

Complex Anti-microbial Ability of Salicylaldehyde Thiosemicarbazone towards Zn^{II}, Ag^I & La^{III} Ions

Abeer A. Ibrahim^{1*}, Mohanad M. Kareem², Mohammed T. Khathi³

¹Inorganic Chemistry Group, Scientific Research Center, Al-Ayen University, Thi-Qar, 64001, Iraq

²Department of Chemistry, College of Science, University of Babylon, Babil-Hilla, 51002, Iraq

³Department of Chemistry, College of Science, University of Thi-Qar, Thi-Qar, 64001, Iraq

Email: abeer.abduljaleel@alayen.edu.iq

Abstract

Three mono, di, and tri valence novel complexes of Zn²⁺, Ag⁺, and La³⁺ of the general formula [M [L]₃(H₂O)]; were designed and synthesized directly with excellent yield via reaction between thiosemicarbazide linked and 2-hydroxybenzaldehyde or (Salicylaldehyde) under optimized heat reaction conditions. Furthermore, the finding products that follow Schiff bases were elucidated by IR, UV, and ¹H-NMR spectroscopy. Likewise, the antibacterial activities of the ligands and their complexes were determined by in vitro assays against *Gram (+Ve)* and *Germ (-Ve)* bacterial strains besides fungi agents. The results evaluated that the complexes contain leading functional groups such as (OH, NH₂, C=S, C-O, and C=N). The behaviour of the complexes as anti-biology against bacteria and fungi has been scrutinized. The results displayed that Zn²⁺ can degrade *Germ (+Ve)* *S. aureus Bacillus*. However, the Ag⁺ complex illustrates high resistance to the same *germ*, and La³⁺ moderately affects bacteria and fungi.

Keywords: novel complexes, Thiosemicarbazone, ¹H-NMR, and antimicrobial activity

1. Introduction

hydrazinecarbothioamide or (thiosemicarbazide) (CH₅N₃S) and their modified thiosemicarbazones TSCs NH₂NHN-CR₁R₂ act as multi-chelating donor ligands with transition or alkali metals by linking through sulfur, nitrogen, and oxygen atoms¹. TSCs have been examined for their biological versatility activation against bacteria, fungi, and anti-cancers². Salicylaldehyde TSC and its derivatives were additionally mentioned to form excessive stability complexes with transition metallic ions in the solution. STSC-based compounds have lower cytotoxic activity in human cancer cells than a-N-pyridyl TSCs. Their copper (II) complexes are frequently much more effective in inhibiting than the corresponding ligands due to their redox properties³. The chemistry of copper (II) thiosemicarbazone derivatives has received considerable attention; as an antioxidant, Sîrbu and his co-works prepared copper (II) thiosemicarbazone complexes with sodium 5-sulfonate-salicylaldehyde thiosemicarbazones, they applied this complexes as an antioxidant response in a highly resistant breast cancer cell. Their findings pave the way for researchers to look into ROS-inducing copper (II) complexes as potential antiproliferative agents in cancer chemotherapy⁴. A new lanthanum (III) and praseodymium (III) complexes of thiosemicarbazones derived had been prepared from the condensation of isatin with 4-phenyl thiosemicarbazide and physio-chemical characterization such as XRD, electronic absorption, and fluorescence, IR, ¹³C-NMR, and TGA were applied⁵. Recently, silver (I) and other central atoms

such as nickel (II) and copper (II) complex N⁴-substituted thiosemicarbazones and ciprofloxacin have been prepared for their effect in silico molecular modeling and pharmacokinetics studies. The results exhibited that silver (I) complexes had lower activity and copper (II) complexes had higher activity against the cancer cell lines tested⁶. Herein, in this study, three types of novel complexes of central transition metals (Zn, Ag, and La) thiosemicarbazones have been prepared directly by reaction of thiosemicarbazide, Salicylaldehyde, besides the ligand reacted with a metal salt to obtain the complexes as mentioned earlier; antimicrobial evaluations have been examined.

2. Experimental

Thiosemicarbazide- Salicylaldehyde legend was prepared by methods described by Pahontu and his co-works⁷ by refluxing for 30 minutes a known quantity of thiosemicarbazide and Salicylaldehyde in methanol solvent. IR, UV, and ¹H-NMR spectroscopy determined the finding products following Schiff bases. Those legends were further used for the complexation reaction with Zn²⁺, Ag⁺, and La³⁺ metal ions.

