

Biological Evolution of Metal Amide Complexes

Raja Ram, S.K. Yadav, H.S.Bhandari ,N. Bhojak*

Green Chemistry Research Centre (GCRC), P.G. Department of Chemistry, Govt. Dungar College (NAAC Grade-A), MGS University
Bikaner, Bikaner , Rajasthan, India.

ABSTRACT

The Present research work describes biological activity of amide group containing ligands and their Mn(II), Ni(II), Co(II) and Cu(II) complexes against *E.coli* and *S.aureus*. The standard disc diffusion method has been employed for investigations. The data obtained during study has been correlated for structure activity relationship and a trend has been pointed for a series of complexes.

Keywords : Antibacterial, Transition Metal

I. INTRODUCTION

Amide ligand possesses a wide range of bioactivities and their chemical, pharmacological applications have been extensively investigated. These emerged as important class of nitrogen and oxygen or sulfur ligands particularly for transition metal ions in the last twenty years. These transition metal complexes have a large variety of biological activities i.e. antifungal, antibacterial, antitumoral or antiviral. Many of these compounds possessed wide spectrum of medicinal properties, including activity against influenza, protozoa, smallpox, certain kinds of tumor, leprosy, bacterial and viral infections, psoriasis, rheumatism, tripanosomiasis, coccidiosis, malaria and as a pesticides and fungicides. These activities due to their ability to chelate trace metals and in few cases, it has been proved that metal ions enhance the biological activity of amide group containing ligands [1-8]. Bacterial infections often produce pain and inflammation. Chemotherapeutic, analgesic and anti-inflammatory drugs are prescribed simultaneously in normal practice. These complexes possessing all three activities i.e. anti-inflammatory, analgesic and antipyretic activities are not common. Anti-inflammatory, analgesic and antipyretic activities are known for some Pyridine and phenol derivatives [8-10]. These transition metal complexes of amide ligands are able to block cartilage destruction during the inflammatory process and thus are a promising class of anti-inflammatory compounds [11]. Manganese complexes have been screened against a number of pathogenic fungi and bacteria with most of them

showing better sensitivity than the ligands [12-14]. Complexes of Iron (III) have been synthesised by quinoline derivative and use in malaria treatment [15].

II. Scope of the Present research work

The investigations on antimicrobial activity of different types of compounds are not only useful for the development of new drugs but it is also essential to ascertain the toxic nature of the compound. In this research paper the biological activity in terms of their growth inhibition property on specific known bacterial of the four synthesized amide ligands and of their metal complexes with Mn (II), Ni (II), Co (II) and Cu (II) have evaluated by standard "disc diffusion" method. The bacterial subcultures of *E. coli* and *S. aureus* have been used as test organisms and all the samples are tested against these stains at different concentration.

III. Experimental

The evaluation of antimicrobial activities involved following general steps:

1. Treatment of glass apparatus and its sterilization

All the glass apparatus, including petridishes were cleaned with chromic acid followed by washing with distilled water. These were then sterilized by heating at 120°C in an oven fully wrapped in inert foil for 6-8 hours.

2. Preparation of the media and its sterilization.

Nutrient agar and Czapek Dox agar slants were used as culture media for bacterial cells and fungal spores respectively.

Composition of Nutrient agar medium is as;

Peptone	=	5g
Sodium chloride	=	5g
Beef extract	=	1.5g
Yeast extract	=	1.5g
Agar	=	15g
Distilled water	=	1000ml (pH=7.4±0.2)

Czapek Dox Agar medium was composed of;

Sodium nitrate	=	2g
Dipotassium hydrogen Phosphate	=	1g
Magnesium sulphate	=	0.05g
Potassium chloride	=	0.05g
Ferrous sulphate	=	0.01g
Sucrose	=	30.0g
Agar	=	15g
Distilled Water	=	1000ml (pH=7.3±0.2)

For the preparation of media, all the ingredients except agar were dissolved in half of the water with gentle warming wherever required. In the other half of distilled water, agar was dissolved by heating with constant stirring. The two solutions were mixed and heated to make a homogenous solution. The one liter solution of each media was filtered through cotton and a clear solution was obtained. This was then sterilized properly plugged in a conical flask by autoclaving at 120°C for 30 min.

