International Journal of Education and Science Research Review
ISSN 2348-6457
www.ijesrr.org Volume-1, Issue-5 October- 2014 Email- editor@ijesrr.or

ANTIBACTERIAL ACTIVITY OF LANTHANIDE (III) COMPLEXES OF AMIDE GROUP CONTAINING LIGANDS

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ABSTRACT:
The antibacterial activity of some amide group containing ligands and their complexes with Sm(III) and Tb (III) ions were tested against two bacterial strains: *Escherichia coli*, *Staphylococcus aureus*. All of the complexes possess inhibitory action against the tested strains. The activity of the studies compounds depends on their concentration. The complexes of aminothiazole derivatives were found to have more anti bacterial activities than aminopyridines derivatives.

INTRODUCTION:

Aminopyridines and aminothaizoles form a wide range of bioactive compounds and also act as precursor for the synthesis of bioactive materials. Their chemistry and pharmacological applications have been extensively investigated. These have emerged as important class of nitrogen and oxygen or sulfur ligands particularly for transition metal ions in the last two decades. The real impetus towards developing their coordination chemistry is their physicochemical properties and significant biological activities. These compounds present a wide variety of biological activity such as antitumoral, fungicidal, bactericidal or antiviral. Their activity has frequently been thought to be due to their ability to chelate trace metals and in few cases it has been proved that metal ions enhance the biological activity of aminopyridines and aminothaizoles [1-3].

The antibacterial properties of lanthanide (III) complexes have attracted the interest of few researchers (4-9).

Few novel complexes of copper have been synthesized and their biological activities evaluated using agar diffusion method and agar dilution method. The results were compared with two well known antibiotics, namely, tetracycline and nystatin [10].

A series of β-diketone hydrozone derivatives have been synthesized through condensation of β-diketone with aromatic aldehydes followed by reaction with phenylhydrazine and their complexes with lanthanide ions have been prepared. The prepared complexes were screened for antibacterial and antifungal properties and have exhibited potential activity [11].

The study of the metal complexes of antipyrine in antineoplastic medication, molecular biology and bioengineering has become hotspots in recent years. A new Schiff base formed from pyridoxal, a vitamin and 4-aminoantipyrine is reported and the antibacterial activity of the newly synthesized Schiff base formed from 4-aminoantipyrine with vitamin B is explored. The Schiff base ligand forms very stable complexes with the lanthanide metals La, Ce, Pr, Nd, Sm, Gd, Tb, Dy and Er, their structural, spectroscopic, biological properties have been reported [12,13]. Recently a series of Lanthanide (III) complexes have been isolated and characterized based on elemental analysis, molar conductance, IR etc. the ligands behave in bidentate fashion coordinating through hydrazide >C=O and nitrogen of >C=N. A coordination number of ten is assigned to the complexes. Antibacterial and antifungal studies indicate an activity of the ligands on complexation [14,15].

Tetracycline complexes of lanthanide have been synthesized and characterized by analytical, IR, electronic, and thermogravimetric analysis. The ligands and the complexes were tested in vitro to evaluate their activity against the bacteria *Escherichia coli* and *Staphylococcus aureus* [16].

The survey of literature shows that rare earth elements have inhibitory activity against bacteria and they are uses in many ways in medical field. The antibacterial action depends on the concentration of the lanthanide ions.

In this paper we report the anti bacterial activity of few doped systems of Sm(III) and Tb (III) - amide ligands.

METAL:

All the solvents used were of analytical grade. Standard solution of the Sm (III) metal has been prepared by dissolving appropriate amount of its carbonate in distilled water. Standard solution of the Tb (III) metal has been prepared by dissolving appropriate amount of its chloride in distilled water.

LIGANDS:

1. N-(2'-pyridyl)-4-hydroxybenzamide (N2P4HB)
2. N-(2'-pyridyl)-3,5-dinitrobenzamide (N2P3,5DB)
3. N-(2'-pyridyl)-4-carboxamide but-1-oic acid (N2P4C1BA)
4. N-(2'-thiazolyl)-4-hydroxybezamide (N2T4HB
5. N-(2'-thiazolyl)- 3,5-dinitrobenzamide (N2T3,5DB)
6. N-(2'-thiazolyl)-4-carboxamide but-1-oic acid (N2T4C1BA)

METHODOLOGY:

The antibacterial activity of ligands and their corresponding complexes with lanthanide ions were assayed simultaneously against the bacteria *Escherichia coli* and *Staphylococcus aureus* by disc diffusion method. Nutrient agar and nutrient broth were used as culture media for bacterial cells.

PREPARATION OF MEDIA AND ITS STERILIZATION:

Composition of Nutrient agar medium was taken as Hi veg Peptone (5g /l), Hi veg extract NO. 1 (3.0g/l), Agar (15g/l), Distilled water (1000ml, pH=6.8±0.2 at 25^{o}C). Composition of Nutrient broth taken Hi veg Peptone (5g/l),Hi veg extract NO. 1 (3.0g/l), Distilled water (1000ml, pH=6.9±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. Nutrient broth was prepared by direct dissolving it in mentioned quantity of distilled water. These were than sterilized properly and plugged in a conical flask by autoclaving at 120°C and 15 lbs pressure for 30 min.