3. Instrumentation

FTIR spectra of thiosemicarbazide ligand and complex's main functional groups were recorded on Shimadzu FTIR-7600 infrared spectrometer (4000-400 cm⁻¹). UV- A Shimadzu spectrophotometer accomplished visible spectra. The ¹H-NMR spectra were applied using Bruker AV III HD NMR in (500 MHz) CDCl₃ with TMS as the internal standard.

4. Biological evaluation

For biological evaluation, it adopted Lalitha, manual methods. Before use, each batch of media was checked for its ability to support the growth of the most relevant control strains (*E.coli* and *S.aureus*). The media powder was dissolved in distilled water. It was put in the autoclave for sterilization, and the agar media was cooled to 40 -50°C in the water bath. Plates were poured to a depth of 4 mm on a surface that has been demonstrated to be level and horizontal. Suspension from the tested organism was prepared by emulsifying a few colonies in sterile normal saline and compared with the turbidity of 0.5 McFarland standards. The cotton swab was used for inoculating suspension on Muller-Hinton agar 29 surfaces after being dipped into standardized

suspension and squeezed gently to remove excess from the swab. Under aseptic conditions and using sterile forceps, the following impregnated discs (1-5) were applied on the agar zinc, lanthanum, and Silver surface. The distance was 24 mm between discs and 10 mm between discs and plate edges. The plate will incubate aerobically in an incubator at 37°C overnight. The plate was examined, and the ruler measured the zone diameter in (mm). The recorded zones were measured as resistant (R) or sensitive (S) ⁸.

5. Results and Discussion

The reaction between thiosemicarbazide and Salicylaldehyde yields multi chelating agent

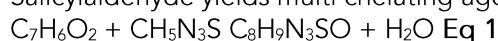


Table 1 Physical and analytical data of the ligands and complexes

Molecule formula	Yield %	MP °C	IR (cm ⁻¹)	$\pi-\pi^*$ Transition	n- π Transition
C ₈ H ₉ N ₃ SO	20.4	220	OH (3200), NH ₂ (3300), C=S (1570), C-O (1365), C=N (1660).	230	312
C ₈ H ₈ N ₃ ZnOS	83.75	212	OH (3200), NH ₂ (3278), C=S(1600), C-O(1317) C=N (1543),Zn-O(474), N-N(1107),Zn-S(497), Zn-N(405)	260	314
C ₈ H ₈ N ₃ LaOS	72.41	216	OH (3000), NH ₂ (3500), C=S(1600), C=N (1111), C-O (1360), La-O(500), N-N(1408),La-S(500), La-N(480)	266	350
C ₈ H ₈ N ₃ AgOS	75.52	214	OH(3178), NH ₂ (3286), C=S(1604), C-O(1300),C=N(1570), Ag-O(478), N-N(1114),Ag-S(440), Ag-N(478)	277	228

The main functional groups of IR spectral bands of H₂L¹-H₂L¹⁰ with their Zn²⁺, Ag⁺, and La³⁺ complexes are displayed in table 1. From table 1, it has been shown that thiosemicarbazide and Salicylaldehyde (thiosemicarbazones) act as mono, di, and tri ligands for the aforementioned central atoms through a deprotonated phenolic oxygen atom, azomethine nitrogen atom, and sulfur atom forming five and six-membered metalocycles. From IR spectra, the OH functional group showed a broad band ca from 3000 to 3200 cm⁻¹, which belonged to the phenolic group. C-O stretching vibration bands were shifted from the ligand from 1365 cm⁻¹ to a lower frequency around 1317, 1360, and 1300 cm⁻¹ in complexes spectra. It was further confirmed by appearing M-O functional group in the complex structure from 405 to 500 cm⁻¹. A strong band was determined around 166 cm⁻¹ was reduced to lower frequencies due to the direction of the coordination of the azomethine nitrogen to the central metal atom. The coordination frequency was calculated from 1500 to 1570cm⁻¹. In the same way, ν (C=S) stretching frequency assigned to the thiocarbonyl group was shifted because of the coordination of the sulfur atom to the metal ion. (Ref ^{9,10,11,12}).

