SYNTHESIS AND CHARACTERIZATION OF SEMICARABAZONE LIGAND.

Submitted in partial fulfilment of the requirements for the award of Bachelor of Science Degree in Chemistry

By:

A. ABISHAKE

Reg.No:38030001

B. SUGUMAR

Reg.No:38030017

DEPARTMENT OF CHEMISTRY

SCHOOL OF SCIENCE AND HUMANITIES

SATHYABAMA INSTITUTE OF SCIENCE AND TECHNOLOGY JEPPIAAR NAGAR, RAJIV GANDHI SALAI, CHENNAI – 600119.

TAMILNADU. MARCH 2021

SATHYABAMA

INSTITUTE OF SCIENCE AND TECHNOLOGY

(DEEMED TO BE UNIVERSITY)

Accredited with "A" grade by NAAC I 12B Status by UGC I Approved by AICTE

Jeppiaar Nagar, Rajiv Gandhi Salai, Chennai – 600 119

www.sathyabama.ac.in

DEPARTMENT OF CHEMISTRY

BONAFIDE CERTIFICATE

This is to certify that this Project Report is the bonafide work of B.Sugumar. (38030017) and A.Abishake (38030001) who carried out the project entitled **"SYNTHESIS AND CHARACTERIZATION OF SEMICARBAZONE LIGAND.** under my supervision from December 2020 to April 2021.

Guide

Dr. V. ROJA

Assistant Professor

Department of Chemistry

Head of the Department

Dr. J. KARTHIKEYAN Ph.D.,

Associate Professor

Department of Chemistry.

Submitted for Viva voce Examination held on_____

INTERNAL EXAMINER **EXTERNAL EXAMINER**

DECLARATION

We **A. ABISHAKE. and B. SUGUMAR**, hereby declare that the Project Report entitled **SYNTHESIS AND CHARACTERIZATION OF SEMICARBAZONE LIGAND.** done by us under the guidance of **Dr. V. ROJA MSc., M. Phil.** Assistant Professor Department of Chemistry, Sathyabama Institute of Science and Technology is submitted in partial fulfilment of the requirements for the award of Bachelor of Science degree in Chemistry.

DATE:

PLACE:

A. ABISHAKE.

B. SUGUMAR.

ACKNOWLEDGEMENT

I am pleased to acknowledge my sincere thanks to Board of Management of SATHYABAMA for their kind encouragement in doing this project and for completing it successfully. I am grateful to them.

I convey my thanks to Dr. M. Sundareswari, Dean, School of Science and Humanities and Dr. J. Karthikeyan, Head of the Department, Department of Chemistry for providing me necessary support and details at the right time during the progressive reviews.

I would like to express my sincere and deep sense of gratitude to my Project Guide, Dr. V . ROJA. for her valuable guidance, suggestions and constant encouragement which paved way for the successful completion of my project work.

I wish to express my thanks to all Teaching and Non-teaching staff members of the Department of Chemistry who were helpful in many ways for the completion of the project.

I take this opportunity to thank my family members and friends for their constant encouragement without which this assignment would not be possible.

A. ABISHAKE.

B. SUGUMAR.

ABSTRACT

A new semicarbazone derivative phenyl semicarbazone with the molecular formula $C_{19}H_{22}Cl_2N_4O$ is synthesized by using N,N-bis (2-chloro ethyl) aminobenzaldehyde. Semicarbazones are important compound obtained by condensation of semicarbazides with suitable aldehydes or ketones, semicarbazones are used as ligands as the cytotoxic agent. Synthesis of new semicarbazones always play a new role in many fields like chemical , agricultural and industrial. Semicarbazones are potent intermediates for the synthesis of pharmaceutical and bioactive materials and they are used in medicinal chemistry. The biological activities of semicarbazone are considered to be related to their ability to form chelates with metals. Semicarbazone ligands usually through their oxygen ,nitrogen, and sulphur donor atoms in their (N,S) bidentate form or (N,N,S or O,N,S) tridentate form, to form metallic complexes. The function al groups of the synthesized compound will identified by using FTIR Spectroscopy method at a range of 400-4000cm^{-1} . The quantitative analysis of the compound was identified by UV-VIS Spectroscopy.