3. Pouting of the media into sterilized petridishes and its solidification

The 15-20 ml of sterilized media was poured homogeneously into sterilized petridishes and used for the inoculation.

4. Inoculation of the media with the test organisms.

Bacterial cells (0.5 ml) was added on the petridishes, prepared by the method as described above and spreaded with the help of a sterile spreader. These petridishes were kept in laminar for 10 minutes for inoculation.

5. Preparation of the solutions and control

Solutions of concentration range in between 25 to 100 ppm have been prepared by diluting stock solution appropriately and used for study of antimicrobial activity.

6. Preparation of test plates

Filter paper discs were soaked into above solution of test compound and these paper discs were placed on the petridish and incubated at 37°C temperature for 24 hours.

7. Measurement of the zone of inhibition

Zone of inhibition was measured for each compound separately with respect to control and also compared to a standard drug.

Recommended procedure for the determination of Antimicrobial activity

A saturated solution of Nutrient agar (75 g) was prepared in double distilled water and it was autoclaved for 15 min, then poured in petriplates in the laminar. After its solidification loan of bacteria (i.e. *Escherichia coli* and *Staphylococcus aureus*) against which antimicrobiological activity is to be investigated has been applied. Solutions were prepared of all the eight ligand and their complexes with Mn (II), Ni (II), Co (II) and Cu (II). A separate paper disc was soaked in each solution for 10 minutes. Thus prepared paper disc was placed into petriplate and finally prepared petriplates were kept in incubator at 37°C for 24 hour. After 24 hour, petriplates were removed and checked for measuring zone of inhibition in mm.

IV. Result and Discussion

Antibacterial activity of all amide group containing ligand and their complexes with Mn(II), Co(II), Ni(II) and Cu(II) have been reported on two microbia i.e., *E.coli* and *S.aureus*.

The results of antibacterial activity have been given in table 1 and have also been represented in Fig. and Photographs of Ligand and complexes.

Following few results which have been observed during investigation are as:

1. All the amide group containing ligands and their complexes possess at least one type of biological activity up to substantial level.

2. On the basis of results of antimicrobial activity a trend of structure activity relationship have reported for different amide ligand systems.

(a) (Against *E.coli*)

N46DM2PB>N2PA>N46DM2PA>N2PB

(b) (Against *S.aureus*)

N46DM2PB>N26DH4PB>N2PA>N6H2MC4P

B=N6H2MC4PA=

N26DH4PA>N2PB=N46DM2PA

4. Results of structure activity relationship of different Mn(II), Co(II), Ni(II) and Cu(II) complexes of amide group containing ligands against *E.coli* and *S.aureus* are as:

(a) (Against *E.coli*)

(i) [Co-(N2PB)₃]Cl₂>[Mn-(N2PB)₂]Cl₂>[Cu-(N2PB)₃]Cl₂>[Ni-(N2PB)₃]Cl₂

(ii) [Co-(N2PA)₃]Cl₂>[Cu-(N2PA)₃]Cl₂>[Mn-(N2PA)₂]Cl₂>[Ni-(N2PA)₃]Cl₂

(iii) [Cu-(N46DM2PB)₃]Cl₂>[Mn-(N46DM2PB)₂]Cl₂>[Co-(N46DM2PB)₃]Cl₂>[Ni-(N46DM2PB)₃]Cl₂

(iv) [Mn-(N46DM2PA)₂]Cl₂>[Co-(N46DM2PA)₃]Cl₂= [Ni-(N46DM2PA)₃]Cl₂

(v) [Cu-(N6H2MC4PB)₃]Cl₂>[Mn-(N6H2MC4PB)₂]Cl₂> [Ni-(N6H2MC4PB)₃]Cl₂

(vi) [Cu-(N6H2MC4PA)₃]Cl₂> [Co-(N6H2MC4PA)₃]Cl₂> [Ni-(N6H2MC4PA)₂]Cl₂

(vii) [Cu-(N26DH4PB)₃]Cl₂> [Mn-(N26DH4PB)₂]Cl₂> [Co-(N26DH4PB)₃]Cl₂> [Ni-(N26DH4PB)₃]Cl₂

