



Synthesis and Antibacterial Screening of Novel 1(4-Aminophenyl)-2(p-Chlorophenyl Thiocar - bamido)-1-Ethanol

Ajay Balu Wadekar

Assistant Professor

Department of Chemistry, shri. Dnyaneshwar Maskuji Burungale Science and Arts College Shegaon

Abstract: Present research work deals with synthesis and antibacterial screening of novel 1(4-aminophenyl)-2(p-chlorophenyl thiocarbamido)-1-ethanol against different pathogenic bacterial strains. Throughout this work Gram-positive and Gram-negative pathogenic bacteria's (like *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus pyogenes* and *Proteus vulgaris*) are used for evaluation of antibacterial activity by disc diffusion method at 0.002 to 0.01 concentrations range. The effect of the structure of the investigated compounds on the antimicrobial activity is discussed. It shows remarkable antibacterial activity against *Escherichia coli* (causes diarrhea) and *Staphylococcus aureus* (causes pus formation) and *Proteus vulgaris* (wound and urinary tract infections) while weakly act against *Streptococcus pyogenes*. The potency of the drug is increased due to substitution.

Keywords: 1(4-aminophenyl)-2-(p-chlorophenyl thiocarbamido)-1-Ethanol, Gram Positive bacteria, gram negative bacteria, antibacterial activities

I. INTRODUCTION

The escalating prevalence of antibiotic-resistant bacterial strains poses a significant threat to global public health, necessitating the development of novel antimicrobial agents with enhanced efficacy and broader spectra of activity. In this context, heterocyclic and sulfur-containing compounds have emerged as promising scaffolds in medicinal chemistry due to their diverse biological properties and structural adaptability [1-7]. Thiocarbamido derivatives, characterized by the presence of the thiocarbamoyl functional group, represent a versatile class of compounds known for their pharmacological potential. The incorporation of various substituents onto the thiocarbamido backbone has been shown to modulate their physicochemical properties and biological activity, particularly in the realm of antibacterial efficacy [8-12]. These derivatives are believed to exert their antimicrobial effects through multiple mechanisms, including disruption of bacterial cell wall synthesis, inhibition of enzymatic pathways, and interference with nucleic acid function. Recent studies have highlighted the significance of structural modifications such as the introduction of aromatic rings, electron-donating or withdrawing groups, and heteroatoms in enhancing the antibacterial potency of thiocarbamido compounds [13-17]. Such substitutions not only influence lipophilicity and membrane permeability but also improve target specificity and reduce toxicity. Many researchers evaluated antibacterial activity of substituted thiocarbamido derivatives [18-25]. Considering these things in mind present research scheme designed to synthesis and antibacterial screening of novel 1(4-aminophenyl)-2(p-chlorophenylthiocarbamido)-1-ethanol against different pathogenic bacterial stains by disc diffusion method. This study seeks to identify potent candidates that could serve as leads for the development of new antimicrobial agents in the fight against resistant pathogens.

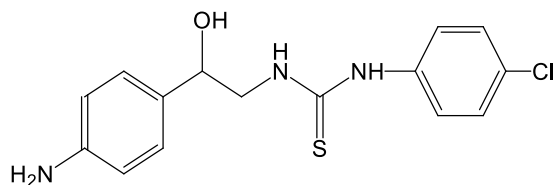
I. RESEARCH METHODOLOGY

All AR grade chemicals were used throughout experiment.

2.1 Synthesis

Synthesis of 1(4-aminophenyl)-2(p-chlorophenylthiocarbamido)-1-ethanol

4-(2-amino-1-hydroxyethyl) aniline and p-chlorophenyl isothiocyanate are reflux in acetone medium for 2 hrs to obtain 1(4-aminophenyl)-2(p-chlorophenyl thiocarbamido)-1-ethanol. After completion of reaction, to isolate 1(4-aminophenyl)-2(p-chlorophenyl thiocarbamido)-1-ethanol from solvent. After distillation of acetone the product is isolated which is recrystallized from ethanol to get white colour crystalline solid with m.p. 85°C.