KEYWORDS: Synthesis, characterization, phenylsemicarbazide, *N*,*N* bis (2-chloroethyl) aminobenzaldehyde, phenyl semicarbazone, UV spectrum FTIR spectrum.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF ABBREVIATIONS

RB – Round Bottom Flask

UV- Ultraviolet Visible Spectroscopy

IR- Infrared Spectroscopy

CHAPTER-1

1- INTRODUCTION

Semicarbazones are important compounds obtained by condensation of semicarbazides with suitable aldehyde or ketones. Semicarbazones have a considerable interest in the field of chemistry and biology due to their antibacterial, antifungal, antiviral and antiviral and antimicrobial activities through their binding to metals in semicarbazones usually behave as chelating ligands and react with metallic cations giving complexes. Semicarbazone ligands co-ordinate to transition metals through their oxygen, nitrogen and sulphur donor atoms in their (N,S) bidentate form or (N,N,S or O,N,S) tridenate form, it from metallic complexes, The synthesis of transition metal complexes with semicabazone ligand are important due to their pharmacological properties. Semicarbazones are compounds with versatile structural features and co-ordinate to the metal in both natural and anionic forms.

Semicarbzones used as ligand as the cytotoxic agent, spectrophotometric agents as well for the analysis of metal ions and in qualitative organic analysis of carbonyl compounds. The conversion of aldehydes and ketones into amine like derivative is an exothermic process and pH dependent reaction A variety of semicarbazone derivatives could be prepared is quantitative yields, by mixing stoichiometric amounts of respective semicabazides.

CHAPTER-2

REVIEW OF LITERATURE

2.1 HISTORY:

Semicarazones are an organic compound containing the unsaturated group C:N.NH.CO.NH_2 semicarbazones are classified as imine derivative because they are formed from the reaction of an aldehyde or ketone with the terminal –NH_2 group of semicarbazide. Which behaves very similarly to primary amines. Some semicarbazones, such as Nitrofurazone, and thiosemicarbazones are known to have anti-viral and anti-cancer activity, usually mediated through binding to copper or iron in cells. Many semicarbazones are crystalline solids, useful for the identification of the parent aldehyde/ketones by melting point analysis.

2.2 CONCEPT:

2.2.1: Semicarbazone and thiosemicarazone; their wide range of pharmacological profile and clinical application.

Heloisa Beraide (2004) in his semiarbazones and thiosemicarbazones, their wide pharmacological profile and clinical application paper get that semicarbazones exhibit target selectivity along with a wide pharmacological profile.

2.2.2: Synthesis and reducing power of assay methyl semicarbazone derivatives.

P.Yogeeswari *et.al*.,(2004) have explained a series of 3-chloro-2-methypheny substituted semicarbazones. For the anticonvulsant activities. It shows that the semicarbazone derivatives shared good anticonvulsant potency in the (sc/sty) screen.

2.2.3: Synthesis of 3-D chloro-2-methylphenyl substituted semicarbazone

M.Singhal *et.al*., (2014) Elsevier have reports the synthesis and reducing power assay of methyl semicarbazone derivatives, using methylphenyl semicarbazide compound and designed a now pharmacophore “chalcone semicarbazone by pharmacophore hybridization approach of drug design. In his, It was found hat methoxy and hydroxyl substituted chalcone

semicarbazone exhibited potent reducing power reducing power and unsubstituted compound showed less reducing potential.

2.2.4: Synthesis of novel pyrozole –phenyl semicarbazone derivatives.

Fateme *e*t.*al.,* (2021) have reported the “Synthesis of novel pyrazole –phenyl semicarbozone derivatives aspotential Alpha-glucosidase inhibitor; kinetics and molecular dynamics stimulation study, in which semicarbazone derivatives were designed synthesized and screened for in vitro α-glucosidase inhibitory activity. Molecular dynamic simulations explains the dynamic behavior and structural changes of the systems by calculation of (RMSD) Root mean square deviation and (RMSF) root mean square fluctuation.

2.2.5: Antituberculous activity of some aryl semicarbazone derivatives.