(viii) [Cu-(N26DH4PA)₃]Cl₂= [Co-(N26DH4PA)₃]Cl₂> [Mn-(N26DH4PA)₂]Cl₂= [Ni-(N26DH4PA)₂]Cl₂

(b) (Against *S.aureus*)

(i) [Cu-(N2PB)₃]Cl₂> [Co-(N2PB)₃]Cl₂> [Mn-(N2PB)₂]Cl₂> [Ni-(N2PB)₃]Cl₂

(ii) [Cu-(N2PA)₃]Cl₂= [Mn-(N2PA)₂]Cl₂> [Co-(N2PA)₃]Cl₂= [Ni-(N2PA)₃]Cl₂

(iii) [Co-(N46DM2PB)₃]Cl₂> [Cu-(N46DM2PB)₃]Cl₂> [Ni-(N46DM2PB)₃]Cl₂> [Mn-(N46DM2PB)₂]Cl₂

(iv) [Cu-(N46DM2PA)₃]Cl₂> [Co-(N46DM2PA)₃]Cl₂> [Mn-(N46DM2PA)₂]Cl₂> [Ni-(N46DM2PA)₃]Cl₂

(v) [Co-(N6H2MC4PB)₃]Cl₂> [Mn-(N6H2MC4PB)₂]Cl₂> [Cu-(N6H2MC4PB)₃]Cl₂> [Ni-(N6H2MC4PB)₃]Cl₂

(vi) [Cu-(N6H2MC4PA)₃]Cl₂= [Co-(N6H2MC4PA)₃]Cl₂= [Ni-(N6H2MC4PA)₃]Cl₂> [Mn-(N6H2MC4PA)₂]Cl₂

(vii) [Co-(N26DH4PB)₃]Cl₂> [Cu-(N26DH4PB)₃]Cl₂= [Mn-(N26DH4PB)₂]Cl₂> [Ni-(N26DH4PB)₃]Cl₂

(viii) [Co-(N26DH4PA)₃]Cl₂> [Cu-(N26DH4PA)₃]Cl₂= [Ni-(N26DH4PA)₃]Cl₂> [Mn-(N26DH4PA)₃]Cl₂

5. Antibacterial activity of Mn(II), Co(II), Ni(II) and Cu(II) complexes of amide group containing ligand is in general, greater against *E.coli* than *S.aureus*. with few exceptions

V. Conclusion

Biological activity of amide group containing ligands and their Mn(II), Ni(II), Co(II) and Cu(II) complexes has been investigated. The standard disc diffusion method has been employed for study. *E.coli* and *S.aureus* as bacterial subcultures have been used for study of antibacterial activity of the compounds. The study indicates that most of ligands having better antibacterial activity than complexes (except of few complexes).

VI. Acknowledgements

Authors are thankful to University Grant Commission (UGC) CRO Bhopal for financial assistance and BIFR, Bikaner for antimicrobial activities.

