalytic precipitation for sensitive detection of Pb(II). *Analytical Methods*, 10, 51–58.
- Ebrahimi, M., Raoof, J.B., Ojani, R. (2018). Design of an electrochemical DNA-based biosensor for selective determination of cadmium ions using a DNA hybridization indicator. *International Journal of Biological Macromolecules*, 108, 1237–1241. doi:10.1016/j.ijbiomac.2017.11.023.
- Elcin, E., Öktem, H.A. (2020). Inorganic Cadmium Detection Using a Fluorescent Whole-Cell Bacterial Bioreporter. *Analytical Letters*, 53, 2715–2733.
- Environmental Management Bureau. (2016). Water Quality Guidelines and General Effluent Standards of 2016. https://emb.gov.ph/wp-content/uploads/2019/04/DAO-2016-08_WATER-QUALITY-GUIDELINES-AND-GENERAL-EFFLUENT-STANDARDS.pdf.
- Fu, X., Lou, T., Chen, Z., Lin, M., Feng, W., Chen, L. (2012). “Turn-on” Fluorescence Detection of Lead Ions Based on Accelerated Leaching of Gold Nanoparticles on the Surface of Graphene. *ACS Applied Materials & Interfaces*, 4, 1080–1086. doi:10.1021/am201711j.
- Gao, A., Tang, C-X., He, X-W., Yin, X-B. (2013). Electrochemiluminescent lead biosensor based on GR-5 lead-dependent DNzyme for Ru(phen)₃²⁺-intercalation and lead recognition. *The Analyst*, 138, 263–268. doi:10.1039/c2an36398d.
- Guo, Z., Chen, B., Wang, Z., Jiang, X. (2015). An electrochemiluminescence biosensor for mercury ion detection based on gamma-polyglutamic acid-graphene-luminol composite and oligonucleotides. *Sensors and Actuators B: Chemical*, 209, 579–585.
- Han, S., Zhou, X., Tang, Y., He, M., Zhang, X., Shi, H., Xiang, Y. (2016). Practical, highly sensitive, and regenerable evanescent-wave biosensor for detection of Hg²⁺ and Pb²⁺ in water. *Biosensors and Bioelectronics*, 80, 265–272. doi:10.1016/j.bios.2016.01.070.
- He, Y., Hu, X., Gong, Z., Chen, S., Yuan, R. (2020). A novel electrochemiluminescence biosensor based on the self-ECL emission of conjugated polymer dots for lead ion detection. *Microchimica Acta*, 187. doi:10.1007/s00604-020-4212-0.
- Huang, C-W., Yang, S-H., Sun, M-W., Liao, V-H-C. (2013). Development of a set of bacterial biosensors for simultaneously detecting arsenic and mercury in groundwater. *Environmental Science and Pollution Research*, 22, 10206–10213.
- Kaur, G., Verma, N. (2018). Colorimetric determination of Cu²⁺ ions in water and milk by apo-tyrosinase disc. *Sensors and Actuators B: Chemical*, 263, 524–532. doi:10.1016/j.snb.2018.02.160.
- Lin, Y-H., Tseng, W-L. (2010). Ultrasensitive Sensing of Hg²⁺ and CH₃Hg⁺ Based on the Fluorescence Quenching of Lysozyme Type VI-Stabilized Gold Nanoclusters. *Analytical Chemistry*, 82, 9194–9200.
- Luan, Y., Lu, A., Chen, J., Fu, H., Xu, L. (2016). A Label-Free Aptamer-Based Fluorescent Assay for Cadmium Detection. *Applied Sciences* 6, 432.

- Magalona, M.L., Peralta, M.M., Lacsamana, M.S., Sabularse, V.C., Pelegrina, A.B., De Guzman, C.C. (2019). Analysis of Inorganic Arsenic (As(III) and Total As) and Some Physicochemical Parameters in Groundwater Samples from Selected Areas in Bulacan, Batangas, and Laguna, Philippines. *KIMIKA*, 30, 28–38. doi:10.26534/kimika.v30i2.28-38.
- Mercado, C.J.G., Atienza, L.M., Juanico, C.B., Depositario, D.P.T, Hurtada, W.A. (2021). Bioaccumulation and Non-Carcinogenic Health Risk Assessment of Heavy Metals in Selected Fish Species from South Bay of Laguna Lake. *Acta Medica Philippina*. 55(7). doi:10.47895/amp.vi0.3031.
- Olivares, R.U., Maria, E.J.S., Sombrito, E.Z. (2019). Environmental Assessment of Metal Pollution in Manila Bay Surface Sediments. *Philippine Journal of Science* 149, 13.
- Pan, J., Li, Q., Zhou, D., Chen, J. (2018). Ultrasensitive aptamer biosensor for arsenic (III) detection based on label-free triple-helix molecular switch and fluorescence sensing platform. *Talanta*, 189, 370–376. doi:10.1016/j.talanta.2018.07.024.