1(4-aminophenyl)-2(p-chlorophenyl thiocarbamido)-1-ethanol

2.2 Antibacterial activity

The antibacterial activities of 1(4-aminophenyl)-2(p-chlorophenyl thiocarbamido)-1-ethanol were tested to evaluate their efficiencies against gram positive and gram negative pathogenic bacteria's. All the chemical and media were purchased from M/s. Hi-Media Pvt. Ltd., Mumbai, India. The organisms used were taken for studies are Gram-positive bacteria (two different standard strains of *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Enterococcus faecalis*, *Streptococcus pyogenes*, *Bacillus cereus*) and Gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Proteus vulgaris*, *Enterobacter aerogenes*). For the evaluation of in-vitro antimicrobial activity. In the present study, we used agar disc diffusion method to find out the activity of newly synthesized 1(4-aminophenyl)-2(p-chlorophenyl thiocarbamido)-1-ethanol against the microbes. Then the minimum inhibitory concentrations were measured by serial dilution method for those compounds only which were found to be active.

2.3 Preparation of sample solution

To study antimicrobial activity of synthesized molecule dissolve and prepared their solution in ethanol medium. Thus, ethanol was taken and tested as control. To check the potency of compounds, the solutions were prepared with 50 alpha gm/ml concentration. 1 ml of this solution was added to 5 ml of nutrient broth solution containing organism to be tested. Tubes with organism and medium with solvent were used as controls. These tubes were kept for incubation at 37°C for 24 hrs. Most of the compounds under study exhibited total inhibition of the test cultures within 24 hours of incubation. The tube containing compounds showing inhibition (antimicrobial activity) was clear and the tube which was kept as control where no compound was added showed growth. Therefore, for all the antibacterial screenings, the concentrations of 0.002 M, 0.004, 0.006, 0.008 and 0.01M of 1(4-aminophenyl)-2(p-chlorophenyl thiocarbamido)-1-ethanol used, which is in the range of the substance to be used as antibiotic.

2.4 Disc diffusion method

Every time fresh sterile nutrient agar medium was prepared. The proceedings were carried out aseptically. In each sterile Petridis 15-20 ml of molten medium was added. Simultaneously 0.05-0.1 ml (approx. 2-3 drops) of 24 hours fresh diluted culture of organism under study was added to each Petri plate. The nutrient broth culture and nutrient agar media were mixed thoroughly by rotatory motion of agar plate on a plane surface. It was allowed to solidify at room temperature. Then sterilized Whitman filter paper No. 1 discs (6 mm diameter) thoroughly moistened with the same concentration of each of the compound were placed on the surface of the plate. Disc moistened with ethanol was used as control. They were allowed to diffuse in the media and then the plates were incubated at 37°C for 24 hrs. The diameter of the zones of inhibition was observed.

II. RESULTS AND DISCUSSION

Newly synthesized 1(4-aminophenyl)-2(p-chlorophenyl thiocarbamido)-1-ethanol molecule was studied for their antimicrobial activities. All the pathogens tested during analysis are human pathogens. The activities of compounds were tested against all the pathogens by disc diffusion method. Anti-bacterial activity of 1(4-aminophenyl)-2(p-chlorophenyl thiocarbamido)-1-ethanol against gram positive and gram negative pathogens respectively shown in Table-1 and Table-2.

Table-1: Zone of Inhibition of 1(4-aminophenyl)-2(p-chlorophenyl thiocarbamido)-1-ethanol in mm for Gram-positive and Gram-negative pathogenic bacteria's

Conc. M	<i>Staphylococcus aureus</i> ,	<i>Escherichia coli</i>	<i>Streptococcus pyogenes</i>	<i>Proteus vulgaris</i>
0.01	15	18	10	15
0.008	12	14	12	13
0.006	10	09	08	--
0.004	11	10	09	08
0.002	08	08	--	07

All the organisms studied are human pathogens; from the resultant data reveals that the synthesized compound showed remarkable and considerable antimicrobial activities. Here zone of inhibition decreases along with decreasing concentration for 0.01M to 0.002M. Tables-1 reveals that, 1(4-aminophenyl)-2(p-chlorophenyl thiocarbamido)-1-ethanol shows high zone of inhibition against *Staphylococcus aureus*, *Escherichia coli* and *Proteus vulgaris* while weak zone of inhibition found against *Staphylococcus pyogenes*. Wherein *Staphylococcus pyogenes* and *Proteus vulgaris* does not show zone of inhibition at 0.002 N and 0.006 M concentration respectively.