VII. REFERENCES

- [1]. Garg BS, Bhojak N, Sharma RK, Bist JS, et al. Separation and pre concentration of metal ions and their estimation in vitamin, steel and milk sample using o-vanillin-immobilized silica gel. *Talanta* 1999; 48(1): 49-55.
- [2]. Garg BS, Bhojak N, Nandan D, et al. Micellar spectrofluorimetric determination of lead (II) in natural water, waste water and egg samples with N-(2'-pyridyl)-2-hydroxybenzamide. *Ind. J. Chem.* 2005; 44A: 1504.
- [3]. Bhojak N, Gudasaria DD, Khiwani N, et al. Microwave Assisted Synthesis Spectral and Antibacterial Investigations on Complexes of Mn(II) With Amide Containing Ligands. *E-Journal of Chemistry* 2007; 4(2):232-237.
- [4]. Raja Ram, Verma KK, and Bhojak N et al. Microwave assisted synthesis, spectral and antibacterial investigations on complexes of Co (II) with amide containing ligands. *International Journal of New Technologies in Science and Engineering.* 2015;2(6):92-100.
- [5]. Verma KK, Soni Gupta P, Bhojak N et al. Microwave Assisted Synthesis, Characterisation and Anti microbial activities of few Cobalt(II)Thiosemicarbazones Complexes. *World Journal of pharmacy and pharmaceutical sciences* 2015; 4(11):1673-1683.
- [6]. Raja Ram, Verma KK, Bhojak N et al. Microwave assisted synthesis, spectral and antibacterial investigations on complexes of Ni(II) with amide group containing ligands. *IARJSET* 2015; 2(11): 40-43.
- [7]. Singh B and Bhojak N Microwave assisted synthesis, spectral and antibacterial investigations on complexes of Mn(II) with amide containing ligands. *RJC* 2008; 1(1):105-109.
- [8]. Yadav N, Bhojak N Microwave assisted synthesis, spectral and antibacterial investigation on Co(II) complexes with amide ligands. *The Int. J. Eng. Sci.* 2013; 2(2): 166-168.
- [9]. Hernandez MRM, Mederos A, Domínguez S et al. Speciation study of the anti-inflammatory drug tenoxicam (Htenox) with Cu(II): X-ray crystal structure of [Cu(tenox)₂(py)₂]•EtOH. *J. Inorg. Biochem.* 2003; 95(2-3): 131-140.
- [10]. Franklin PX, Pillai AD, Vasu KK et al. 2-Amino-5-thiazolyl motif: A novel scaffold for designing anti-inflammatory agents of diverse structures. *Eur. J. Med. Chem.* 2008; 43(1): 129-134.
- [11]. Vukovic N, Sukdolak S, Solujic S et al. Synthesis and Antibacterial Evaluation of Some Novel 2-Aminothiazole Derivatives of 4-Hydroxy-chromene-2-one. *Arch. Pharm.* 2008; 341(8): 491-496.
- [12]. Rover S, Cesura MA, Huguenin P et al. Synthesis and Biochemical Evaluation of N-(4-Phenylthiazol-2-yl)benzenesulfonamides as High-Affinity Inhibitors of Kynurenine 3-Hydroxylase. *Med. Chem.* 1997; 40(26): 4378-4385
- [13]. Shazia R, Mohammed I, Anwar N, et al. Transition metal complexes as as potential therapeutic agents, *Academic journals.org BMBR*, 2010; 5: 38-45.
- [14]. Bharti S K, Singh S K et al. Metal based drugs: current use and future potential pharmaceutical chemistry Research lab. Department of pharmaceuticals, institute of technology, Banaras Hindu Uni. India 2009;1(2): 39-51.
- [15]. Shalita A R, Comparison of salicylic acid and Benzoyl peroxide wash in the treatment of acne vulgaris, *Clinical therapeutics*, 1989; 2: 267-268.
- [16]. Pathel G J, Hathe M V et al. Synthesis, Characterization and chelating properties of benzoxazolidin -2-one/4- aminosalicylic acid clubbed molecules, *Electrochem. J. Chem.*, 2006; 3(13): 319-326.

