



Received on 07 March, 2014; received in revised form, 18 April, 2014; accepted, 01 July, 2014; published 01 November, 2014

SYNTHESIS, SPECTRAL STUDIES AND ANTIMICROBIAL SCREENING OF SOME TRANSITION METAL COMPLEXES WITH SUBSTITUTED ACETOPHENONE THIOSEMICARBAZONE

Shyam Kumar Meena* and Meenakshai Jain

Department of Chemistry, Govt. P.G. College Dholpur, Rajasthan, India.

Department of Chemistry, University of Rajasthan, Jaipur, Rajasthan, India.

Keywords:

Synthesis, Spectral studies, Transition metal complexes, acetophenone thiosemicarbazone, Antibacterial activity.

Correspondence to Author:

Shyam Kumar Meena

Lecturer in Chemistry
Govt. P. G. College Dholpur
Rajasthan, 328001, India


E-mail:

shyammeena_1984@yahoo.co.in

ABSTRACT: Complexes of Fe, Cu and Zn have been prepared by reacting metal chloride/sulphate with p-hydroxyacetophenone thiosemicarbazone, p-fluoroacetophenone thiosemicarbazone, p-bromoacetophenone thiosemicarbazone as ligands and their complexes were screened for their IR, NMR, and antifungal and antibacterial studies. Acetophenone thiosemicarbazone ligands were prepared by the reaction of substituted acetophenone with thiosemicarbazone in the presence of hot ethanol. All the transition-ligands 1:2 complexes have been isolated in the solid state, are stable in air, and characterized on the basis of their elemental and spectral data. They were found to be active against influenza, protozoa, small pox, and certain kinds of tumor. Their metal complexes were used, in various biological systems, polymers, dyes, anti-inflammatory, analgesic and anti-oxidative action. The Schiff bases and their metal complexes were used in various biological activities such as antimicrobial, antifungal, antiviral, insecticides, and antitumor activity.

INTRODUCTION: The Schiff's base and their metal chelates is effective anticancer, antitumor, anti tuberculosis, antipyretic agent as well as anti fertility. Schiff's base possess industrial application as catalysts, dyes, fiber, perfumes an aesthetic, plant growth inhibitors cosmetics corrosion inhibitors, oxygen absorbents, polymers, lubricating agents, for removing metal impurities of oil and drying accelerators.¹⁻⁷

The metal complexes with Schiff's base derived from chalcone and thiosemicarbazone have been extensively studied and have exhibited medicinal properties⁸. Copper (II) complexes have found possible medicinal uses in the treatment of many diseases including cancer.⁹ Semicarbazone of various transition metals have been investigated owing to their coordination capability and pharmaceutical activity¹⁰⁻¹². Schiff's bases make them more effective in attaining high coordination structure¹³. Since Domagk's original report¹⁴ on the anti-tubercular activity of thiosemicarbazones, the number of papers on the pharmacology of these compounds has expanded dramatically. They have also been found to be active against influenza¹⁵, small pox¹⁶, and certain kinds of tumor¹⁷ and have

<p>QUICK RESPONSE CODE</p> 	<p>DOI: 10.13040/IJPSR.0975-8232.5(11).4880-86</p> <hr/> <p>Article can be accessed online on: www.ijpsr.com</p>
<p>DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.5(11).4880-86</p>	

been suggested as possible pesticides and fungicides¹⁸. Their activity has frequently been thought to be their ability to chelate with tracer metal.

MATERIALS AND METHODS:

The transition metal complexes of substituted acetophenone thiosemicarbazone were derived from the reaction an aqueous solution of metal salt. Acetophenone thiosemicarbazone ligands were prepared by the reaction of substituted acetophenone with thiosemicarbazone in the presence of hot ethanol. All the transition-ligands 1:2 complexes have been isolated in the solid state, are stable in air, and characterized on the basis of their elemental and spectral data.

Thiosemicarbazone ligands behave as bidentate ligands by coordinating through the Sulfur of the isocyanides group and nitrogen of the cyanide residue. The acetophenone thiosemicarbazone ligands and their transition complexes have been screened for their IR, NMR, and antifungal and antibacterial studies.