Electronic absorption spectral data of the ligand (L) and complexes showed bands from 266 to 277 and

228 to 350nm (Table 1) the band representative benzene and other functional groups that appeared in benzene. The absorption band of complex functional groups is expanded to a high wavelength value compared to that of the TSc. $\pi-\pi^*$ band values were shown from 230 to 277nm. However, n- π strong band values were observed from 228 – 350 nm ¹³.

6. NMR Spectra

Many ligands and their diamagnetic complexes have been studied using NMR spectroscopy to determine their structure and nature.

The NMR spectra of the complexes were recorded, and DMSO-d₆ was used as a solvent;

Thiosemicarbazones ligand molecule formula C₈H₉N₃SO, Formula Weight = 195.24, elemental analysis by composition = C (49.21%), H (4.65), N (21.52%), O (8.19%), S (16.42%), with Surface Tension equal to = 52.1 ± 7.0 dyne/cm, and Index Refraction = 1.652 ± 0.05. The ¹H NMR spectroscopy of the ligand TSC shows nine protons from 9.88 to 6.79 and six signals for chemical shift. ¹HNMR shows OH protons at 11.29 ppm, δ = 9.88 (S, 1 H, NNHCS), 8.38 (S, 1H, CH=N), 8.09 (S, 1H, NH₂) ppm, and δ 8.2 (m, 4H, C₆H₄). However, singlet signals at δ = 2.51 and 3.47 ppm for DMSO solvent.

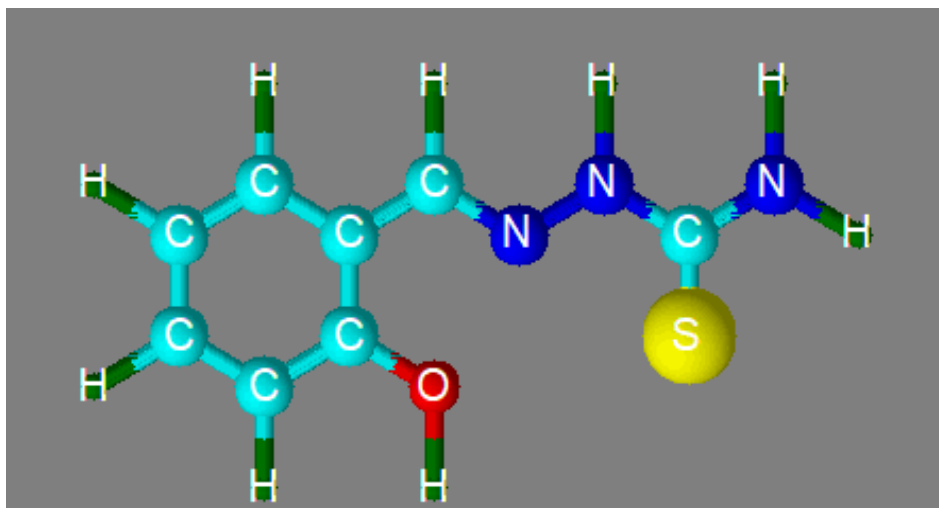


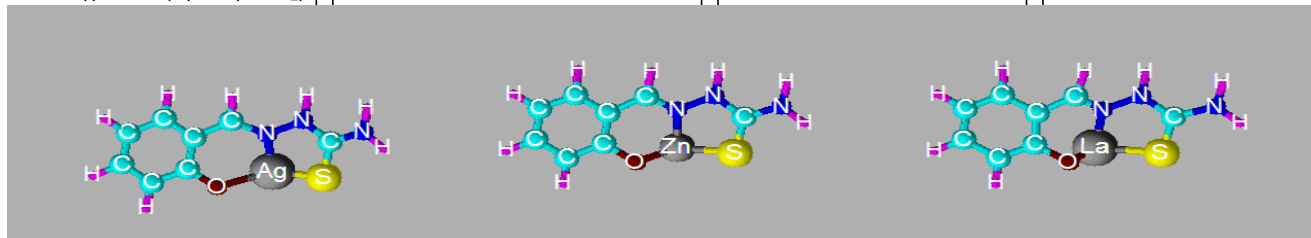
Fig 1 Thiosemicarbazone Legend Structure

Zinc- Thiosemicarbazones complex molecule formula $C_8H_8ZnN_3SO$. Formula Weight = 259.64, elemental analysis by composition = C (37.01%), H (3.11%), N (16.18%), Zn (25.19%), and S (12.35%). 1H NMR (500.10 MHz, DMSO- d_6): δ = 11.36 (br. s, 1H, OH), 9.88 (s, 1H, NNHCS), 8.37 (s, 1H, CH=N), 8.07 (s, 1H, NH₂) ppm.

