J. Chemtracks 23 (1&2) 33-38, 2021

Abstracted / Indexed in
A division of the American Chemical Society
Chemical Abstract U.S.A.

ISSN 0973-239X
CODEN:JCOHF7
IMPACT FACTOR : 4.950

Comparative Studies of the bioactive nature of some metal complexes of morpholine dithiocarbamates

Smita Chaturvedi and Vinod Kumar
Department of Chemistry, Agra College, Agra
Email : smitachat15@gmail.com ; vinodkchem@gmail.com

Manuscript received online 26 March 2018, Revised on 06 June 2018, accepted on 02 April 2019

Abstract: Some metal complexes of morpholine-dithiocarbamates were synthesized and characterized by various physico-chemical techniques (i.e. IR, Magnetic, Mass, TGA etc). After studying their structural aspect, which is not mentioned in the present piece of work, their bioactive characterization and their comparative bioactivity was determined by *in vitro* technique. The present work deals with the metal complexes (Na, Cu, Ni, Mn, Zn) of dithiocarbamates and their antifungal and antibacterial studies against (*Fusarium moniliforme*, *Aspergillus flaves*) and bacteria (*E. coli*, *Pseudomonas aeruginasa*, *Bacillus subtilis*, *staphylococcus aurous*).

(Keywords : Morpholine-dithiocarbamates, IR, Magnetic, Mass and TGA)

Introduction

Dithioacid complexes have been reported for a great number of metal ions and are used in biological system. Research[1-4] over the past quarter of century showed that they have profound effect on biological systems. These complexes plays a vital role in metabolic and toxicological function in biological system.

A large number of biological literature has been built up on the dithiocarbamates and a number of reviews have been published an their activity as fungides[5-8] and antibacterial[9-12].

The most important group of derivatives are the salt of methyl, diethyl and ethylene bis (dithio carbamic) acids. At present they are produced in various countries for use in agriculture to control plant disease under the trade name–Manab, Zinab, Ziram etc. The corresponding metal derivatives (dithiocarbamates) are obtained in quantitative yield by interaction of metal salt with soluble alkali-dithiocarbamates.

$$(R_2 - N - \overset{\overset{S}{\|}}{C} - S)_n M$$

M → Metal ions; Cu^{2+}, Zn^{2+}, Mn^{2+}, etc.
R = Alkyl or aryl group
n = Orcidation state of the metal.

Experimental

All the chemical used for synthesis and for biocidal studies are AR grade unless stated otherwise.

In the present work the result of the already synthesized and characterized metal morpholine dithiocarbamate-derivatives are investigated for their relative biocidal behavior and a comparative analysis of all the metal complexes and the ligand have been reported.

Selection of the microorganism used for the study

Before doing the individual investigation on fungi and bacteria, the question arises, that in the vast field of fungi and bacteria which one should be selected to perform the experiments. To solve this difficulty a random experiment was carried out. A metal complex of a the dithiocarbamates, (i.e., a Cu complex) was selected. Solutions of different concentrations, (i.e., 10,50, 100, 200 and 500 ppm) were prepared in appropriate

solvents. These solution were mixed with Czapeck's Dox agar medium and poured in a sterilized petridish in which a pinch of soil was taken. Control plate containing only one to two c.c.s of solvent were also prepared for comparison.

All these petridishes were kept in B.O.D. incubator at 28 $\pm 2^0$C for about 7 days with periodic observation. The results obtained are shown in the table given below:

Table : 1

S. No.	Microorganism	Concentration			
		Control	10 ppm	50 ppm	100 ppm
1	*Aspergillus flavus*	+	+	-	-
2	*A. fumigatus*	+	+	-	-
3	*A. sydowi*	+	+	-	-
4	*Penicillium citrinum*	+	+	-	-
5	*Alternaria alternata*	+	+	-	-
6	*Fusarium moniliforme*	+	+	-	-
7	*Bacillus subtilis*	+	+	-	-
8	*Pseudomonas aeruginosa*	+	+	-	-
9	*Escherichia coli*	+	+	-	-
10	*Sarcina leutia*	+	+	-	-
11	*Acrobactor aerogens*	+	+	-	-
12	*Micrococcus* sp.	+	+	-	-
13	*Staphylococcus aureus*	+	+	-	-

(+ & - indicate the growth and growth inhibition respectively)

From the data of the table it can be conveniently decided as to which of the microoganisms can be selected for detailed evaluation and decide the MIC (minimum inhibitory concentration) of the copper compound under test, which has been found to be 50 ppm, for testing the other complexes. The test solutions having concentration > 50 ppm were prepared.