Synthesis of substituted acetophenone thiosemicarbazones (2a-d) Table-1

P-Fluoroacetophenonethiosemicarbazone
P-Fluoroacetophenonethiosemicarbazone was prepared after the method of compaigne and Archer.¹⁹ F- Fluoroacetophenone (2.52 ml, 20 mmol) was dissolved in ethanol (50ml) in a round bottomed flask and heated on a water bath for 5-10 minutes. This hot solution was treated with a hot ethanolic solution (50 ml) of thiosemicarbazone (1.80g, 20mmol) and refluxed for 4-5 hrs on water bath using reflux water condenser. The change in color of solution indicates the formation of P-Fluoroacetophenone thiosemicarbazone (2a-d). on cooling the reaction mixture the cream coloured product crystallized out which was filtered off under water suction and further recrystallized from absolute ethanol and finally dried over anhydrous cacl₂ in a vacuum desiccators.

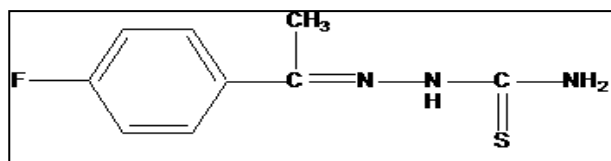


FIG: 1

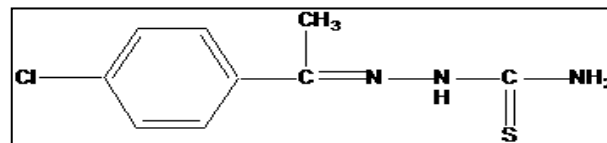


FIG: 2

Synthesis of 4-substituted aceto phenone thio semicarbazones metal complexes (3a-d):

Bis (F-Fluoroacetophenonethiosemicarbazone) iron (II)

P-Fluoroacetophenonethiosemicarbazone (1.816g, 8mmol) was dissolved in ethanol (20ml) and heated on a water bath. This solution was slowly treated with an aqueous solution of metal salt Feso₄.6H₂O (0.6076g, 4mmol) in 2:1 molar ratio with string. Reaction mixture was refluxed on water bath for 1-2 hrs and left overnight to yield the crystalline dark green coloured crystals, which was filtered off under suction washed with water till filtrate become colourless. The product was finally washed with dilute ethanol and dried over fused cacl₂ in vacuum desiccators.

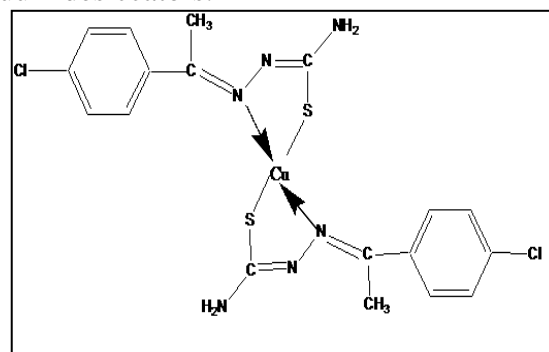


FIG: 3

BIS(PCHLOROACETOPHENONETHIOSEMICARBAZ ONE) CUPPER (II) (3A-D) TABLE-2

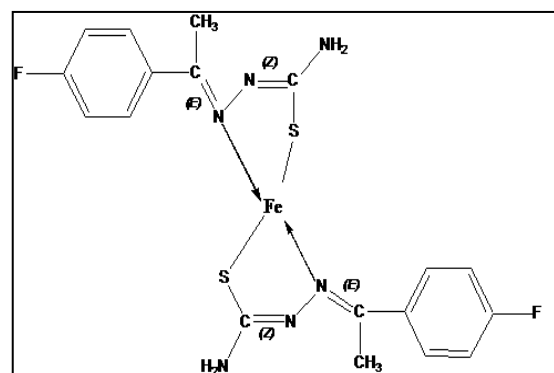


FIG: 4

BIS(PFLUOROACETOPHENONETHIOSEMICARBAZ ONE) IRON (II) (4A-D) TABLE-3

RESULTS AND DISCUSSION:

Substituted acetophenones

In the IR spectra of substituted acetophenone a sharp absorption band from 1780-1650 cm⁻¹ is

observed due to acetophenone $>C=O$ and at 1620 cm^{-1} due to $>C=C<$ stretching vibration.