Lanthanum- Thiosemicarbazones complex molecule formula $C_8H_8LaN_3SO$. Formula Weight = 333.13, elemental analysis by composition = C (28.84%), H (2.42%), La (41.7%), N (12.61%), O (4.8%), and S (9.63%). 1H NMR (500.10 MHz, DMSO- d_6): δ = 11.36 (br. s, 1H, OH), 10.28 (s, 1H, NNHCS), 8.37 (s, 1H, CH=N), 7.94 (s, 1H, NH₂) ppm.

Silver Thiosemicarbazones complex molecule formula $C_8H_8AgN_3SO$, Formula Weight = 302.10, elemental analysis by composition = C (31.81%), H (2.67%), N (13.91%), Ag (35.71%), and S (10.61%).

1H NMR (500.10 MHz, DMSO- d_6): δ = 12.05 (br. s, 1H, OH), 10.21 (s, 1H, NNHCS), 8.55 (s, 1H, CH=N), 8 (s, 1H, NH₂) ppm.¹⁴ Additionally, the chemical shift due to the aromatic ring of TSCs protons (m, 4H, C₆H₄) appears at δ = 7.89, 7.81, and 7.98 ppm, respectively in the ligands, which shifts gently up the field in complexes. This could be due to the decline in electron density after the complex is formed. DMSO solvent singlet signals for all complexes appeared at δ = 2.50 – 4.03 ppm.

Fig 2 Zn²⁺, Ag⁺ and La³⁺ Complexes Structures

Antimicrobial activity

Against two types of bacteria and fungi are summarized in the (Table 2). The antibacterial activity was carried out for four samples TSC, Zn²⁺, Ag⁺, and La³⁺ complexes. The diameter of the inhibition zone (mm) and disc diameter was measured for each treatment. The result revealed that the Zn²⁺ complex has high sensitivity against *Garm (+Ve) S. aureus* the length up to 20 mm. In addition, the Ag⁺ result indicated low sensitivity against bacteria and fungi. Conversely, La³⁺ reveals a moderate effect against Germ (+Ve) *S. aureus* and low sensitivity to *E. coli* and *Aspergillus*. Moreover, the results illustrate that complexes have more activity and ligands have no function against microbiology. N Fahmi and his co-workers argued that chelation significantly reduces the polarity of the metal ion, owing to the partial disclosure of its positive charge with the donor groups and the possibility of electron delocalization across the entire chelate ring. This chelation may also increase the lipophilicity of the central metal atom, permitting it to pass through the lipid layer of the cell

membrane¹⁵.

Table 2 screening of antimicrobial activity of TSC and its complexes

	TSC	Zn ²⁺	La ³⁺	Ag ⁺
<i>Garm (+Ve) S. aureus Bacillus</i>	6 (R)	20 (S)	9 (S)	Zero (R)
<i>Garm (-Ve) E. Coli Escherichia</i>	15 (S)	11 (S)	7 (R)	9 (R)
<i>Aspergillus</i>	Zero (R)	6 (R)	7 (R)	8 (S)

S sensitive, clear zone, R resistance no zone

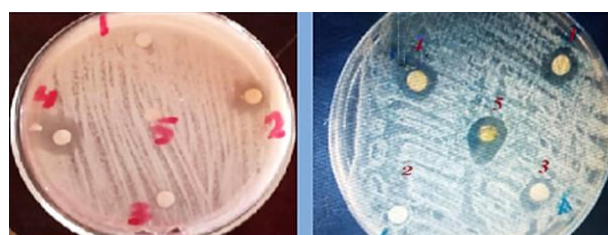


Fig 3 Antimicrobial Activity of TSC and Its Complexes Number 1 for La-TSC, Number 3 TSC, Number 4 Zn-TSC And Number 5 Ag-TSC

7. Conclusion

Three complexes of Zn^{2+} , Ag^+ and La^{3+} , with the Thiosemicarbazone coordinated as a bidentate and tridentate ligand, have been prepared as Schiff base intermediate. The final products were characterized by IR, UV, and 1H NMR, their functional groups as OH, NNHCS, CH=N, NH_2 , and aromatic rings. The results from the batch experiments indicated that complexes of Zn^{2+} , Ag^+ and La^{3+} have high sensitivity against bacteria and fungi than the effect of ligand TSC. What is more, their examination has applied to bacteria and fungi.