D. Srirm. *et*.,*al.,* (2004) have reported tthat he course of their work on the synthesis of their work, on the synthesis of new drugs for tuberculosis, they had identified Ni-C_4- acetamido phenyl) –N_4-(2-nitro benzylidene) Semicarbazone (1b) , which inhibited in the vitro mycobacterium, tuberculosis H_{37} Rv; 100% inhibited at 1.56µg/ml. Their published paper was first of its kind in which aryl semicarbazones were reported to possess antimicrobacterials potency greater tha ethionamide, ethabutol, ciprofioxalin and kanamycin.

2.2.6: Synthesis, spectral characterization and crystal structure of copper(ii) complexes of hydroxyaleto-phenone-N (4)-phenyl semicarbazone.

U.L. Kala. *et*,*al* (2006) in their published article reported that the six new copper(ii) complexes of 2-hydroxyacetophenon-N($_4$)-phenyl semicarbazone have been synthesized and physic-chemically characterized. The tridentate character of the semicarbazone is inferred from IR spectra. The metal-ligand bonding parameters evaluated showed strong in-plane σ and in-plan π-bonding. The structure of the compound, cul phen has been resolved single crystal X-ray diffraction studies. Their compound adopts a distorted square pyramidal geometry with a N_2O_2 core as the base.

2.2.7: Studies on the Mechanism of oxime and semicarbazone formation.

William P. Jencks in his article explains that, at neutral pH hydroxylamine and semicarbazide will react rapidly with a number of aldehydes and ketones to form addition compounds which lack the ultraviolet and infrared absorption of the original carbonyl compound. These addition compound undergo a slow acid catalyzedetehydration to form oxime or formation at acid pH

appears to be due to a nitrogen base on the carbonyl compound and is not dependent on general acid catalysis.

2.2.8: Microvave –assisted synthesis and bioevalution of some semicarbazone.

Laila Jafri. *et*.,*al* (2012) in their papers they explain that in continuation of their efforts in finding potential therapeutic agents, a variety of biologically siginificant semicarbazones were synthesized by the reaction of different carbonyl compounds with phenyl semicarbazides through microwave irradiation initially they studied 18 semicarbazones antimicrobial, antitumor and antioxidant potential. None of the tested compounds showed any antibacterial activity; however some compounds showed significant antifungal activity. Similarly all compounds showed antitumor activity when tested against tenors grown on potato dieses. The final results showed that the semicarbazones derived from 2-nitrobenxaldehyde and acetophenone were the most activity 2,2-diphenyl-1-picrylhydrazyl-9 (DPPH) free radical scavengers.

2.2.9: Synthesis and spectral characterization of cobalt(iii) complexes of *N*(4)-phenylsemicarbazone.

Binu Varghese *et*.*al*., (2019) have reported, an interesting series of five new cobalt complexes of 2-benzoylphrideine-*N*-4-phenyl semicarbazone (HL^1) and 2-acetylpyridine-*N*-4-phenyl semicarbazone (HL^2) had been synthesized and physic chemically characterized. Cobalt (iii) and various tridentate ligands from mainly mixed bis(ligand) complexes. However, their IR Spectrum of HL^1 and HL^2 indicates that in the solid state it remains in keto forms. The IR spectra of complexes do not show any intense adsorption bonds around 1698cm^{-1} and 1683cm^{-1} due to the carbonyl stretching of the semicarbazone moiety. This shows that in solution, It tautomerises to the enol from and co-ordinates to the metal in the enolate from.

2.2.10: Synthesis and antimicrobial activity of semicarbazone and thiosemicarbazone derivative.

Renala. B *et*.,*al* (2007) have reported that seventeen semicarbazne and thiosemicarbazone derivatives were prepared and tested in vitro against a chloroquine resistant strain of plasmodium falciparum (w_2) to evaluate their antiplasmodial potential. In that three thiosemicarbazones were found to be active against the parasite and non-toxic to human peripheral blood mononuclear cells (PBMC). The thiosemicarbazone was able to reduce the

parasitaemia by 61% on 7 day after the infection with out any sign of toxicity to the animals. These in vitro and in vivo results made an interesting lead for further development.

2.3 Applications of Semicarbazone:

Semicarbazone plays an essential role in agriculture, pharmaceutical and industrial chemistry and they are used as catalysts in various biological systems, polymers and dyes, besides some uses antifertility and enzymatic agents. Lipophilicity, which controls the rate of entry in to the cell is modified by coordination.

