

## Documents

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**Structural, optimization of and mechanistic insights into a new thiosemicarbazone derivative as a highly sensitive and selective chemosensor for Hg<sup>2+</sup> recognition using DFT, COSMO-RS, RSM, and molecular dynamics simulation approaches**

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**Abstract**

A new thiosemicarbazone derivative, N-(2-hydroxyphenyl)-2-[1-(pyridin-4-yl)ethylidene]hydrazinecarbothioamide (HPEH), has been synthesized, characterized, and further developed as a highly selective and sensitive colorimetric chemosensor for Hg<sup>2+</sup> recognition in environmental water samples. Structural conformers of HPEH were successfully identified using a combination of the potential energy surface (PES) and time-dependent density functional theory (TD-DFT) methods. The synthesized HPEH was successfully characterized further and analyzed based on its harmonic vibrational frequencies, NMR spectra, and electronic transitions using the DFT approach. Sigma profiles were generated using the COSMO-RS approach to identify a compatible medium for HPEH to act as a chemosensor. The conditions for the highly sensitive and selective detection of Hg<sup>2+</sup> by HPEH were successfully optimized using the statistical response surface methodology approach. The optimum sensing of HPEH occurred in an 8:2 v/v DMSO/pH 7.8 solution at a 20:60 μM HPEH/Hg<sup>2+</sup> concentration and after a reaction time of 18 min, with statistically significant independent variables ( $p < 0.05$ ) for all parameters. Under optimal conditions, the lowest Hg<sup>2+</sup> concentration detected by HPEH was 3.56 μM, indicating that HPEH can serve as an alternative and comparable probe for the detection of Hg<sup>2+</sup> in aqueous systems. Using the optimized results, the interaction between HPEH and Hg<sup>2+</sup> in the chemosensor system was successfully modeled, and the model was subsequently used with the TD-DFT, non-covalent interaction-reduced density gradient (NCI-RDG), and molecular dynamics approaches to gain mechanistic insights into the interaction. The results showed that the newly synthesized HPEH, in addition to being cost-effective, could serve as a suitable alternative and comparable chemosensor for Hg<sup>2+</sup> recognition in water samples, with the advantages of being efficient, portable, and eco-friendly, and offering rapid analysis without the need of specialized training. © 2023 Elsevier B.V.

**Author Keywords**

Chemosensor; COSMO-RS; DFT; Molecular dynamic; RSM; TD-DFT

**Index Keywords**

Cost effectiveness, Density functional theory, Molecular dynamics, Nuclear magnetic resonance spectroscopy, Phenols, Potential energy, Quantum chemistry, Reaction kinetics, Structural optimization; Chemosensors, COSMO-RS, DFT, Dynamics simulation, Mechanistics, RSM, Structural optimisations, Synthesised, Thiosemicarbazones, Time dependent density functional theory; Chemosensor

**References**

- Crichton, R., Ward, R., Hider, R.  
**Metal chelation in medicine**  
(2017) *R. Soc. Chem.*,
- Gupta, N., Singhal, D., Singh, A.K., Singh, N., Singh, U.P.  
**A highly selective chromogenic sensor for Mn<sup>2+</sup>, turn-off fluorometric for Hg<sup>2+</sup> ion, and turn-on fluorogenic sensor for F<sup>-</sup> ion with the practical application**  
(2017) *Spectrochim. Acta. Part A, Mol. Biomol. Spectroscopy*, 176, pp. 38-46.
- Zahir, F., Rizwi, S.J., Haq, S.K., Khan, R.H.  
**Low dose mercury toxicity and human health**  
(2005) *Environ. Toxicol. Pharmacol.*, 20, pp. 351-360.