References

1. M. J. M. Campbell, *Coordination Chemistry Reviews* **15** (1975) 279–319 ([https://doi.org/10.1016/S0010-8545\(00\)80276-3](https://doi.org/10.1016/S0010-8545(00)80276-3))
2. R. Hueting, R. Tavaré, J. R. Dilworth, & G. E. Mullen, *Journal of Inorganic Biochemistry* **128** (2013) 108–111 (<https://doi.org/10.1016/j.jinorgbio.2013.07.017>)
3. T. S. Lobana, S. Khanna, & R. J. Butcher, *Zeitschrift für Anorganische und Allgemeine Chemie* **633** (2007) 1820–1826 (<https://doi.org/10.1002/zaac.200700199>)
4. A. Sîrbu, O. Palamarcu, M. V. Babak, J. M. Lim, K. Ohui, E. A. Enyedy, S. Shova, D. Darvasiová, P. Rapta, W. H. Ang, & V. B. Arion, *Dalton Transactions* **46** (2017) 3833–3847 (<https://doi.org/10.1039/c7dt00283a>)
5. A. Rai, S. K. Sengupta, & O. P. Pandey, *Spectrochimica Acta - Part A: Molecular and Biomolecular Spectroscopy* **61** (2005) 2761–2765 (<https://doi.org/10.1016/j.saa.2004.09.031>)
6. S. Ahmed, M. A. Jayathuna, D. Mahendiran, S. Bharathi, & A. Kalilur Rahiman, *Applied Organometallic Chemistry* (2022) (<https://doi.org/10.1002/aoc.6782>)
7. E. Pahontu, V. Fala, A. Gulea, D. Poirier, V. Tapcov, & T. Rosu, *Molecules* **18** (2013) 8812–8836 (<https://doi.org/10.3390/molecules18088812>)
8. M. K. Lalitha, *Indian Association of Medical Microbiologists* (2007) 1–47
9. V. Stavila, R. L. Davidovich, A. Gulea, & K. H. Whitmire, *Coordination Chemistry Reviews* **250** (2006) 2782–2810 (<https://doi.org/10.1016/j.ccr.2006.02.032>)
10. A. P. Gulya, V. I. Prisacar', V. I. Tsapkov, S. A. Buracheva, S. N. Spynu, N. P. Bezhenar', D. Poirier, & J. Roy, *Pharmaceutical Chemistry Journal* **41** (2007) 596–599 (<https://doi.org/10.1007/s11094-008-0023-z>)
11. A. Gulea, D. Poirier, J. Roy, V. Stavila, I. Bulimestru, V. Tapcov, M. Birca, & L. Popovschi, *Journal of Enzyme Inhibition and Medicinal Chemistry* **23** (2008) 806–818 (<https://doi.org/10.1080/14756360701743002>)
12. N. S. Youssef, A. M. A. El-Seidy, M. Schiavoni, B. Castano, F. Ragaini, E. Gallo, & A. Caselli, *Journal of Organometallic Chemistry* **714** (2012) 94–103 (<https://doi.org/10.1016/j.jorganchem.2012.03.018>)
13. S. İlhan, *Russian Journal of Coordination Chemistry/Koordinatsionnaya Khimiya* **35** (2009) 347–351 (<https://doi.org/10.1134/S1070328409050066>)
14. M. Hricovíni, M. Mazúr, A. Sîrbu, O. Palamarcu, V. B. Arion, & V. Brezová, *Molecules* **23** (2018) (<https://doi.org/10.3390/molecules23040721>)
15. N. Fahmi, I. J. Gupta, & R. V. Singh, *Phosphorus, Sulfur, and Silicon and the Related Elements* **128** (1997) 1–9 (<https://doi.org/10.1080/10426509708031559>)