Co-ordination may lead to significant reduction of drug –resistance.

Semicarbazones also used as spectrophotometric agents as well for the analysis of metal ions and are frequently used in the qualitative organic analysis of carbonyl compounds.

ANTI-FUNGAL AND ANTI-BACTERIAL ACTIVITY:

Microbial resistance towards drug creates a very serious problem since last 3 decades because of the development of resistance many drug are now useless which were very effective (coher 1992:Cunha 1998) The toxic effect produced by these anti-biotic is also reducing their significance. So for the need for a anti-microbial is always being there.

ANTI CANCER ACTIVITY:

Semicarbazones are also used is the treatment of cancer against EAC(Enrlich Ascites Carcinoma) The EAC cells are experimental tunormodels used worldwide in cancer research.

Semicarbazones are crystalline solids. Useful for the identification of the parent aldehydes/ketones by melting point analysis.

Semicarbazone in medicinal and pharmacy ,Application in synthesis and chemical analysis , Application in Co-ordination chemistry,

CHAPTER -3

AIM AND SCOPE OF THE PROJECT INVESTIGATION:

The aim of the project is to synthesis and characterization of the semicarbazone ligand. Basically semicarbazone are used in various field mainly in chemical and biological field. Synthesis of new semicarbazone always play a new role in both fields like industrial, agricultural and medicinal. Semicarbazone are crystalline solids, useful for the identification parent aldehyde/ketones by melting point analysis. In today's decades the semicarbazones are used in treatment because they have anti-viral, antimicrobial , anti-cancer activities, usually mediated through binding copper or iron in cells. In future the semicarbazones will be one of the part in medicinal field for curing cancer.

CHAPTER-4

MATERIALS AND METHODS

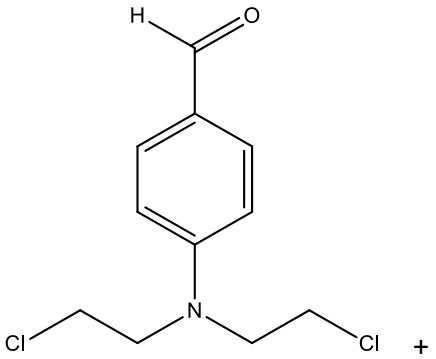
4.1 MATERIALS:

All chemicals used were of analytical reagent grade (AR) and the reagents were purchased from **Merck (INDIA)** and used as received . The meterials used were phenyl semicarbazide, N,N bis (2-chloroethyl) amino benzaldehyde and ethanol.

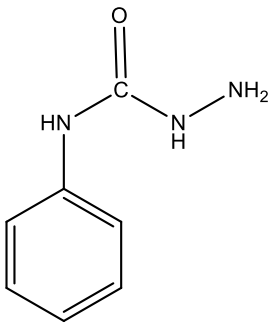
4.2 METHOD:

SYNTHESIS OF SEMICARBAZONE:

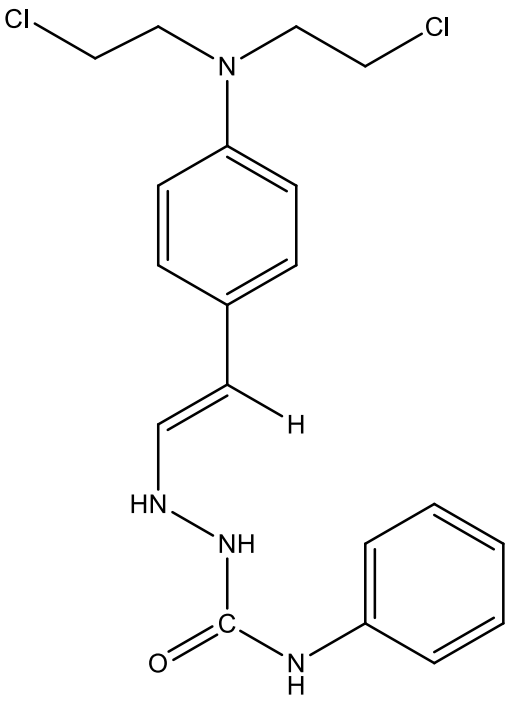
0.15g of phenylsemicarbozone (0.01mole) and 0.24g of N,N bis (2-chloroethyl) amino benzaldehyde were transferred to separate 100 ml beaker. Add (5-10ml) of ethanol to both the beakers and stir it until they completely dissolved. Now transfer both solution to the 250ml RB flask. The mixture was refluxed for 1-2 hrs and the solid product formed was separated by filtration, washed several times with 50% ethanol and the dried.