III. CONCLUSION

In present work found investigated about antimicrobial activity against various pathogenic bacteria at 0.002M to 0.01M concentrations. presently 1(4-aminophenyl)-2(p-chlorophenyl thiocarbamido)-1-ethanol reveals that remarkable and considerable antibacterial activity. Specially it shows remarkable antibacterial activity against *Escherichia coli* (causes diarrhea) and *Staphylococcus aureus* (causes pus formation) and *Proteus vulgaris* (wound and urinary tract infections) while weakly active against *Streptococcus pyogenes*. so these molecules can be used as alternative for the treatment of diseases caused by the above mentioned pathogens only if they do not have toxic and other side effects after the details study. The potency of the drug is increased due to substitution.

REFERENCES

- [1] Arslan, H.; Kulcu, N.; Florke, U. 2003. Synthesis and characterization of copper(II), nickel(II) and cobalt(II) complexes with novel thiourea derivatives. *Transit. Metal Chem.* 28, 816-819.
- [2] Mansuroglu, D.S.; Arslan, H.; Florke, U.; Kulcu, N. 2008. Synthesis and characterization of nickel and copper complexes with 2,2-diphenyl-N-(alkyl(aryl)carbamothioyl)acetamide: The crystal structures of HL1 and cis-[Ni(L-1)(2)]. *J. Coord. Chem.* 61, 3134-3146.
- [3] Ozer, C.K.; Arslan, H.; VanDerveer, D.; Binzet, G. 2009. Synthesis and characterization of N- (alkyl(aryl)) carbamothioyl)cyclohexanecarboxamide derivatives and their Ni(II) and Cu(II) complexes. *J. Coord. Chem.*, 62, 266-276.
- [4] Binzet, G.; Arslan, H.; Florke, U.; Kulcu, N.; Duran, N. 2006. Synthesis, characterization and antimicrobial activities of transition metal complexes of N,N-dialkyl-N'-(2-chloro- benzoyl)thiourea derivatives. *J. Coord. Chem.*, 59, 1395-1406.
- [5] Ugur, D.; Arslan, H.; Kulcu, N. 2006. Synthesis, characterization and thermal behavior of 1,1-dialkyl- 3-(4-(3,3-dialkylthioureidocarbonyl)benzoyl)thiourea and its Cu(II), Ni(II), and Co(II) complexes. *Russ. J. Coord. Chem.*, 32, 669-675.
- [6] Emen, M.F.; Arslan, H.; Kulcu, N.; Florke, U.; Duran, N. 2005. Synthesis, characterization and antimicrobial activities of some metal complexes with N'-(2-chloro-benzoyl)thiourea ligands: The crystal structure of fac-[CoL3] and cis-[PdL2]. *Pol. J. Chem.*, 79, 1615-1626.
- [7] Arslan, H.; Florke, U.; Kulcu, N.; Emen, M.F. 2006. Crystal structure and thermal behaviour of copper(II) and zinc(II) complexes with N-pyrrolidine-N'-(2-chloro-benzoyl)thiourea. *J. Coord. Chem.*, 59, 223-228.
- [8] Henderson, W.; Nicholson, B.K.; Dinger, M.B.; Bennett, R.L. 2002. Thiourea monoanion and dianion complexes of rhodium(III) and ruthenium(II). *Inorg. Chim. Acta*, 338, 210-218.
- [9] Sacht, C.; Datt, M.S.; Otto, S.; Roodt, A. 2000. Synthesis, characterisation and coordination chemistry of novel chiral N,N-dialkyl-N-menthyloxycarbonylthioureas. Crystal and molecular structures of N,N-diethyl-N-(-)-(3R)-menthyloxycarbonylthiourea and cis-(S,S)-[Pt(L)Cl(DMSO)] [where HL= N-(+)-(3R)-menthyloxycarbonyl-N'-morpholiniothiourea or N-benzoyl-N',N'-diethylthiourea]. *J. Chem. Soc., Dalton Trans.*, 24, 4579-4586.
