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Antimicrobial studies of nickel(II) complexes derived from 5-chloro-2-hydroxy acetophenone N^4 methyl thiosemicarbazone

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ABSTRACT

A new series of novel metal complexes of Ni (II) 5-chloro 2-hydroxy acetophenone *N*(4) methyl thisemicarbazone with heterocyclic base adducts were synthesized and evaluated for antimicrobial activity against *Pseudomonas Putida, Escherichia Coli, Aspergillus Niger and Candida Albicans*. Antimicrobial activity was carried out at 10^{-3} and 10^{-4} M concentrations using Amphicilin and Bicip as standard drugs. Overall results indicated that the metal complexes are better antimicrobial agents as compared to their thiosemicarbazone i.e. ligand. Compound Ni.L.Phen showed better antimicrobial activity.

KEYWORDS

5-Chloro 2-hydroxy acetophenone;
Thiosemicarbazone;
Bioactive metal complexes;
Antimicrobial activity.

INTRODUCTION

In recent years, thiosemicarbazones and their transition metal complexes have been studied due to their wide pharmacological interest[1,2]. Among these transition metals, Ni (II) is recognized as an essential trace element for bacteria, plants, animals and humans. It has number of applications in industrial homogeneous catalysis[3].

Also the most promising areas in which thiosemicarbazone compounds are developed is their use against cancer[4-6]. The presence of metal ion in thiosemicarbazone complexes increases the activity or contributes to migrate the side effects of the organic parent compounds[7]. The main known effects related to their anticancer activity are reactive oxygen species (ROS) production[8], topoisomerase II inhibition[9], mitochondria disruption[10] and a multidrug resistance protein (MDRI) inhibition[11,12]. 3-aminopyridine-2-carboxaldehyde thiosemicarbazone has been developed as an anticancer drug and has in clinical phase II on several cancer types[13,14].

MATERIALS AND METHOD

The complex Ni.L.B (Where B, is heterocyclic base like pyridine, 2-2'-bipyridine, 1, 10 phenanthroline, α-picoline, β-picoline) was prepared by reported procedure[15] and on the basis of spectral and physicochemical characterization an expected structure for four and five coordinate complexes of Ni (II) 5-chloro 2-hydroxy acetophenone N^4 methyl thisemicarbazone with heterocyclic base adducts are shown below.

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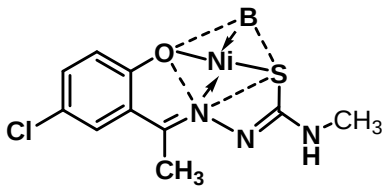
Expected structure



Where, B = Heterocyclic base; i.e. Pyridine, α-Picoline and β-Picoline.

Biological activity (Agar well diffusion method)

The antibacterial activity was determined using the agar well diffusion method. The prepared culture plates were inoculated with different bacteria and fungus by using plate method. Wells were made on the agar surface with 6mm cork borer. The solutions of complexes were poured into the well using sterile syringe. The plates were incubated at 37±2°C for 24 hours for bacterial activity and 48 hours for fungul activity. The plates were observed for the zone formation around the wells. The zone of inhibition was calculated by measuring the diameter of the inhibition zone around the well (in mm) including the well diameter. The activity was determined using two different concentrations 10^{-3} M and 10^{-4} M. In order to compare activity of the synthesized complexes, followed the same procedure with metal chlorides. The activity index was calculated to express the activity in comparison to the antibiotics[16]. The diameters of the inhibition zones for all tested compounds are presented in TABLE 1.

TABLE 1 : Antimicrobial activity of synthesized compounds

Compounds	Pseudomonas Putida		Escherichia Coli		Aspergillus Niger		Candida Albicans	
	10^{-3}M	10^{-4}M	10^{-3}M	10^{-4}M	10^{-3}M	10^{-4}M	10^{-3}M	10^{-4}M
L	12	10	9	8	12	10	10	9
Ni-L.H_2O	12	12	11	10	12	11	13	12
Ni-L-Py	12	12	15	12	13	12	15	14
Ni-L-Bipy	15	12	14	13	14	13	16	15
Ni-L- Phen	16	15	16	14	17	15	16	15
Ni-L α-Pico	12	11	12	11	11	08	12	11
Ni-L. β-Pico	12	11	13	11	11	10	13	08
Standard	34	36	26	31	18	19	17	20
$NiCl_2.6H_2O$	31	28	26	27	22	26	21	23

(Zone in mm, Std-Amphicilin,Bicip)

% Activity Index of Ni(II) complexes

Compound	Pseudomonas Putida		Escherichia Coli		Aspergillus Niger		Candida Albicans	
	10^{-3}M	10^{-4}M	10^{-3}M	10^{-4}M	10^{-3}M	10^{-4}M	10^{-3}M	10^{-4}M
L	35.29	27.78	34.62	25.81	66.67	52.63	58.82	45.00
Ni.L.H2O	35.29	30.56	42.31	32.26	66.67	57.89	76.47	60.00
Ni.L.Py	35.29	36.11	57.69	38.71	72.22	63.16	88.24	70.00
Ni.L.Bipy	44.12	38.89	53.85	41.94	77.78	68.42	64.12	75.00
Ni.L.Phen	47.06	41.67	61.54	45.16	94.44	78.95	94.12	75.00
Ni.L. α-Pico	35.29	30.56	46.15	35.38	61.11	42.11	70.59	55.00
Ni.L. β-Pico	35.29	27.76	50.00	35.38	61.11	52.63	76.47	40.00
Standard	100	100	100	100	100	100	100	100
$NiCl_2.6H_2O$	91.18	77.78	100	100	122.22	136.84	123.53	115

RESULTS AND DISCUSSION

On the basis of spectral, physicochemical characterization and keeping view of the preferred geometries, square planner for the four coordinate and a distorted square pyramidal for five coordinate complexes have been proposed. All the synthesized adducts have been studied their antimicrobial activity against *Pseudomonas Putida*, *Escherichia Coli*, *Aspergillus Niger* and

Candida Albicans, to find out structure activity relationship.

The results showed that the complexes showed better activity than free ligand. The adducts with bipyridine and 1,10 phenanthroline showed better activity. The most probable reason for this difference might be due to chelation which reduces the polarity of the central metal atom because of the partial sharing of its partial positive charge with donor groups and possible Π-electron delocalization within the whole chelating ring. As a result of this,the lipophilic nature of the central metal atom increases, which favours the permeation of the complexes through the lipid layer of the cell membrane[17]. Out of these seven compounds tested, Ni.L.phen was found more active against four cultures. The N^4 substituted 5-chloro 2-hydroxy acetophenone methyl thiosemicarbazone was found less active than its Ni(II) complex and adducts. Thus increase in coordination number from four to five in nickel complexes increases microbial activity[18]. In gram negative bacteria (*Pseudomonas Putida*, *Escherichia Coli*) the outer membrane. So it might not be ease for the complexes to diffuse inside the bacterial cell. The metal ion chloride salts were more effective than complexes. This shows free metal ions are more effective than binded in complexes.

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