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Synthesis and Characterization of mixed Ligand Cu(II) Complexes of Sulfacetamide-Na with 2, 2-bipyridine and 1, 10-phenonthrolene

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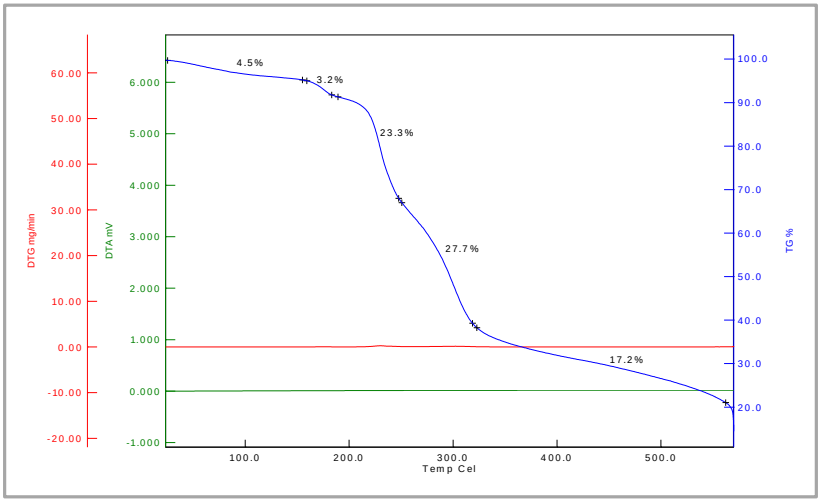
ABSTRACT

Sulfacetamide-Na is used as a primary ligand, and 2, 2-bipyridine, 1, 10-phenanthroline is used as a secondary ligand to synthesize mix ligand Cu(II) complexes. All the synthesized complexes were characterized by IR, UV, and TGA. IR spectra show that sulfacetamide-Na reacts as a monodentate ligand and coordinates through NH_2 nitrogen. Bidentate ligand 2, 2-bipyridine and 1, 10-phenanthroline coordinates through the nitrogen of the ring. UV/Visible electronic spectroscopy shows variation between ligand and complexes. All ligands are colourless, so a flat graph got in the visible range. Complexes show a slope and due to their colored nature. TGA data shows loss of mass of water molecule, chlorine, and ligand. The antibacterial test shows mixed ligand complexes have high antibacterial activity as compared to their ligands.

Graphical Abstract



Thermo gravimetric analysis of $[Cu(sulf\text{-}Na)_2(Met)]$.

Keywords: Mixed ligand complexes, sulfacetamide-Na, Bipyridine, Phenonthrolene, Antibacterial activity, Spectra.

INTRODUCTION

Since sulfonamide drug has been synthesized, its derivatives have been used as antibiotics, antifungal and antiseptic in medical science. Sulfacetamide-Na is one of the derivatives that has antiseptic and antibiotic properties. Sulfacetamide-Na is used in skin infections in the form of lotions or creams and as oral doses in urinary tract infections. Sulfacetamide-Na is also used in the ophthalmic solution for the treatment of eye infection. From the past several decades, metal-drugs have been used in medical science [**1-5**]. The research show that the metal complex of sulfacetamide-Na has more effective antibacterial activity than sulfacetamide-Na. Research shows that NH_2 group of sulfacetamide-Na take part in chelation with metal ion like Cu and Co. (C=O) group and (SO_2) group of sulfacetamide-Na takes participation in complex formation with large metal ions like Cd and Ag [**6-10**].

2, 2-bipyridine and 1, 10-phenonthrolene both are basic bidentate ligand due to two nitrogen atoms are in the rings. Both these ligands has great binding tendency with metal ion therefore these are widely used in the synthesis of mix ligand complexes [**11-15**]. These both ligands Ru-metal complexes shows bacteriostatic properties in which Ru-complex of 2, 2-bipyridine is more effective than Ru-complex of 1, 10-phenonthrolene. Cu is naturally occurring metal so Cu-complex of 2, 2-bipyridine is shows oxidative, hydrolytic, photolytic, and electrolytic cleavage of DNA. Both these ligand enhance the antibacterial and anticancer properties of mixed ligand complexes [**16-20**].

In this work, we have synthesized mixed ligand complexes of sulfacetamide-Na. sulfacetamide-Na used as primary ligand and 2, 2-bipyridine, 1, 10-phenonthrolene, Methionine used as secondary ligand. Three mixed ligand complexes were synthesized [$Cu(sulf)_2(BPy)$], [$Cu(sulf)_2(Phen)$] and [$Cu(sulf)_2(met)$], These complexes were characterized by IR spectroscopy, thermal analysis (TGA) and then tested for their antimicrobial activity [**21-22**].