Substituted acetophenonethiosemicarbazones

Formation of substituted acetophenones thiosemicarbazone was confirmed by the disappearance of absorption band from $1720\text{--}1650\text{ cm}^{-1}$ due to carbonyl group ($>C=O$) and appearance of new absorption bands from $3400\text{--}3350, 3320\text{--}2800,$ and $1200\text{--}1045\text{ cm}^{-1}$ assigned to $-NH_2$, $-NH$ and $>C=S$ stretching vibrations, respectively in their IR spectra. Similarly, in 1H NMR spectra an additional broad singlet at δ 2.85 ppm appears due to $-NH_2$ and a sharp singlet at δ 10.82 ppm due to $-NH-$ protons are observed which further support the formation of compounds. (2a-d).

Metal complexes of substituted acetophenone thiosemicarbazone

In the IR spectra of the ligands and complexes only selected absorption peaks are discussed, which are important for ascertaining the donor sites of ligands. In the IR spectra of metal complexes of substituted acetophenone-thiosemicarbazones the presence of absorption band at 3380 cm^{-1} due to $-NH_2$ (symmetric) and at 3380 cm^{-1} due to $-NH_2$ (asymmetric) modes remain almost unaltered. This clearly indicates the noninvolvement of this group in complexation reaction²⁰⁻²¹ but slight displacement of these frequencies is due to increased positive charge on nitrogen atom arising

from the donation of electron pair from sulfur of thioamide moiety which is involved in chelation²²⁻²³. Sharp absorption band from $3280\text{--}2850\text{ cm}^{-1}$ which was due to $NH-$ in ligands disappear in complexes indicating possible deprotonation on the β -nitrogen after complexation with metal ion²⁴⁻²⁷. A new absorption band in the complexes at $445\text{--}432\text{ cm}^{-1}$ due to $(M-N)$ confirm the metal nitrogen bond in the complexes²⁸⁻²⁹.

All compounds have been characterized on the basis of spectral (IR, NMR) studies and elemental analysis. IR spectra ($400\text{--}4000\text{ cm}^{-1}$) were recorded using a KBr. Central drug research institute (CDRI), Lucknow and Department Of Chemistry, University of Rajasthan, Jaipur. 1H NMR spectra were recorded on Bruker spectrometer (300 MHz) at CDRI, Lucknow using $CDCl_3/DMSO$ as solvent. TMS was taken as internal standard. C, H, N and S analysis of these compounds have been done using Coleman C and H analyzer. Melting points were determined in open glass capillaries and are uncorrected. The purity of compounds was checked by TLC using silica gel-G as adsorbent and visualization was accomplished by UV light or iodine adsorption.

All compounds are crystalline dark coloured solids, have fairly high melting points and are sparingly soluble in common organic solvents and are insoluble in water.

TABLE 1: ANALYTICAL AND PHYSICAL DATA OF SUBSTITUTED ACETOPHENONETHIOSEMICARBAZONES [Y-AR-C(CH₃)=N-NH-CS-NH₂]

Comp.	Y	Mol. formula	colour	Mol. Wt.	m.p.	yield	Elemental analysis % (calcd.) C H N S
2a	H	C ₉ H ₁₁ N ₃ S	Green	193	170	90	55.93,5.74,21.74,16.59
2b	4-F	C ₉ H ₁₀ FN ₃ S	Cream	211	150	85	51.17,4.77,19.89,15.18
2c	4-Cl	C ₉ H ₁₀ ClN ₃ S	Brown	227	125	82	47.47,4.43,18.45,14.08
2d	4-Br	C ₉ H ₁₀ BrN ₃ S	Cream	272	185	86	39.72,3.70,15.44,11.78