- Bontoom, S., Boonkitpatarakul, K., Sukwattanasinitt, M., Niamnont, N.  
**Highly selective detection of Cu<sup>2+</sup> based on a thiosemicarbazone triphenylacetylene fluorophore**  
(2017) *Tetrahedron Lett.*, 73, pp. 2483-2487.
- Liu, Y., Liu, Y., Xu, L., Li, J., Liu, X., Liu, J., Li, G.  
**Highly selective, colorimetric detection of Hg<sup>2+</sup> based on three color changes of AuNPs solution from red through sandy beige to celandine green**  
(2017) *Sens. Actuators B: Chem.*, 249, pp. 331-338.
- Tekuri, V., Sahoo, S.K., Trivedi, D.R.  
**Hg<sup>2+</sup> induced hydrolysis of thiazole amine based Schiff base: Colorimetric and fluorogenic chemodosimeter for Hg<sup>2+</sup> ions in an aqueous medium**  
(2019) *Spectrochim. Acta A Mol. Biomol. Spectrosc.*, 218, pp. 19-26.
- Sie, Y.W., Li, C.L., Wan, C.F., Chen, J.H., Hu, C.H., Yan, H., Wu, A.T.  
**A colorimetric probe for dual sensing of Hg<sup>2+</sup> and Cu<sup>2+</sup> ions in water**  
(2017) *Inorg. Chim. Acta*, 467, pp. 325-329.
- Hosseinjani-Pirdehi, H., Mahmoodi, N.O., Nadamani, M.P., Taheri, A.  
**Novel synthesized azo-benzylidene-thiourea as dual naked-eye chemosensor for selective detection of Hg<sup>2+</sup> and CN<sup>-</sup> ions**  
(2020) *J. Photochem. Photobiol. A Chem.*, 391, pp. 1-8.
- Lee, C.G., Kang, S., Oh, J., Eom, M.S., Oh, J., Kim, M.-G., Lee, W.S., Han, M.S.  
**A colorimetric and fluorescent chemosensor for detection of Hg<sup>2+</sup> using counterion exchange of cationic polydiacetylene**  
(2017) *Tetrahedron Lett.*, 58, pp. 4340-4343.
- Dhaka, G., Jindal, G., Kaur, R., Rana, S., Gupta, A., Kaur, N.  
**Multianalyte azo dye as an on-site assay kit for colorimetric detection of Hg<sup>2+</sup> ions and electrochemical sensing of Zn<sup>2+</sup> ions**  
(2019) *Spectrochim. Acta A Mol. Biomol. Spectrosc.*, 229, pp. 1-9.
- Manna, A.K., Mondal, J., Chandra, R., Rout, K., Patra, G.K.  
**A thio-urea based chromogenic and fluorogenic chemosensor for expeditious detection of Cu<sup>2+</sup>, Hg<sup>2+</sup> and Ag<sup>+</sup> ions in aqueous medium**  
(2018) *J. Photochem. Photobiol. A Chem.*, 356, pp. 477-488.
- Normaya, E., Hamdan, M.F.A., Ahmad, M.N., Aziz, Y.F.A., Bulat, K.H.K.  
**DFT/TD-DFT study on development and optimization of 1-anilino-3-phenyliminourea as a colorimetric chemosensor for Hg<sup>2+</sup> recognition in aqueous medium**  
(2020) *J. Mol. Struct.*, 1206.
- Antony, J.  
**Design of experiments for engineers and scientists**  
(2014), Elsevier Ltd.
- Klayman, D.L., Bartosevich, J.F., Griffin, T.S., Mason, C.J., Scovill, J.P.  
**2-Acetylpyridine thiosemicarbazones. 1. A new class of potential antimalarial agents**  
(1979) *J. Med. Chem.*, 22, pp. 855-862.
- Normaya, E., Farina, Y., Halim, S.N.A., Tiekink, E.R.T.  
(2011),  
3-(2-Hydroxyphenyl)-1-((E)-[1-(pyrazin-2-yl)ethylidene]amino)thiourea monohydrate, *Acta Crystallogr. E: Struct. Rep. Online* 67 o943–o944

- Li, Y., Shi, W., Ma, J., Wang, X., Kong, X., Zhang, Y., Feng, L., Xie, Z.  
**A novel optical probe for Hg<sup>2+</sup> in aqueous media based on monothiosemicarbazone Schiff base**  
(2017) *J. Photochem. Photobiol. A Chem.*, 338, pp. 1-7.
- Likussar, W., Boltz, D.F.  
**Theory of continuous variations plots and a new method for spectrophotometric determination of extraction and formation constants**  
(1971) *Anal. Chem.*, 43, pp. 1265-1272.
- Frisch, M.J., Trucks, G.W., Schlegel, H.B., Scuseria, G.E., Robb, M.A., Cheeseman, J.R., Scalmani, G., Montgomery, J.A. Jr, J.E. Peralta, F. Ogliaro, M. Bearpark, J.J. Heyd, E. Brothers, K.N. Kudin, V.N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J.C. Burant, S.S. Iyengar, J. Tomasi, M. Cossi, J.M. Millam, M. Klene, C. Adamo, R. Cammi, J.W. Ochterski, R.L. Martin, K. Morokuma, O. Farkas, J.B. Foresman, D.J. Fox, Gaussian 09, Revision A.02, Wallingford CT.
- Sundaraganesan, N., Ilakiamani, S., Saleem, H., Wojciechowski, P.M., Michalska, D.  
**FT-Raman and FT-IR spectra, vibrational assignments and density functional studies of 5-bromo-2-nitropyridine, Spectrochim**  
(2005) *Acta Part A Mol. Biomol. Spectrosc.*, 61, pp. 2995-3001.
- Jesus, A.J.L., Rosado, M.T.S., Reva, I., Fausto, R., Eusebio, M.E., Redinha, J.S.  
**Conformational study of monomeric 2,3-butanediols by matrix-isolation infrared spectroscopy and DFT calculations**  
(2006) *J. Phys. Chem.*, 110, pp. 4169-4179.
- Jamroz, M.H.  
(2004), Vibrational energy distribution analysis VEDA 4, SMMG, Warsaw.
- (2020), E.Normaya, M.F.A. Hamdan, M.N.Ahmad, Y.F.A.Aziz, K.H.K. Bulat, DFT/TD-DFT study on development and optimization of 1- anilino-3- phenyliminourea as a colorimetric chemosensor for Hg<sup>2+</sup> recognition in aqueous, *J.Mol.Struct.* 1206 127699 medium
- E.Normaya  
**Gravimetric and electrochemical statistical optimizations for improving copper corrosion resistance in hydrochloric acid using thiosemicarbazone-linked 3-acetylpyridine**  
(2022) *RSC Adv*, 12, pp. 27793-27808.
- Ismail, H.  
(2021), M.N.Ahmad, E. Normaya, A highly sensitive and selective thiosemicarbazone chemosensor for detection of Co<sup>2+</sup> in aqueous environments using RSM and TD/ DFT approaches, *Sci. Rep*, 11 20963
- Ahmad, M.N., Karim, N.U., Normaya, E., Piah, B.M., Iqbal, A., Bulat, K.H.K.  
**Artocarpus altilis extracts as a food-borne pathogen and oxidation inhibitors: RSM, COSMO RS, and molecular docking approaches**  
(2020) *Sci. Rep.*, 10, pp. 1-14.

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