International Journal of
Science and Engineering Investigations vol. 6, issue 61, February 2017
ISSN: 2251-8843

Antibacterial Activities of Isatin-3-Thiosemicarbazone Derivatives and Their Metal Complexes against Different Types of Bacteria

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Abstract- Isatin-3-thiosemicarbazone derivatives and their metal complexes (Zn & Ni) were evaluated *in vitro* for their antibacterial activities against selected five bacterial strains, viz. gram-positive (*Staphylococcus aureus* ATCC 25923, *Staphylococcus huminis*) and gram negative (*Klebsiella pneumoniae*, *Proteus vulgaris*). It was observed that metal complexes had an enhanced activity compared to the ligand against some types of tested bacteria. Binding of the all molecules to DNA is through minor groove.

Keywords- *Isatin-3-Thiosemicarbazone, Antibacterial Activities, Ligand and Metal Complexes of Thiosemicarbazone*

I. INTRODUCTION

Thiosemicarbazideis used in different area 4-Phenylthiosemicarbazide (4-PTSC) thiosemicarbazide utilized as an agrarian compound a pesticide. It likewise has antibacterial properties credited to electron delocalization in the thiosemicarbazide fraction [1].

Thiosemicarbazones are a significant substance due to their chemistry and probably biological activities, like antibacterial, antifungal, antimicrobial, antiviral and anticancer [2, 3].

Thiosemicarbazones have been studied as prophylactic therapeutics per human disease since 1946 [4]. Thiosemicarbazones were the principal antiviral synthesis perceived to have an extensive range antiviral movement against a scope of DNA and RNA infections. In south India as precocious as 1965, They reported that N-methyl isatin-β-thiosemicarbazone as named methisazone or marboran had been used as an efficient antiviral medication for the chemoprophylaxis of pox and this drug was experienced in human volunteers [4]. Isatin-β-thiosemicarbazone derivatives were reported as pretended a range of antiviral activities such as vaccinia viruses and Moloney leukemia [5, 6]. Isatin-β-thiosemicarbazone also, some of its derivatives have high movement against neurovaecinia and certain different poxvirus contaminations in mice [7]. Thiosemicarbazone of isatin was found mightily active [8]. Formation of overripe vaccinia virus progeny can be inhibited by Isatin-β-thiosemicarbazone [9].

Abdel-Rahman et al. [10] reported that Cu(II) complexes incorporating imines derived from amino acids exhibited a stronger antibacterial and antifungal efficiency compared to their corresponding ligands.

II. EXPERIMENTAL SECTION

All chemicals utilized in this study were analytical grade. The ligands and their metal complexes were prepared by report method [11].

With the reports about anti-bacterial activities of the 1H-Indole-2, 3-dione-thiosemicarbazone derivatives, we screened chemical substances 1-9 for their antibacterial effects *in vitro* against five types of bacteria (Table 1).

TABLE I. ANTIBACTERIAL ACTIVITIES OF COMPOUNDS UNDER STUDY

Compounds	*K. pneumoniae*	*S. aureus ATCC* 25923*	*S. aureus*	*P. vulgaris*	*S. huminis*
H_2PTSC^*	7.00	17.50	11.88	12.75	7.50
$[Zn(HPTSC)_2]$	6.17	11.38	9.33	11.00	9.33
$[Ni(HPTSC)_2]$	8.00	7.00	0.00	8.83	7.00
$H_24NPTSC$**	7.30	13.75	14.67	11.5	0.00
$[Zn(H4NPTSC)_2]$	7.00	21.67	18.75	25.00	0.00
$[Ni(H4NPTSC)_2]$	6.667	15.00	14.75	13.25	0.00
H_2BTSC***	7.25	0.00	11.50	9.38	8.00
$[Zn (HBTSC)_2]$	6.50	12.63	10.83	14.69	9.67
$[Ni(HBTSC)_2]$	6.50	8.88	8.00	9.33	0.00

*1H-indole-2,3-dione-3-(N-phenyl thiosemicarbazione)
**1H-indole-2,3-dione-3-[N-(4-nitrophenyl)-thiosemicarbazone]
***1H-indole-2,3-dione-3-(N-benzylthiosemicarbazone)

The media were prepared by adding parts relating to maker's directions by measured 20 g of nutrient agar for 1000 mL distilled water and disinfected in the autoclave at 121°C and air weight for 15 min. Medium was cooled to 45-60 °C and poured in petri dish. Then, the medium was solidified at room temperature in a safety cabinet to prevent contamination [11-13].