TABLE 2: ANALYTICAL AND PHYSICAL DATA OF CU (II) COMPLEXES OF SUBSTITUTED ACETOPHENONETHIOSEMICARBAZONE [Y-AR-C(CH₃)=N-NH-CS-NH₂]₂ CU (II)

Comp.	Y	Mol. formula	colour	Mol. Wt.	m.p.	yield	Elemental analysis % (calcd.) C H N S
3a	H	C ₁₈ H ₂₀ N ₆ S ₂ Cu	Green	440	146	90	47.39,4.41,18.21,14.32
3b	4-F	C ₁₈ H ₁₈ F ₂ N ₆ S ₂ Cu	Cream	482	153	75	44.65,3.69,17.34,13.17
3c	4-Cl	C ₁₈ H ₁₈ Cl ₂ N ₆ S ₂ Cu	Brown	227	141	81	40.95,3.45,15.99,12.32
3d	4-Br	C ₁₈ H ₁₈ Br ₂ N ₆ S ₂ Cu	Cream	272	142	85	31.95,2.95,13.85,10.51

TABLE 3: ANALYTICAL AND PHYSICAL DATA OF FE (II) COMPLEXES OF SUBSTITUTED ACETOPHENONETHIOSEMICARBAZONE [Y-AR-C(CH₃)=N-NH-CS-NH₂]₂ FE (II)

Comp.	Y	Mol. formula	colour	Mol. Wt.	m.p.	yield	Elemental analysis % (calcd.) C H N S
4a	H	C ₁₈ H ₂₀ N ₆ S ₂ Fe	Grey	442	115	70	87.54,4.45,18.50,14.40

4b	4-F	C ₁₈ H ₁₈ F ₂ N ₆ S ₂ Fe	Grey	478	153	75	44.95,3.65,17.45,12.99
4c	4-Cl	C ₁₈ H ₁₈ Cl ₂ N ₆ S ₂ Fe	Brown	511	170	81	35.50,2.90,13.90,9.95
4d	4-Br	C ₁₈ H ₁₈ Br ₂ N ₆ S ₂ Fe	Cream	600	165	85	41.96,3.45,15.99,12.32

TABLE 4: CHARACTERISTIC IR SPECTRAL DATA OF SUBSTITUTED ACETOPHENONE THIOSEMICARBAZONE AND THEIR METAL COMPLEXES

Comp. No.	IR (KBr: ;max cm-1)									
	2	3	4	5	6	7	8	9	10	11
1	-NH ₂	>NH	Ar-H	>C=N	>C=C<	C-X	>C=S	C-S	N-N	M-N
2a	3320	3290	3010	6120	1450	-	1200	-	810	-
2b	3360	3280	3025	1605	1490	720	1150	-	840	-
2c	3410	3300	3045	1625	1456	560	1190	-	805	-
2d	3390	3265	3026	1620	1480	690	1160	-	845	-
3a	3320	-	3048	1604	1465	-	-	1130	865	440
3b	3310	-	3025	1620	1456	1070	-	1050	842	456
3c	3410	-	3014	1618	1472	650	-	1065	854	450
3d	3410	-	3026	1620	1495	745	-	1060	865	426
4a	3300	-	3025	1605	1450	-	-	1165	854	412
4b	3390	-	0310	1602	1460	1150	-	1085	825	410
4c	3385	-	3021	1604	1475	560	-	1065	862	460
4d	3400	-	3025	1624	1480	-	-	1150	845	440