- [10] Lipowska, M.; Hayes, B.L.; Hansen, L.; Taylor, A.; Marzilli, L.G. 1996. Rhenium(V) oxo complexes of novel N2S2 dithiourea (DTU) chelate ligands: Synthesis and structural characterization. *Inorg. Chem.*, 35, 4227-4231.
- [11] Zuckerman, R.L.; Bergman, R.G. 2000. Structural factors that influence the course of overall [2+2] cycloaddition reactions between imidozirconocene complexes and heterocumulenes. *Organometallics*, 19, 4795-4809.
- [12] Henderson, W.; Kemmitt, R.D.W.; Mason, S.; Moore, M.R.; Fawcett, J.; Russell, D.R. 1992. Thia-diazatrimethylenemethane and N,N',P-Triphenylphosphonothioic Diamide Complexes of Platinum(II). *J. Chem. Soc., Dalton Trans.*, 1, 59-66.
- [13] Yuan, Y.F.; Wang, J.T.; Gimeno, M.C.; Laguna, A.; Jones, P.G. 2001. Synthesis and characterisation of copper complexes with N-ferrocenoyl-N'(alkyl)thioureas. *Inorg. Chim. Acta.*, 324, 309- 317.
- [14] Zhang, Y.M.; Wei, T.B.; Xian, L.; Gao, L. M. 2004. An efficient synthesis of polymethylene-bis-aryl thiourea derivatives under the condition of phase-transfer catalysis. *Phosphorus Sulfur Silicon Relat. Elem.*, 179, 2007-2013.
- [15] Zhang, Y.M.; Wei, T.B.; Wang, X.C.; Yang, S.Y. 1998. Synthesis and biological activity of N-aryl-N'-carboxyalkyl thiourea derivatives. *Indian J. Chem. Sect B*, 37, 604-606.
- [16] Zhou, W. Q.; Li, B. L.; Zhu, L. M.; Ding, J. G.; Yong, Z.; Lu, L.; Yang, X. J., 2004. Structural and spectral studies on N-(4-chloro)benzoyl-N'-(4-tolyl)thiourea. *J. Mol. Struct.*, 690, 145-150.
- [17] Eweis, M.; Elkholy, S.S.; Elsabee, M.Z. 2006. Antifungal efficacy of chitosan and its thiourea derivatives upon the growth of some sugar-beet pathogens. *Int. J. Biol. Macromol.*, 38, 1-8.
- [18] Arslan, H.; Florke, U.; Kulcu, N. 2003. N'-(4-Chlorobenzoyl)-N,N-diphenylthiourea. *Acta Cryst. E*, 59, O641-O642.
- [19] Arslan, H.; Florke, U.; Kulcu, N. 2003. Synthesis, characterization, and crystal structure of 1-(4- chloro-benzoyl)-3-naphthalen-1-yl-thiourea. *J. Chem. Crystallogr.*, 33, 919-924.
- [20] Arslan, H.; Florke, U.; Kulcu, N. 2004. The crystal and molecular structure of 1-(biphenyl-4- carbonyl)-3-p-tolyl-thiourea. *Acta Chim. Slov.*, 51, 787-792.
- [21] Arslan, H.; Kulcu, N.; Florke, U. 2006. Normal coordinate analysis and crystal structure of N,N- dimethyl-N'-(2-chloro-benzoyl)thiourea. *Spectrochim. Acta, Part A*, 64, 1065-1071.
- [22] Arslan, H.; Florke, U.; Kulcu, N. 2007. Theoretical studies of molecular structure and vibrational spectra of O-ethyl

- benzoylthiocarbamate. *Spectrochim. Acta, Part A*, 67, 936-943.
- [23] Arslan, H.; Ozpozan, N.; Ozpozan, T. 1999. Thermal studies of p-toluidino-p-chlorophenylglyoxime and of some corresponding Ni(II), Cu(II) and Co(II) complexes. *Thermochim. Acta*, 329, 57-65.
- [24] Avsar, G.; Kulcu, N.; Arslan, H. 2002. Thermal behaviour of copper(II), nickel(II), cobalt(II) and palladium(II) complexes of N,N-dimethyl-N'-benzoylthiourea. *Turk. J. Chem.*, 26, 607- 615.
- [25] Ugur, D.; Florke, U.; Kulcu, N.; Arslan, H. 2003. 3-[4-(3,3-diethylthioureidocarbonyl)-benzoyl]-1,1- diethylthiourea. *Acta Cryst. E.*, 59, O1345-O1346.