Table 1. Biological activity of amide group containing, ligands and complexes (medium-Nutrient Agar)

S.No.	Ligands/Complexes	Zone of inhibition (in mm)	
		<i>E.coli</i>	<i>S. aureus</i>
1.	N2PB	0.0	0.0
	[Co-(N2PB) ₃]Cl ₂	9.0	5.5
	[Mn-(N2PB) ₂]Cl ₂	6.0	5.0
	[Cu-(N2PB) ₃]Cl ₂	5.0	6.0
	[Ni-(N2PB) ₃]Cl ₂	0.0	0.0
2.	N2PA	5.5	5.5
	[Co-(N2PA) ₃]Cl ₂	7.5	5.5

	$[\text{Mn}-(\text{N2PA})_2]\text{Cl}_2$	6.6	6.0
	$[\text{Cu}-(\text{N2PA})_3]\text{Cl}_2$	7.0	6.0
	$[\text{Ni}-(\text{N2PA})_3]\text{Cl}_2$	5.0	5.5
3.	N46DM2PB	6.0	7.0
	$[\text{Co}-(\text{N46DM2PB})_3]\text{Cl}_2$	4.5	7.5
	$[\text{Mn}-(\text{N46DM2PB})_2]\text{Cl}_2$	5.0	0.0
	$[\text{Cu}-(\text{N46DM2PB})_3]\text{Cl}_2$	5.5	6.5
	$[\text{Ni}-(\text{N46DM2PB})_3]\text{Cl}_2$	0.0	4.5
4.	N46DM2PA	4.5	0.0
	$[\text{Co}-(\text{N46DM2PA})_3]\text{Cl}_2$	5.5	6.0
	$[\text{Mn}-(\text{N46DM2PA})_2]\text{Cl}_2$	6	4.5
	$[\text{Cu}-(\text{N46DM2PA})_3]\text{Cl}_2$	5.5	6.5
	$[\text{Ni}-(\text{N46DM2PA})_3]\text{Cl}_2$	5.5	0.0

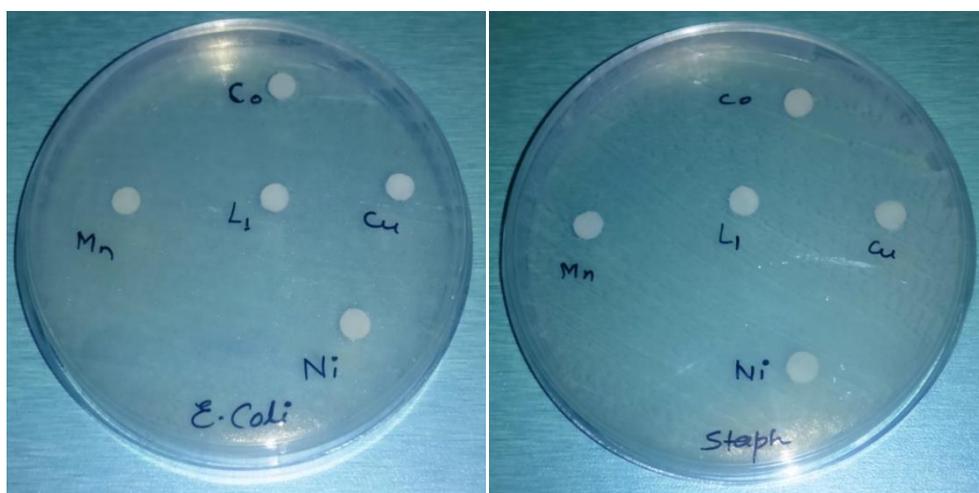


Figure 1. Biological activity of amide group containing, ligands and complexes (medium-Nutrient Agar)