+



4-(bis(2-chloroethyl)amino)benzaldehyde *N*-pheylhydrazinecarboxamide



(E)-2-(4-bis(2-chloroethyl)amino)styryl)-*N*-phenylhydrazinecarbozamide.

Fig:1: Reaction for the synthesis of phenyl semicarbazone.

CHAPTER-5

RESULTS AND DISCUSSION

5.1 UV- VIS SPECTROSCOPY DATA FOR SEMICARBAZONE

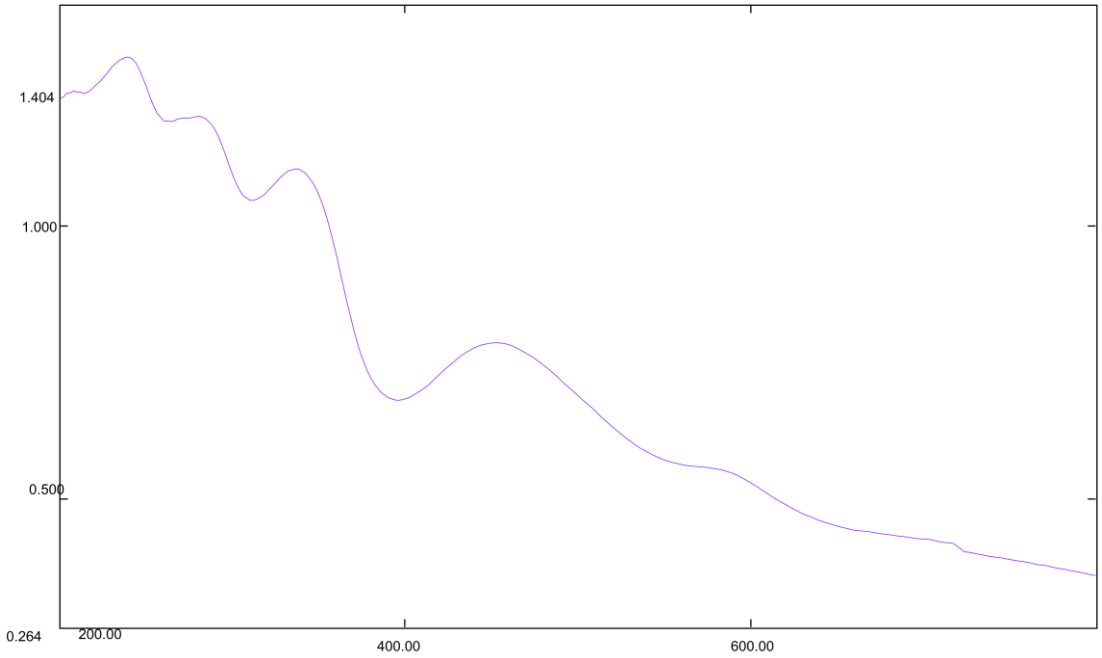
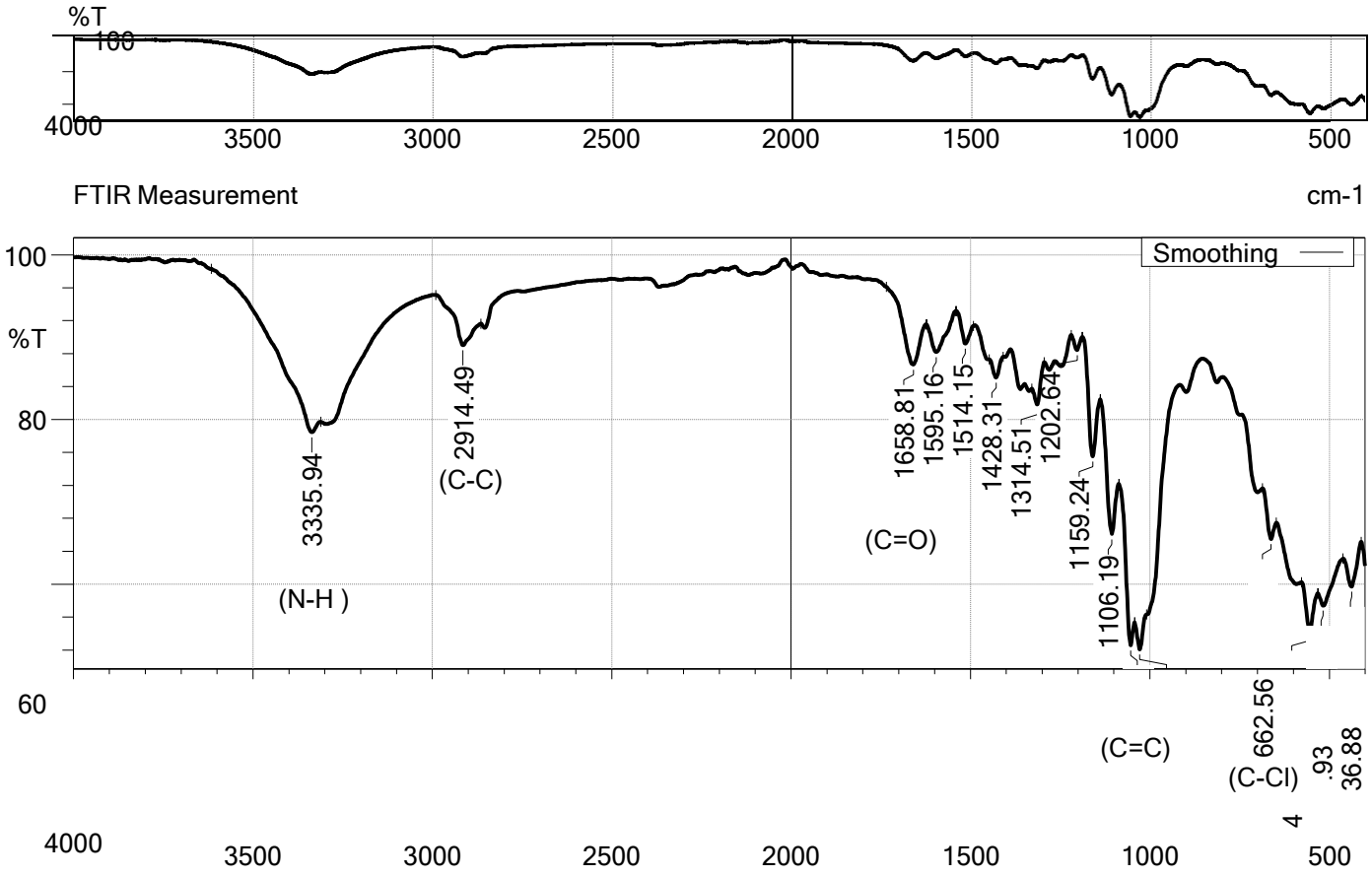