The culture of the following available pathogenic fungi and bacteria were taken as test microorganism:

Fungi:

(i) *Fusarium moniliforme*
(ii) *Aspergillus Flavus*

Bacteria:

(i) *Eschierichia Coli*
(ii) *Psedomonas aeruginosa*
(iii) *Bacillus subtilis*
(iv) *Staphylococcus aureus.*

Methods of testing the biocidal activity of fungi:

(i) Agar Plate Technique:

The antifungal activity of dithiocarbamate and their selected metal complexes was studied against the selected fungi, by agar plate technique. The experimental procedure was more or less the same as applied in the case of soil, the main difference being the addition of a little amount of antibiotic in the Czepeck's Dox medium to prevent the unwanted bacterial growth. Before transferring the Czepeck's Dox medium containing the known concentrations 50, 100 & 200 ppm. of the complexes of dithiocarbamate under investigation (Cu^{2+}, Ni^{2+},Co^{2+}, Mn^{2+}, & Zn^{2+}), to the sterilized petridesh, about 5ml of spore suspension of the desired fungus was also added.

Result and Discussion:

The percentage inhibition (I) was calculated by measuring the diameter of the fungal colony grown in the control and test plates by the following expression given by vincent[12].

$$I = \frac{(C - T)x\ 100}{C}$$

where,
C = diameter of fungus colony in the control plate.
T = diameter of fungus colony in treated (teat) plate
I = percentage inhibition

The observation of diameter of fungal growth measured in mm. and claculated percentage inhibition (for metal complexes of dithiocarbamate) are given respectively in tables : 2 and 3.

Inferences on the basis of the observations collected in the tables are:

(i) The dithiocarbamate and their metal complexes are fungi-toxic and their activity increases as the concentration increases.
(ii) Metal complexes of dithiocarbamate show greater activity than that of the free ligands.
(iii) The growth inhibition capacity of the metal complexes of dithiocarbamate follow the order, for both the fungi is more or less the same: Zn > Cu > Mn > Ni > Co

These observations have indicated that metal complexes have manifold fungi toxicity compared to the free ligand.

The increased antifungal activities of Zn & Mn complexes may be attributed to the presence of chlorine atom[13] in the coordination sphere.

(2) Filter paper disc diffusion plate method:

The antibacterial activity of the selected complexes was studied against the selected bacteria with the help of this technique.

This method is also known as 'Paper disc plate method[14]. In this method sterilized whatmann no. 1 filter paper discs of 5 mm diameter were soaked in the solutions of different concentrations of complexes under investigation and placed carefully on the previously sterilized petridishes containing seeded (charged with the desired bacteria) nutrient agar medium. These plates were incubated under standard conditions (about 32^0C in BOD incubator) for 48 hours with periodic observations. The diameter of inhibition zone was measured after incubation period.

The result obtained in the case of the bacteria for the complexes of dithiocarbamate are more or less in agreement with the results obtained in the case of fungi. The data so recorded are given in the tables: 4.

In the antibacterial studies it is evident that metal complexes have grater activity than that of the free ligand. The increased activity of the metal chelates[15] in comparison to their constituent's metal and ligands is probably due to the following facts.

(i) By increasing the liposoluble nature of the biologically active ligand or the metal in the form of metal complex in comparison to the metal ion or the ligand molecule alone.

(ii) By replacement of the metal ion of the metal enzyme present in biological system with the foreign metal ion of the more liposoluble metal complex by way of tanschelation.

(iii) By the replacement of protein molecule form the metal enzyme by the foreign ligand of the more liposoluble metal ligand complex, thus rupturing the enzyme affecting the biological function.

(iv) Due to the combined activity effect of both ligands and the metal in the chelate or due to the more liposoluble nature of the coordinated metal ion forming a stable, neutral metal chelate.

However, among all the above possible factors the more rapid diffusion of the metal complex as a whole through the cell walls of the microorganisms may be one of the other important factors.

The active constituents may act on protein synthesis within the cell, effecting the biological processes[16].

Conclusion : The synthesized and characterized metal complexes of dithiocarbamates were analyzed for their bio active nature with the help of different established technique i.e. Agar plate method and fitter paper disc diffusion method; On the basis of these studies the trend for morpholine-dithiocarbamates metal complexes in both the fungi and as well as in the bacterial growth inhibition are. Zn > Mn > Ni > Co > Na

Table No. 2

COMPOUND	*Fusarium Monillforme**			*Aspergillus Flavus***		
	200 ppm	**100 ppm**	**50 ppm**	**200 ppm**	**100 ppm**	**50 ppm**
morpholine-dte	12	15	17	14	16	18
Cu	5	8	10	7	10	13
Ni	8	10	13	11	14	16
Co	9	10	12	10	14	15
Mn	6	8	11	8	11	14
Zn	5	9	10	7	12	13

- Diameter of fungus colony in control plate for *Fusarium moniliforme* = 21mm
- Diameter of fungus colony in control plate for *Aspergillus flavus* = 25mm
- morpholine-dithiocarbamates = Sodium morpholine dithiocarbamate

Table No. 3: Antifungal activity (%inhibition) of Morpholine-dto & its Metal derivatives.