TABLE 5: CHARACTERISTIC ¹H NMR SPECTRAL DATA OF SUBSTITUTED ACETOPHENONE THIOSEMICARBAZONE AND THEIR METAL COMPLEXES

Compd. No.	Mol. formula	¹ H NMR spectral data (δ,ppm)			
		Ar-H(m)	NH(br)	NH ₂ (s)	CH ₃ (b)
2b	C ₉ H ₁₀ FN ₃ S	7.6	7.0	2.1	0.9
2c	C ₉ H ₁₀ ClN ₃ S	7.3	7.0	2.1	0.9
2d	C ₉ H ₁₀ BrN ₃ S	7.5	7.5	2.0	0.9
3b	C ₁₈ H ₁₈ F ₂ N ₆ S ₂ Cu	6.6	-	2.2	2.1
3c	C ₁₈ H ₁₈ Cl ₂ N ₆ S ₂ Cu	7.6	-	2.1	2.0
3d	C ₁₈ H ₁₈ Br ₂ N ₆ S ₂ Cu	7.7	-	2.6	2.2
4b	C ₁₈ H ₁₈ F ₂ N ₆ S ₂ Fe	7.0	-	2.0	2.0
4c	C ₁₈ H ₁₈ Cl ₂ N ₆ S ₂ Fe	7.3	-	2.0	2.0
4d	C ₁₈ H ₁₈ Br ₂ N ₆ S ₂ Fe	7.5	-	2.0	2.0

BIO-EFFICACY: Some representative compounds were screened for their antibacterial and antifungal efficacy. Bis (F-Fluoroacetophenonethiosemicarbazone) iron (II)