Fig:2: UV-Visible spectrum of phenyl semicarbazone.

The UV-Visible spectroscopy refers to the adsorption or reflectance spectroscopy used for the quantitative determination of different analytes. The UV-Visible spectra of the compound shows the maximum adsorption peaks at 400nm. This maximum adsorption of phenyl semicarbazone was assigned to the(n- π*) transition. The UV-Visible spectrum to phenyl semicarbazone is shown in *Fig*:*3*.

5.2 FTIR DATA FOR SEMICARBAZONE:



:

Fig3: FTIR-Spectrum of phenyl semicarbazone

The FTIR spectrum analysis of the semicarbazone was performed in the range 400-4000cm^{-1}. The is shown in figure 3 depicts the spectrum. FTIR spectroscopy is a powerful tool for the identifying functional groups and determining the molecular structure of a newly synthesized compound. The chemical structure of the phenyl semicarbazone was conformed by the analysis of IR spectrum which revealed the presence of various functional groups.

TABLE:**1**

Observed IR spectral data and assignment in the range 4000-400cm^{-1}

Bond Type	Observed frequency for phenyl semicarbazone
-N-H-stretching	3335.94
-C-C-stretching	2914.48
-C=O-stretching	1658.81
-C=O-stretching	1105.11
-C-Cl-stretching	662.56

CHAPTER 6

SUMMARY AND CONCLUSION

Semicarbazones are important compounds obtained by condensation of semicarbazides with suitable aldehyde or ketones. Semicarbazone ligands co-ordinate to transition metals through their oxygen,nitrogen and sulphur donar atoms in their (N,S) bidentate from, or tridenate form, to from naturals complexes.

Semicarbazones also used as spectrophotometric agents as well as for the analysis of metal ions. Synthesis of new semicarbazones always plays a new role in fields like industrial, agricultural, and medicinal. In future the semicarbazones

will be one of part in medicinal field for curing cancer . A new semicarbazone derivative phenylsemicarbazone with the molecular formula $C_{12}H_{22}Cl_2N_4O$ is synthesized by using N,N-bis(2-chloroethyl) aminobenzaldehyde from the collected data of IR the ranges performed from 400-4000cm^{-1}. Similarly the UV-Visible spectra of the compounds shows the maximum adsorption peak at 400nm.

CHAPTER-7

7. REFERENCE:

1. LEVEILLE,J,etal. Characterzation of Tc – 99m L,L –ECD. for brain profusion imaging, part-2 ,Biodistribution and brain imaging in human, J. Nucl. Medical. 30 (1989) (1892—1901)
2. PILLAI.M.R.A .etal. Radiochemical studies of technetium complex of tetradentate amine phenols, Appl. Radiat. Isot 41(1990) 557—561
3. ESHIMA ,B. Wral. Tc—99m Renal tubular function agents, currents status, seminar. Nucl. Med. XX(1990) 28--40
4. Shikn K.A, Baser MA, Mde Na, Asian journal of chemistry 2001; 13:496
5. Karia FD, Parsania Ph. Synthesis, biologial and thermal properties of schiff bases of biophenol, C.A Asian Journals of chemistry 1999: 11(3) 991-995
6. Sridhar SK, Pandaya Sn, De deroq E. Bollettino chimico Farmaceutico 2001: 140, 302 Pmid: 11680082
7. DRAGANA DEKANSKI etal., High antioxidative potential and low toxic effects of selenosemicarbazone metal complexes . J. Serb. Chem. Soc. 78 (10) 1503–1512 (2013).
8. Chiara P etal., New approach towards the synthesis of selenoSemicarbazone, useful compounds for Chagas' disease .euro. J.of Chem109 107-113.

9. Filipovi etal ., Biological activity of two isomeric N-hetero aromatic selenoSemicarbazone and their metal complexes Monatsh Chem (2014) 145:1089–1099
10. Dilworth J.R , Peach, J.M., Heslop , J.M Dennelly S.P Compunds for imaging an therapy, OS 201, 0098353 (2011)
11. Brown A.V crouse, G.D , Saparks, T.c Mc leoan C.t… Rigsbec , E.M Lamber, W.T ., Niyaz Y.M , Pesidual compositions, 2012.
12. Danter, W.R Inhibitor compounds and cancer treatment methods, Os 2010001540 (2010)
13. Dorgan HN, DURAN A, Yemini E. Synthesis and anti-bacterial activity of 1-(3-hydroxy-2- naphthoyl)-4-subsitutedthiosemicarbazides. Drug metabol drug ineract1999; 15:187-95.
14. Singal M, Paul A. Anti-bacterial evaluation of synthesized methyl semicarbazone derivative, int jPharm Sci Res 2011 a; 2: 2602-04.
15. Pandeya SN, Yogeeswari P, Thirumurugan. Antitubercular activity of arylsemicarbazone derivative. Bioorg Med ChemLet 2000; 14: 3923-24.
16. Singhal M, Paul A. Synthesis, characterization and Anti-pyretic evaluation of some Novel Chalconeswmicarbazone derivative. Res J Pharmaco 2011c: 5: 47-52.
17. Singh HP, Chauhan CS, Pandeya SN, Sharma CS, Srivastava *et al*., 2010. Synthesis, analgesic and Anti-inflammatory activity of semicarbazones. Euro J Med Chem 2000;35:879-86.
18. Sriram D, Yogeeswari P, Thirumurugan. Antitubercular activity of arylsemicarazone derivative, Bioorg Med Chemett 2000; 14:3923-24.
19. Singhal M, Paul A. Anti-ozidant activity of synthesized methyl semicarbazone derivative by DPPH scavenging assay. Global J Pharmacol 2011b;60-66.
20. Wang SX, Zhang FJ, Li,YL, Feng QP. Syntheisis, Characterization and anti-bacterial activity of tranition metal complexes with 5-Hydroxy-7,4'-Dimethoxyflavone.