$1x10^{-5}$ Mole substance was dissolved in 1mL dimethyl sulfoxide. To ensure the solvent experienced no effect on the bacterial growth, a control was performed with the test medium supplemented with DMSO and it was observed that DMSO gave no effect on the microorganisms. [11-13]. Experiment was performed in triplicates.

After the media rigidity, the bacterial strain was spread using the swab then studied compounds were spread for each type of bacteria by using paper disc method. All plates were incubated at 37 °C for 24 h and checked for the growth of inhibition zones. The presence of clear zones around the disc indicated that both the ligand and complex were active and the diameter of inhibition zone for studied compounds were measured [11-14].

III. 3. RESULTS AND DISCUSSION

A. Antibacterial Activities

In our study, isatin-thiosemicarbazone as a ligand and metal complexes (Zn & Ni) were evaluated *in vitro* as antibacterial activities against 5 bacterial strains. Three of them are gram-positives *(S. aureus ATCC 25923, S. aureus, S. huminis)* and two of them are gram negatives (*K. pneumoniae , P. vulgaris*).

In Table 1 and Fig. 1, one can observe that HPTSC, $[Zn(HPTSC)_2]$ and $[Ni(HPTSC)_2]$ against *K. pneumoniae* have inhibition zones 7.00, 6.17, 8.00 (mm), and relatively these inhibition zones considered moderate according to the diameter of inhibition zone, and against *S. aureus ATCC 25923*, HPTSC, $[Zn(HPTSC)_2]$ and $[Ni(HPTSC)_2]$ also have different antibacterial activities with inhibition zones 17.50, 11.38, 7.00 (mm), where these inhibition zones of both HPTSC and $[Zn(HPTSC)_2]$ relatively considered good according to the diameter of inhibition zone but for $[Ni(HPTSC)_2]$ was weak comparatively. As shown in Fig. 1, inhibition zones of both HPTSC and $[Ni(HPTSC)_2]$ were statistically different according to the statistical calculation. Against *S. aureus* both HPTSC and $[Zn (HPTSC)_2]$, they have good antibacterial activity with inhibition zones 11.88, 9.33 (mm), whereas $[Ni(HPTSC)_2]$ have no inhibition zone. H_2PTSC, $[Zn(HPTSC)_2]$ and $[Ni(HPTSC)_2]$ have good antibacterial activities against *P. vulgaris* with inhibition zones 12.75, 11.00, 8.83 (mm) according to the diameter of inhibition zones, and against the last tested bacteria *S. huminis* for H_2PTSC, $[Zn (HPTSC)_2]$ and $[Ni(HPTSC)_2]$ still have antibacterial activities with different inhibition zones 7.50, 9.33, 7.00 (mm). Obtained results of different inhibition zones indicate that HPTSC and its metallic complexes $[Zn(HPTSC)_2]$ and $[Ni(HPTSC)_2]$ exhibited different antibacterial activity against selected bacteria according to the diameter of presence inhibition zones that were measured.

$H_2$4NPTSC compound and its metallic $[Zn(H4NPTSC)_2]$ and $[Ni(H4NPTSC)_2]$ have enhanced antibacterial activities respectively against *S. aureus ATCC 25923* with an inhibition zones 13.75, 21.67, 15.00 (mm), against *S. aureus* 14.67, 18.75, 14.75 (mm) and against *Proteus P. vulgaris* 11.5, 25, 13.25 (mm) compared to the inhibition zones against *K. pneumoniae* which are 7.30, 7.00, 6.67 (mm). As shown in Fig. 2, it was observed that against both *S. aureus ATCC 25923* and *P. vulgaris* 4NPTSC and its metallic complexes $[Zn(H4NPTSC)_2]$ and $[Ni(H-4NPTSC)_2]$ were statistically different.