COMPOUND	*Fusarium Monillforme**			*Aspergillus Flavus***		
	200 ppm	**100 ppm**	**50 ppm**	**200 ppm**	**100 ppm**	**50 ppm**
morpholine-dte	42.89	28.57	19.05	44.00	36.00	28.00
Cu	76.19	61.90	52.38	72.00	60.00	48.00
Ni	61.90	52.38	38.09	56.00	44.00	36.00
Co	57.14	52.38	42.86	60.00	44.00	40.00
Mn	71.43	61.90	47.62	68.00	56.00	44.00
Zn	76.19	57.14	52.38	72.00	52.00	40.00

Table No. 4
Diameter (mm) of the Zone formed Around the Disc in the test Plates for Morpholine-dtc & its Metal Derivatives (Antibacterial activity).

COMPOUND	*E. Coli*	*Pseudomonas aeruginosa*	*Bascillus subtilis*	*Staphylococcus aureus*
morpholine-dte	12	16	13	18
Cu	14	17	16	20
Ni	13	16	14	19
Mn	17	10	15	19
Co	15	16	17	18
Zn	18	17	19	20

morpholine-dtc = Sodium morpholine dithiocarbamate

References

1. O.P. Pandey, S.K. Sengupta and S.C. Tripathi, Indian J. Chem. *32(2)*, 145 (1987); Chem. Abst. *107*, 125858V (1987).
2. H. Martin, the Scientific principles of Crop Protection, *4th Ed.,* Edward Arnold ltd., London, 128 (1959).
3. Hafezeh Nabipour, Shahriar Ghammamy, Shahriar Ashuri, Zahra Shokri Aghbolaghc, J. Org. Chem *2*, 75-80, (2010).
4. Ahmet Cagri Karaburun, Zafer Asim Kaplancikli, Nalan Gundogdu-Karaburun, Fatih Demirci, Letters in Drug Design & Discovery *8 (9)*, 811-815, (2011).
5. Catherine Rafin, Etienne Veignei, Michel Sancholle, Denis Postel, Christophe Len, Pierre Villa, Gino Ronco, Journal of Agricultural and food Chemistry *48 (11)*, 5283-5287, (2000).
6. Christophe Len, Anne-S Boulogne-Merlot, Denis Postel, Gino Ronco, Pierre Villa, Christel Goubert, Eric Jeufrault, Bernard Mathon, Herve Simon, Journal of Agricultural and Food Chemistry *44 (9)*, 2856-2858, (1996).
7. H Nabipour, Sh Ghammamy, A Rahmani, Micro & Nano Leters *6 (4)*, 217-220, (2011).
8. Veenu Bala, Gopal Gupta, Vishnu L Sharma, Mini reviews in medicinal chemistry *14 (12)*, 1021-1032, (2014).
9. MK Bharty, RK Dani, P Nath, A Bharti, NK Singh, Om Prakash, Ranjan K Singh, RJ Butcher, Polyhedron *98*, 84-95, (2015).
10. Mahrokh Baghershiroudi, Kazem D Safa, Khosro Adibkia, Farzaneh Lotfipour, Synthetic Communications *48(3)*, 323-328, (2018).
11. N Manav, AK Mishra, NK Kaushik, Spectrochimica Acta Part A : Molucular and Biomolecular Spectroscopy *65 (1)*, 32-35, (2006).
12. J.M. Vincent, "Farmer's Bull., U.S.D.A. Inhabitors", Nature, *159*, 850 (1947).
13. J.R. Postgate, "Methods in Microbiology" Vol. I, J.R. Nooris and D.W. Ribbons, Academic press, London (1969).
14. H.H. Thornberry, "A paper disc plate method for the quantitative evaluation of fungicidal and bactericidal phytopathology", *60*, 1373 (1950).
15. F.P. Dwyer and D.P. Mellor, "Chelating Agents and Metal Chelates", Academic press, InC, 111, Fifth Avenue, New York, 42-43 (1964).
16. A. Kucers and N. MckBennett "The Use of Antibiotics A Comprehensive Review with Clinical Emphasis", 3rd Ed., p.19, William Heinemann Medical Books Ltd. London (1979).

An International Peer Reviewed Research Journal of Chemistry
Abstracted / Indexed in : Chemical Abstract U.S.A.
JC- 1434/2K21 (ISSN:0973-239X), INDIA
Journal Chemtracks Vol. 23 (1&2), 33-38, January to December 2021