INOCULATION OF THE MEDIA WITH TEST ORGANISM

The 15-20 ml of sterilized media was poured homogenously into sterilized petridishes and used for the inoculation. Bacterial cells were added on the petridishes prepared by the method as described above and spreaded with the help of a sterile spreader or loop. These petridishes were kept in incubator for at least 16-18 hours for incubation. Bacterial culture was also bee prepared by adding of bacterial cells in nutrient broth at room temperature then the broth was kept in laminar for 15 min. for inoculation.

Solutions of concentration 100 ppm and 200 ppm have been prepared by diluting stock solution appropriately and used for study of antimicrobial activity. After incubation of the broth culture for few hours, these inoculums were well spread over the agar surface with help of sterilized cotton swab. Then filter paper discs were soaked in to above test compound and these discs were placed on the petridishes and incubated at 37^{o}C temperature for 24 hours.

MEASUREMENT OF ZONE OF INHIBITION:

Zone of inhibition was measured for each compound separately with respect to control and also compared to a standard drug. Saturated solution of Nutrient agar and nutrient broth were prepared in double distilled water and autoclaved for 30-45 min, than 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 was applied. Solutions of different strength (i.e. 100 ppm and 200 ppm) were prepared of all the three aminopyridines and three aminothiazoles complexes with Gd (III). A separate paper disc was soaked in each solution for 120 minutes and thus finally prepared petridishes were kept in incubator at 37^0C for 24 hours. After 24 hours, petridishes were removed and checked or measuring zone of inhibition in mm.

Antimicrobial activity of six systems of aminopyridines and aminothiazoles derivatives has been carried out on *E. coli and S. aureus*.

CONCLUSION:

1. Antibacterial activity of aminothiazoles derivatives is greater than aminopyridines derivatives at 200 PPM against *Escherichia coli*. Similar trend is followed against *Staphylococcus aureus.*

2. Comparative activity for different ligands with same lanthanide (III) ion at 200 PPM and following results were obtained against *Escherichia coli* are as

(i) For Sm (III) aminopyridine complexes
N2P3,5DB > N2P4C1BA > N2P4HB
(ii) For Tb (III) aminopyridine complexes
N2P4C1BA > N2P4HB ~ N2P3,5DB
(iii) For Sm (III) aminothiazole complexes
N2T4HB > N2T4C1BA > N2T3,5DB
(iv) For Tb (III) aminothiazole complexes
N2T4HB ~ N2T3,5DB > N2T4C1BA

3. Comparative activity for different ligands with same lanthanide (III) ion at 200 PPM and following results were obtained against *Staphylococcus aureus* are as

(i) For Sm (III) aminopyridine complexes
N2P4C1BA > N2P3,5DB > N2P4HB
(ii) For Tb (III) aminopyridine complexes
N2P4HB > N2P3,5DB > N2P4C1BA
(iii) For Sm (III) aminothiazole complexes
N2T4HB > N2T3,5DB ~ N2T4C1BA
(iv) For Tb (III) aminothiazole complexes
N2T3,5DB > N2T4HB ~ N2T4C1BA

TABLE :- 1
ANTIBACTERIAL ACTIVITY OF SAMARIUM COMPLEXES OF DERIVATIVES OF AMINOPYRIDINE AND AMINOTHIAZOLES

S.NO.	COMPOUNDS	ZONE OF INHIBITION AT DIFERENT CONCENTRATION			
		Escherichia coli		*Staphylococcus auerus*	
		100 ppm	200 ppm	100 ppm	200 ppm
1	Sm (III)- N2P4HB	5	10	6	30
2	Sm (III)-N2P3,5DB	Nil	14	5	10
3	Sm (III)-N2P4C1BA	5	12	6	12
4	Sm (III)-N2T4HB	Nil	10	5	24
5	Sm (III)-N2T3,5DB	Nil	12	5	14
6	Sm (III)-N2T4C1BA	5	14	5	14

TABLE :-2
ANTIBACTERIAL ACTIVITY TERBIUM COMPLEXES OF DERIVATIVES OF AMINOPYRIDINE AND AMINOTHIAZOLES

S.NO.	COMPOUNDS	ZONE OF INHIBITION AT DIFERENT CONCENTRATION			
		Escherichia coli		*Staphylococcus auerus*	
		100 ppm	200 ppm	100 ppm	200 ppm
1	Tb (III)-N2P4HB	Nil	6	5	8
2	Tb (III)-N2P3,5DB	5	6	6	6
3	Tb (III)-N2P4C1BA	5	8	Nil	5
4	Tb (III)-N2P4HB	Nil	8	Nil	5
5	Tb (III)-N2P3,5DB	6	8	5	6
6	Tb (III)-N2P4C1BA	Nil	6	5	5

ACKNOWLEDGEMENTS
The authors are thankful to Central Drug Research Institute for providing spectral studies.

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