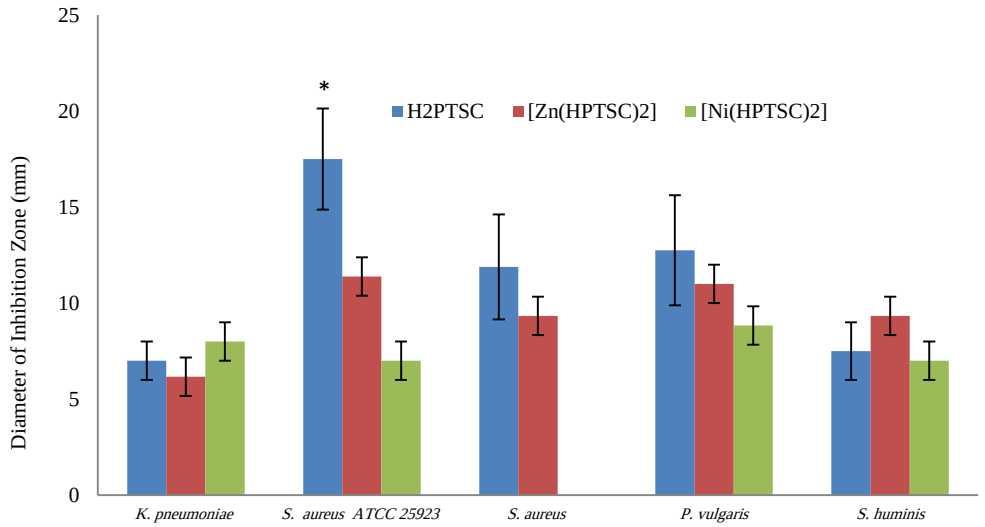

Figure 1. Inhibition zone of H_2PTSC, $[Zn(HPTSC)_2]$ and $[Ni(HPTSC)_2]$ against different types of bacteria

H_2BTSC, [Zn(HBTSC)$_2$], and [Ni(HBTSC)$_2$] compounds have different inhibition zones against selected bacteria as shown in Table 1, namely against Klebsiella pneumoniae the inhibition zones with 7.25, 6.50, 6.50 (mm), against *S. aureus ATCC 2592*, HBTSC has no inhibition zone whereas its metallic [Zn(HBTSC)2] and [Ni(HBTSC)2] complexes have inhibition zones with 12.63, 8.88 (mm).

H_2BTSC, [Zn(HBTSC)$_2$] and [Ni(HBTSC)$_2$] compounds have inhibition zones against *S. aureus* which are 11.50, 10.88, 8.00 (mm), against *P. vulgaris* the inhibition zones are 9.38, 14.69, 9.33 (mm) and against *S. huminis* both HBTSC and [Zn(HBTSC)$_2$] have inhibition zone with 8.00, 9.67 (mm), whereas [Ni(HBTSC)$_2$] has no inhibition zone according to presence or absence of diameter of inhibition zones. As shown in Fig. 3, inhibition zones of H_2BTSC, [Zn(HBTSC)$_2$], [Ni(HBTSC)$_2$] compounds against *P vulgaris* are statistically different.

It has been observed that $H_2$4NPTSC and its metallic complexes [Zn(H4NPTSC)$_2$] and [Ni(H4NPTSC)$_2$] have the better antibacterial activities of studied compounds compared to H_2PTSC, [Zn(HPTSC)$_2$], [Ni(HPTSC)$_2$] and H_2BTSC, [Zn(HBTSC)$_2$], [Ni(HBTSC)$_2$] according the presence diameter of inhibition zone. It is also observed that metal complexes have an enhance activity compared to the ligand against some types of tested bacteria, perhaps because of transition metal that involved in coordination. The antimicrobial bustle of the metal based chemotherapeutic agents of nano-sized Cr(III), Fe(II), Co(II) and Ni(II) Schiff base complexes having N, N, O donor system screened against different types of bacteria and fungi and reported that all metal complexes have superior activity than its free ligand [15].