21. Yuntao Zhou, Irene Piergentili, Jennifer Hong, Michelle P. van der Helm, Mariano Macchione, Yao Li, Rienk Eelkema, Sanzhong Luo. Indoline Catalyzed Acylhydrazone/Oxime Condensation under Neutral Aqueous

Conditions. *Organic Letters* **2020,** *22* (15) , 6035-6040. https://doi.org/10.1021/acs.orglett.0c02128

22.Meixia He, Jean-Marie Lehn. Time-Dependent Switching of Constitutional Dynamic Libraries and Networks from Kinetic to Thermodynamic Distributions. *Journal of the American Chemical Society* **2019,** *141* (46) , 18560-18569. https://doi.org/10.1021/jacs.9b09395

23.Mohini Kamra, Parikshit Moitra, Devasena Ponnalagu, Anjali A. Karande, Santanu Bhattacharya. New Water-Soluble Oxyamino Chitosans as Biocompatible Vectors for Efficacious Anticancer Therapy via Co-Delivery of Gene and Drug. *ACS Applied Materials & Interfaces* **2019,** *11* (41) , 37442-37460. https://doi.org/10.1021/acsami.9b09485

24.Junhao Huang, Saeed Zajforoushan Moghaddam, Esben Thormann. Structural Investigation of a Self-Cross-Linked Chitosan/Alginate Dialdehyde Multilayered Film with in Situ QCM-D and Spectroscopic Ellipsometry. *ACS Omega* **2019,** *4* (1) , 2019-2029. https://doi.org/10.1021/acsomega.8b03145

25.Peng Wang, Guohua Deng, Lanying Zhou, Zhiyong Li, and Yongming Chen . Ultrastretchable, Self-Healable Hydrogels Based on Dynamic Covalent Bonding and Triblock Copolymer Micellization. *ACS Macro Letters* **2017,** *6* (8) , 881-886. https://doi.org/10.1021/acsmacrolett.7b00519

26.Carlo Pifferi, Gour Chand Daskhan, Michele Fiore, Tze Chieh Shiao, René Roy, and Olivier Renaudet . Aminooxylated Carbohydrates: Synthesis and Applications. *Chemical Reviews* **2017,** *117* (15) , 9839-9873. https://doi.org/10.1021/acs.chemrev.6b00733

27.Dominik K. Kölmel and Eric T. Kool . Oximes and Hydrazones in Bioconjugation: Mechanism and Catalysis. *Chemical Reviews* **2017,** *117* (15) , 10358-10376. https://doi.org/10.1021/acs.chemrev.7b00090

28.Ibrahim Yildiz . A DFT Approach to the Mechanistic Study of Hydrozone Hydrolysis. *The Journal of Physical Chemistry A* **2016,** *120* (20) , 3683-3692. https://doi.org/10.1021/acs.jpca.6b02882

29.Naiqian Zhan, Goutam Palui, Jan-Philip Merkl, and Hedi Mattoussi . Bio-orthogonal Coupling as a Means of Quantifying the Ligand Density on Hydrophilic Quantum Dots. *Journal of the American Chemical Society* **2016,** *138* (9) , 3190-3201. https://doi.org/10.1021/jacs.5b13574

30.Daniel P. Ferris, Paul R. McGonigal, Leah S. Witus, Takatoshi Kawaji, Mohammed M. Algaradah, Ahmed R. Alnajadah, Majed S. Nassar, and J. Fraser Stoddart . Oxime Ligation on the Surface of Mesoporous Silica Nanoparticles. *Organic Letters* **2015,** *17*