- Peña-Bahamonde, J., Nguyen, H.N., Fanourakis, S.K., Rodrigues, D.F. (2018). Recent advances in graphene-based biosensor technology with applications in life sciences. *Journal of Nanobiotechnology*, 16.
- Perelonia, K.B., Abendano, C., Raña, J., Opinion, A.G., Villeza, J., Cambia, F. (2017). Heavy Metal Contamination in Water and Fishery Resources in Manila Bay Aquaculture Farms. *The Philippine Journal of Fisheries*, 24, 74–97. doi:10.31398/tjpf/24.2.2016a0014.
- Ren, A., Zhu, D., Xie, W., He, X., Duan, Z., Luo, Y., Zhong, X., Song, M., Yan, X. (2018). A novel reaction-based fluorescent probe for sensitive and selective detection of Cu²⁺. *Inorganica Chimica Acta*, 476, 136–141. doi:10.1016/j.ica.2018.02.015.
- Singh, J., Mittal, S.K. (2012). *Chlorella sp.* based biosensor for selective determination of mercury in presence of silver ions. *Sensors and Actuators B: Chemical*, 165, 48–52.
- Tang, L., Xie, X., Zhou, Y., Zeng, G., Tang, J., Wu, Y., Long, B., Peng, B., Zhu, J. (2017). A reusable electrochemical biosensor for highly sensitive detection of mercury ions with an anionic intercalator supported on ordered mesoporous carbon/self-doped polyaniline nanofibers platform. *Biochemical Engineering Journal*, 117, 7–14. doi:10.1016/j.bej.2016.09.011.
- Tortolini, C., Bollella, P., Antonelli, M.L., Antiochia, R., Mazzei, F., Favero, G. (2015). DNA-based biosensors for Hg²⁺ determination by polythymine–methylene blue modified electrodes. *Biosensors and Bioelectronics*, 67, 524–531.
- Tovar-Sánchez, E., Suárez-Rodríguez, R., Ramírez-Trujillo, A., Valencia-Cuevas, L., Hernández-Plata, I., Mussali-Galante, P. (2019). The Use of Biosensors for Biomonitoring Environmental Metal Pollution. *Biosensors for Environmental Monitoring*. <https://doi.org/10.5772/intechopen.84309>
- Wei, Y., Yang, R., Yu, X-Y., Wang, L., Liu, J-H., Huang, X-J. (2012). Stripping voltammetry study of ultra-trace toxic metal ions on highly selectively adsorptive porous magnesium oxide nanoflowers. *The Analyst*, 137, 2183.
- Xu, J., Wang, Z., Liu, C., Xu, Z., Zhu, B., Wang, N., Wang, K., Wang, J. (2018). A Colorimetric and Fluorescent Probe for the Detection of Cu²⁺ in a Complete Aqueous Solution. *Analytical Sciences*, 34, 453–457. doi:10.2116/analsci.17p517.
- Yadav, R., Kushwah, V., Gaur, M.S., Bhadauria, S., Berlina, A.N., Zherdev, A.V., Dzantiev, B.B. (2019). Electrochemical aptamer biosensor for As³⁺ based on apta deep trapped Ag-Au alloy nanoparticles-impregnated glassy carbon electrode. *International Journal of Environmental Analytical Chemistry*, 100, 623–634. doi:10.1080/03067319.2019.1638371.
- Zaynab, M., Al-Yahyai, R., Ameen, A., Sharif, Y., Ali, L., Fatima, M., Khan, K. A., & Li, S. (2022). Health and environmental effects of heavy metals. *Journal of King Saud University - Science*, 34(1), 101653. <https://doi.org/10.1016/j.jksus.2021.101653>
- Zhang, L., Deng, H., Yuan, R., Yuan, Y. (2019). Electrochemical lead(II) biosensor by using an ion-dependent split DNzyme and a template-free DNA extension reaction for signal amplification. *Microchimica Acta*, 186. doi:10.1007/s00604-019-3857-z.
- Zhou, X., Su, Q., Xing, D. (2012). An electrochemiluminescent assay for high sensitive detection of mercury (II) based on isothermal rolling circular amplification. *Analytica Chimica Acta*, 713, 45–49. doi:10.1016/j.aca.2011.11.003.
- Zhu, Y-F, Wang, Y-S., Zhou, B., Yu, J-H., Peng, L-L, Huang, Y-Q., Li, X-J., Chen, S-H., Tang, X., Wang, X-F. (2017). A multifunctional fluorescent aptamer probe for highly sensitive and selective detection of cadmium(II). *Analytical and Bioanalytical Chemistry*, 409, 4951–4958. doi:10.1007/s00216-017-0436-1.
- Zong, L., Song, Y., Li, Q., Li, Z. (2016). A “turn-on” fluorescence probe towards copper ions based on core-substituted naphthalene diimide. *Sensors and Actuators B: Chemical*, 226, 239–244. doi:10.1016/j.snb.2015.11.089.