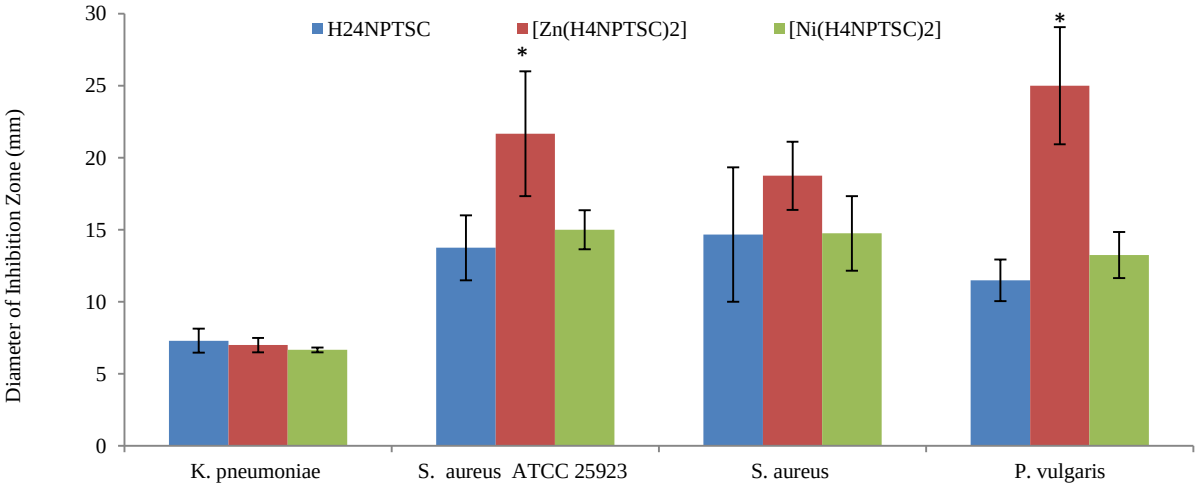

Figure 2. Inhibition zone of $H_2$4NPTSC, [Zn(H4NPTSC)$_2$] and [Ni(H4NPTSC)$_2$] against different types of bacteria