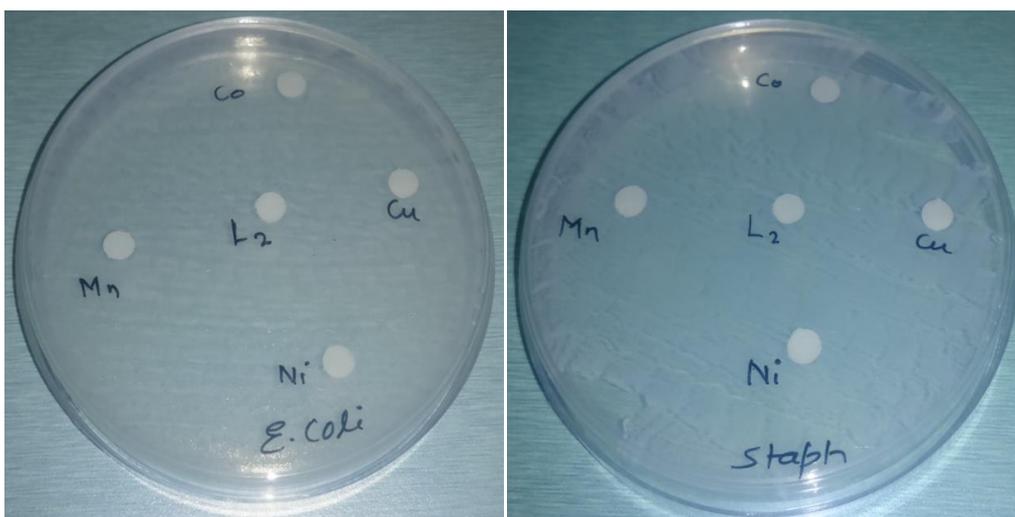


Figure 2. Biological activity of amide group containing ligands and complexes

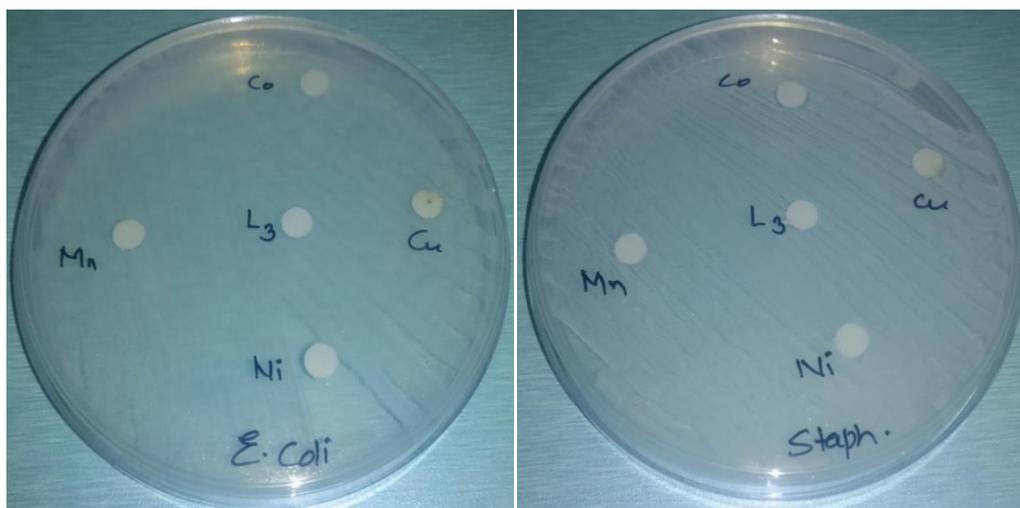


Figure 3. Biological activity of amide group containing ligands and complexes

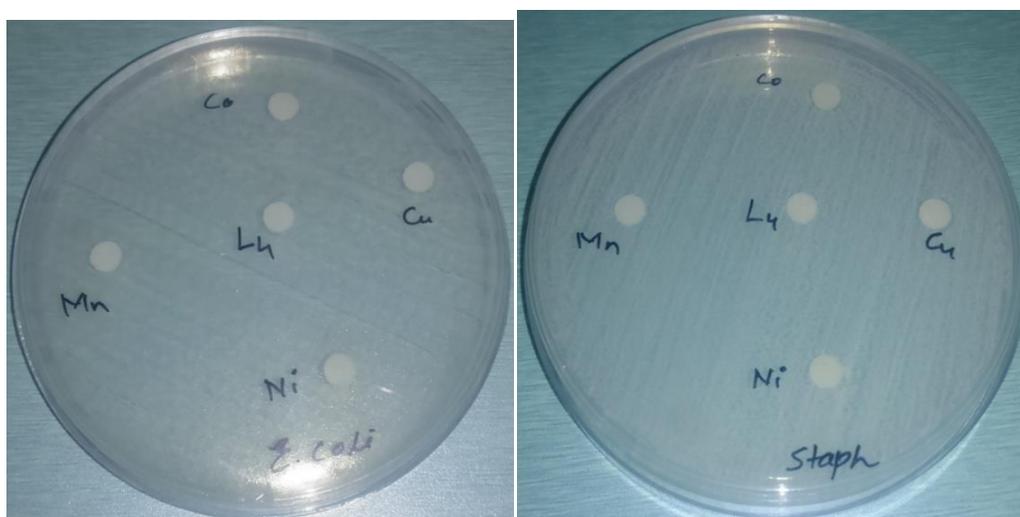