FIG: 5 ANTIBACTERIAL SPECIEES-E.COLI



FIG: 6 ANTIBACTERIAL SPECIEES-STREPTOMYCES

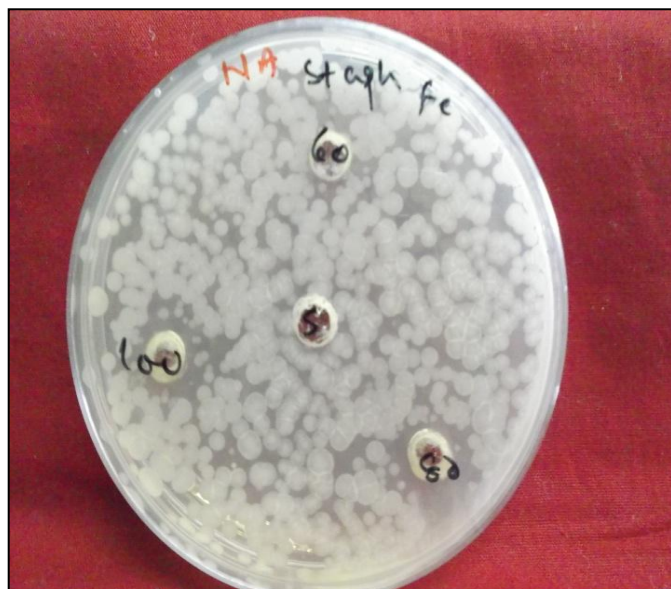


FIG:7 ANTIBACTERIAL SPECIEES-BACILLES CEREUS



FIG:8 ANTIBACTERIAL SPECIEES-STREPTOCOCCUS AUREUS



FIG: 9 ANTIFUNGAL SPECIES-FUSARIUM



FIG: 10 ANTIFUNGAL SPECIES-PENECILLUM



FIG: 11ANTIFUNGAL SPECIES- A.NIGER

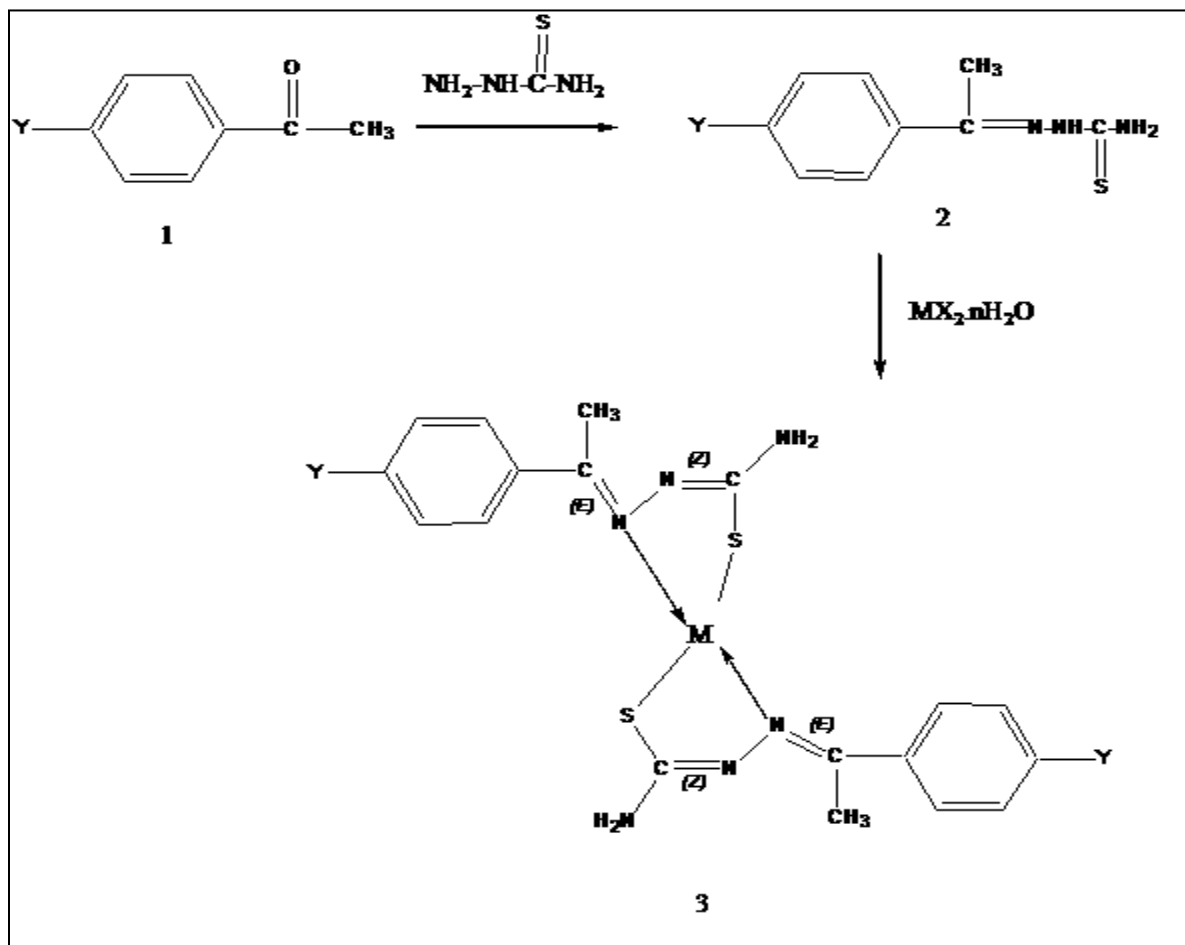


FIG: 12

ACKNOWLEDGEMENT: Authors are thankful to Head Department of Chemistry, University of Rajasthan, Jaipur for providing research facilities. Central Drug Research Institute (CDRI), Lucknow, Seminal Applied Science Pvt. Ltd Jaipur for providing research facilities.

REFERENCES:

1. Kumar Deveshk, "Application of metal complexes of Schiff base with special reference to thiosemicarbazone: a review" 2014,2,13.
2. Singh P. Vinod, Singh Shweta, Singh P. Divya , Tiwari K. , Mishra Monika . "Synthesis, spectroscopic (electronic, IR, NMR and ESR) and theoretical studies of transition metal complexes with some unsymmetrical Schiff bases" Journal of Molecular Structure, 2014, 71-78, 1058
3. Khoo Teng-Jin, Khaled bin break Mohammed, Crouse K.A., Ali A.M., Cowley A.R. , Watkin D.J. , Tarafder M.T.H. "Synthesis, characterization and biological activity of two Schiff base ligands and their nickel(II), copper(II), zinc(II) and cadmium(II) complexes derived from S-4-picolylidithiocarbamate and X-ray crystal structure of cadmium(II) complex derived from pyridine-2-carboxaldehyde" Inorganica Chimica Acta , 2014,413,68-76.
4. Fekri Roghayeh, Shaabani Behrooz, Synthesis and Characterization of Ni (II) Complex with Tridentate Ligand of Schiff's Bases of Salicylaldehyde with Thiocyanate Ligand , J. Appl. Environ. Biol. Sci.2013, 3(8), 75-78
5. Chohan Z. H. "Ni (II), Cu (II) and Zn (II) metal chelates with thiazole Schiff bases synthesis, characterization and bactericidal properties", Met.-Based Drugs, 1999; 6: 75-80.
6. Prakash Anant, Adhikari Devjani "Application of Schiff bases and their metalComplexes-A Review, International Journal of ChemTech Research, 2011, 3, 1891-1896.
7. Cohan Z. H. and Kausar S, "Synthesis, characterization and biological effect of anions on Co (II) and Ni (II) chelates of tridentate Schiff base", J. Chem. Soc. Pak., 2001; 23: 163-167.
8. Marisa, B.F, Franco B., Claudio C , Stéphanie D , Irène M.-B , Giorgio P , Elisabetta P , Silvana P. and Perialberto T., "Copper (II) and Cobalt (III) Pyridoxal Thiosemicarbazone Complexes with Nitroprusside as Counterion", J. Med. Chem., 2005; 48:1671-1675 .
9. Orvig C. and Abrahams M. J., "Biochemical and inorganic copper chemistry", Chem. Rev., 1999; 99: 2201.
10. Nadkarny V. V., Rao R. S., and Fernandes P. S., "Synthesis of a few acid hydrazides: sulfonyl hydrazides and their derivatives from 2-phenyl-1, 2, 3-triazole-4-carboxylic acid and [(4-nitrophenyl thio] acetic acid as antibacterial", J. Indian Chem. Soc., 1976; 53: 833-36.
11. Garg A., Tendon J. P., "Magnetic and spectroscopic studies of chromium (III) complexes of semicarbazones and thiosemicarbazones", Synth. React. Inorg. Met.-Org. Chem., 1990; 20: 707-15.
12. Oza C. k., Jain M., Jain N., Verma D., "Synthesis characterization, Antimicrobial, Activities, and structural studies of lanthanide (III) complexes with 1-(4-chloro phenyl)-3-(4-fluoro/hydroxyl phenyl) prop-2-en-1-thiosemicarbazone", Phosphorus, Sulfur Silicon Relat. Elem., 2010; 185: 377-386.
13. Mishra N. C., Mohapatra B. B. and Guru S., "Mixed ligand complexes of bis (ethylmalonato) cobalt (II), copper