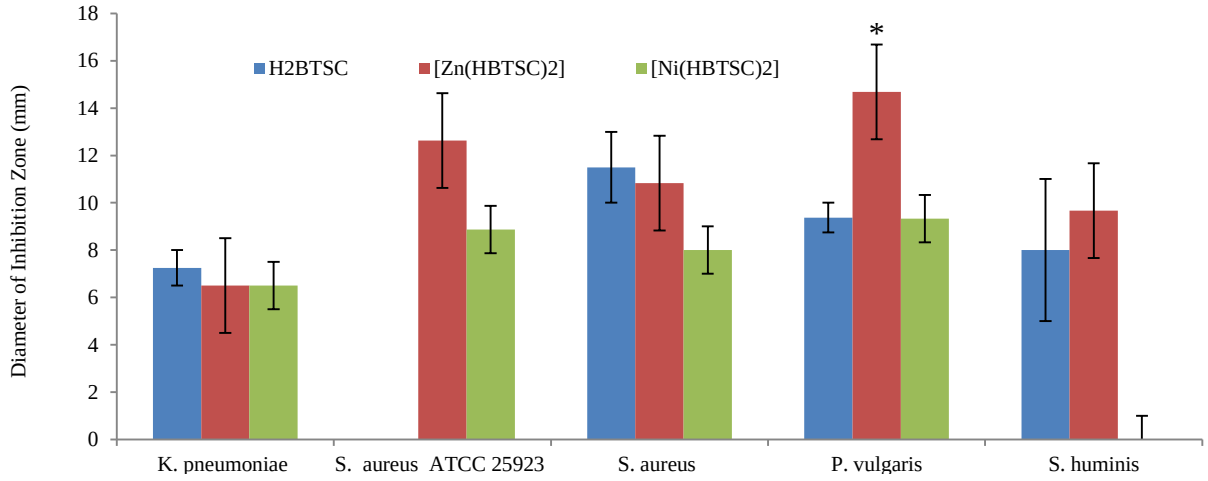

Figure 3. Inhibition zone of H_2BTSC, [Zn(HBTSC)$_2$] and [Ni(HBTSC)$_2$] against different types of bacteria

IV. CONCLUSION

In this paper, Isatin–thiosemicarbazones derivatives and their metal complexes are evaluated in *vitro* against 5 bacterial strains. Obtained results indicated that the studied compounds have different antibacterial activities against some types of selected bacteria, and being compared to the ligand metal complexes have an enhance activity against some types of selected bacteria, that could be explained by the different nature of the transition metal involved in coordination.

REFERENCES

[1] A.K. Nandi, S. Chaudhri, S.K. Mazumdah, S. Ghosh, J. Chem. Soc. Per. Trans. 2. 11 (1984) 1729-1733.

[2] J.F.M. Da Silva, S.J. Garden, A.C. Pinto, J. Braz. Chem. Soc. 12 (2001) 273-324.

[3] E.M. Jouad, G. Larcher, M. Allain, A. Riou, G.M. Bouet, M.A. Khan, X.D. Thanh, J. Inorg. Biochem. 86 (2001) 565-571.

[4] K. Venkatesh, B. Venkanna, K.B. Chandra Sekhar, K. Mukkanti, J. Chem. Pharm. Res. 7 (2015) 437-445.

[5] D.C. Quenelle, K.A. Keith, E.R. Kern, Antivirus Res. 71 (2006) 24-30.

[6] L. Sebastian, A. Desai, M.N. Shampur, Y. Perumal, D. Sriram, R. Vasanthapuram, J. Vir. 5 (2008) 1-12.

[7] D.J. Bauer, P.W. Sadler, Brit. J. Pharm. 15 (1960) 101-110.

[8] T.R. Bal, B. Anand, P. Yogeeswari, D. Sriram, Bioorg. Med. Chem. Lett. 15 (2005) 4451-4455.

[9] H. Adibi, M.M. Khodaei, P. Pakravan, R. Abiri, J. Pharm. Chem. 44 (2010) 219-227.

[10] L.H. Abdel-Rahman, A.M. Abu-Dief, M. Ismael, M.A.A. Mohamed, N.A. Hashem, J. Mol. Struc. 1103 (2016) 232- 244.

[11] F. Kandemirli, M.I. Choudhary, S. Siddiq, M. Saracoglu, H. Sayiner, T. Arslan, A. Erbay, B. Köksoy, Quantum Chemistry-Molecules for Innovations, Quantum Chemical Calculations for Some Isatin Thiosemicarbazones, InTech - Open Access Publisher, (2012) pp. 25-58.

[12] K. Venkatesh, P. Rayam, K.B. Chandra Sekhar, K. Mukkanti, Int. J. Appl. Bio. Pharm. Tec. 7 (2016) 258-266.

[13] B. Prathima, R.Y. Subba, P.V. Chalapathi, Y.P. Reddy, R.A. Varada, In.t J. Pharm. Pharm. Sci. 4 (2012) 167-174.

[14] M. Yidliz, B. Dulger, S.Y.K. Yancu, B.M. Yanpici, J. Ind. Chem. Soc. 81 (2004) 7-12.

[15] L.H. Abdel-Rahman, A.M. Abu-Dief, E.F. Newair, S.K. Hamdan, J. Photochem. Photobiol. B: Biology. 160 (2016) 18-31.