Figure 4. Biological activities of amide group containing, ligands and complexes

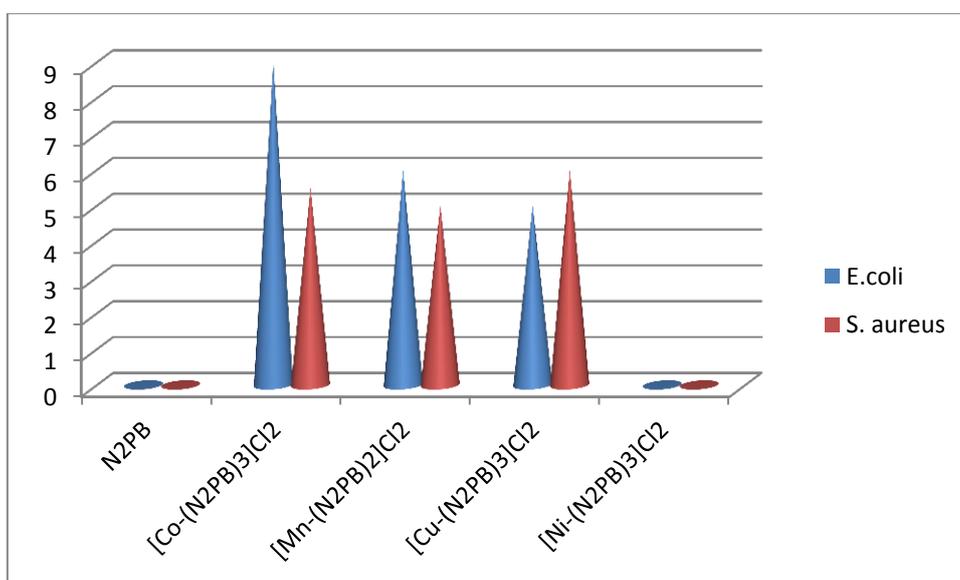


Figure 5. Biological activities of amide Ligands and their metal complexes.

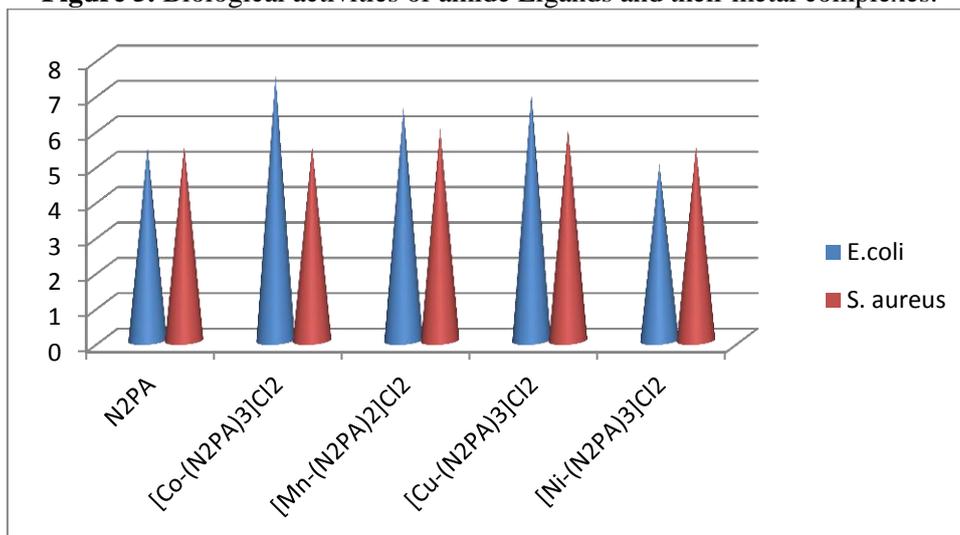


Figure 6. Biological activities of amide Ligands and their metal complexes.