- (II) and zinc (II) with nitrogen donor ligands”, *J. Indian Chem. Soc.*, 1980; 57: 552-3.
14. Domagk, G.; Behnisch, R.; Mietzsch, F.; Schmidt, H. “New compound *active neagaint tuberculosis bacilli in vitro*” *Naturwissenschaften*, 1946; 33: 315.
 15. Orlova N.,Aksenova V.A.,Selidovkin D.A.,Bogdanova N.S.,and Perkin G.N.,Syntheses and spectroscopic studies of potential antitumor copper (II) complexes with 5-phenylazo-3-methoxy salicylidene thiosemicarbazone and N⁴ substituted thiosemicarbazones,”*Russ.Pharm. Toxicol*, 1968,348.
 16. Bauter D J, Stvincent L., Kempe C.H., Downle A.W., “Prophylactic treatment of small pox contact with N-methylisatin betathiosemicarbazone (compound33T57, marboran)” *Lancet*, 1963; 2: 494-6.
 17. Petering, H. G., Bus Kirk, H. H., Underwood, G. E , “Antitumor action of 2-oxo-3-ethoxybutyraldehyde bis(thiosemicarbazone) and similar compounds”, *Cancer Research*, 1964; 24: 367-72.
 18. By Johnson, Charles W., Joyner, Joseph W., Perry, R. P, “The inhibitory effect of four thiosemicarbazones on *Cryptococcus neoformans* “, *Antibiotics and Chemotherapy* (Washington, D. C.), 1952; 2: 636-8.
 19. Compaigne E.E., Archer W.L., *J.Am.Chem.Soc.* 1952,74,5801.
 20. Parihari, R. K., Patel, R. K., Patel, R. N. “Synthetic and structural studies of the transition metal complexes of manganese-, cobalt- and zinc(II) with m-nitrobenzaldehyde thiosemicarbazone and some neutral ligands “,*Journal of the Indian Chemical Society*, 2000; 77(6): 289-290.
 21. Varshney A., Tandon J. P., Crowe, A. J, “Synthesis and structural studies of tin (II) complexes of semicarbazones and thiosemicarbazones”, *Polyhedron* 1986; 5(3): 739-42.
 22. Amita Singh, Lalita; Dhakarey, Rajesh; Saxena, G. C., “Magnetic and spectral behavior of semicarbazone derivatives of manganese (II), copper (II), iron (III) and chromium (III) and their antimicrobial screening “, *Journal of the Indian Chemical Society*, 1996; 73(7): 339-342.
 23. Mohanty, L. M., Mishra, R. C., Mohapatra, B. K., ‘Studies on hydrazones, semicarbazones, thiosemicarbazones and oximes as ligands. Part-I. Some divalent metal complexes of benzoin phenylhydrazone and thiosemicarbazone”, *Journal of the Indian Chemical Society*, 1995; 72(5): 311-13.
 24. Sengupta, S. K., Pandey, O. P., Srivastava, A. K., Srivastava, S. K.,”Synthesis and structural studies of mono(cyclopentadienyl)titanium(IV) derivatives of acetylferrocenyl thiosemicarbazones “, *Indian Journal of Chemistry, Section A: Inorganic, Bio-inorganic, Physical, Theoretical & Analytical Chemistry*, 1999; 38A(10): 1066-1069.
 25. Bhardwaj, N. C., Singh, R. V. “Penta- and hexacoordinated aluminum (III) complexes of thiosemicarbazones”,*Journal of the Indian Chemical Society* 1994; 71(1):35-8.
 26. Mishra, R. C., Mohapatra, B. K., Panda, D., “Studies on hydrazones, semicarbazones, thiosemicarbazones and oximes as ligands. Part VII: Some divalent metal complexes of benzalacetone thiosemicarbazone”, *Journal of the Indian Chemical Society*, 1983; 60(8): 782-3.
 27. Patil, M. S., Deore, H. O., Kulkarni, M. M., Shah, J. R, “Structural studies on nickel(II), cobalt(II), iron(II), copper(II), manganese(II), iron(III), chromium(III) and vanadyl(2+) chelates of 2-hydroxy-1-naphthaldehyde semicarbazone” *Journal of the Indian Chemical Society*, 1983; 60(9): 817-20.
 28. Speca A. N., Karayannis, N. M., Pytlewski, L. L., “Chromium (III) and iron (III) perchlorate chelates with the mono-N-oxides of 2, 2'-bipyridine and 1, 10-phenanthroline”, *Inorganica Chimica Acta*, 1974; 9(1): 87-93.
 29. Kaul B.B. and Pandeya K.B., “Synthesis and spectral studies of platinum metal complexes of benzoin thiosemicarbazone”, *Journal inorg. Nuclear chemistry*, 1977; 40:1035.

How to cite this article

Meena SK and Jain M: Synthesis, Spectral Studies and Antimicrobial Screening of Some Transition Metal Complexes with Substituted Acetophenone Thiosemicarbazone. *Int J Pharm Sci Res* 2014; 5(11): 4880-86.doi: 10.13040/IJPSR.0975-8232.5 (9).4880-86.

All © 2014 are reserved by International Journal of Pharmaceutical Sciences and Research. This Journal licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 3.0 Unported License.

This article can be downloaded to **ANDROID OS** based mobile. Scan QR Code using Code/Bar Scanner from your mobile. (Scanners are available on Google Playstore)