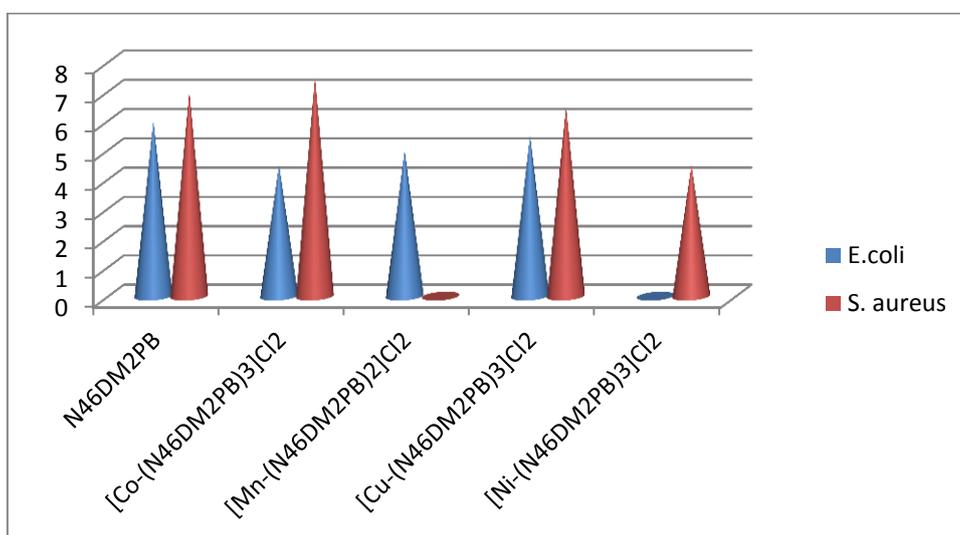


Figure 7. Biological activities of amide Ligands and their metal complexes.

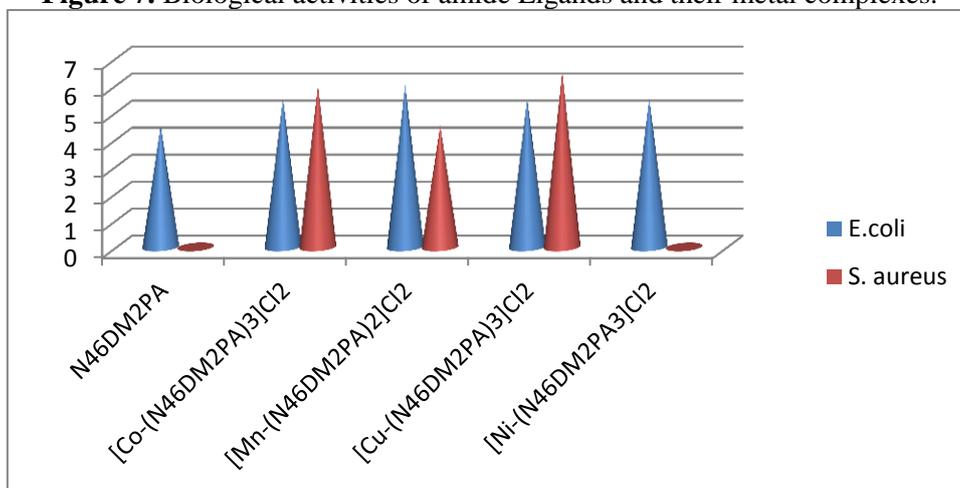


Figure 8. Biological activities of amide Ligands and their metal complexes.