MATERIALS AND METHODS

[$Cu(sulf)_2(BPy)$]: 10 mL methanolic solution of $CuCl_2.2H_2O$ (1 mmol) was added to methanolic solution of 2 mmol of sulfacetamide in 15 mL solvent at RT. After string, a few minutes light green color was obtained, then added 1 mmol methanolic solution of 2, 2-bipyridine in 10 mL solvent at RT. Drak-blue colored precipitates were formed, which was filtered and washed with methanol.

[$Cu(sulf)_2(Phen)$]: Made a clear solution of 2 mmol of $CuCl_2.2H_2O$ in 10 mL methanol, then added 2 mmol sulfacetamide-Na solutions in 15 ml methanol. Green colored solution was obtained. To this, one mmol 1, 10-phenanthroline was added, which suddenly resulted from dark greenish to blue precipitates, which was filtered, washed with methanol, and dried at RT.

[$Cu(sulf)_2(met)$]: Aqueous solution of $CuCl_2.2H_2O$ (1 mmol) in 10 mL solvent was added to 15 mL aqueous solution of 2 mmol sulfacetamide-Na at RT. After Few minutes of stirring greenish solution was obtained, and then added 15ml aqueous solution of methionine (1 mmol) at RT. Bluish grey colored precipitates were obtained, which was filtered, washed with water and dried it in oven at 50°C temperature.

RESULTS AND DISCUSSION

Infrared spectra: IR data of [$Cu(sulf)_2(BPy)$] and[$Cu(sulf)_2(Phen)$] are given in table 1. The frequency of N-H in sulfacetamide-Na at 3381 cm^{-1} shifted to 3360 cm^{-1} in [$Cu(sulf)_2(BPy)$] complex and 3350 cm^{-1} in [$Cu(sulf)_2(Phen)$] complex. This can be suggested that nitrogen of NH_2 of sulfacetamide-Na participates in chelation. The ring stretching frequencies C=C and C=N at 1500, 1421 cm^{-1} of free phenanthroline shifted to 1512, 1425 cm^{-1} in [$Cu(sulf)_2(Phen)$] complex and 1575,1452 cm^{-1} of free bipyridine were shifted to 1595, 1502 cm^{-1} in [$Cu(sulf)_2(BPy)$] complex. This

data indicating that nitrogen atoms of these both heterocyclic molecules form coordination bond with the metal ion. The characteristic out of plane hydrogen bending modes of free phenanthroline observed at 852 and 738 cm^{-1} which shifted to 856 and 726 cm^{-1} in $[Cu(sulf)_2(Phen)]$ and for bipyridine at 756, 621 cm^{-1} were shifted to 771 and 677 cm^{-1} in $[Cu(sulf)_2(BPy)]$ complex (Figure 1-7).

IR data of [Cu(sulf)2(Met)] are given in table 2. (N-H) frequency of sulfacetamide-Na observed at 3381 cm^{-1} shifted to lower at 3360 cm^{-1} in complex and (N-H) group frequency of methionine 2955 cm^{-1} shifted upward in the complex. This data confirms the chelation of nitrogen with a metal ion. The symmetric and antisymmetric vibrational frequency of (COO^-) shifted upwards and downwards, respectively in the complex. This confirms the coordination of oxygen with a metal ion.

Table 1. IR data of $[Cu(sulf)_2(BPy)]$ and$[Cu(sulf)_2(Phen)]$

Assignment	Absorbance wave number cm^{-1}				
	$[Cu(sulf)_2(BPy)]$	$[Cu(sulf)_2(Phen)]$	Sulfa-Na	BPy	phen
V(NH); amine group	3360	3350	3381	-	-
V(C=N); in Bpy	1595	-	-	1575	-
V(C=N); in Phen	-	1512	-	-	1500
V_{as} (S=O); sulfonyl group	1440	1462	1383	-	-
V_s (S=O); sulfonyl group	1137	1145	1147	-	-
V(C=O) ; amido group	1680	1679	1680	-	-
V(M-N)	557,416	457,484	-	-	-

Table-2. IR data of [Cu(sulf)2(Met)]

Assignment	Absorbance wavenumber cm^{-1}		
	$[Cu(sulf)_2(Met)]$	Sulfa-Na	Methionine
V(NH);amine group	3375-sulfa 3238-meth	3381	2955
V_{as} (S=O); sulfonyl group	1464	1383	-
V_s (S=O); sulfonyl group	1149	1147	-
V(C=O) ; amido group	1689	1680	-
$V_{as}(COO^-)$; in methionine	1621	-	1618
$V_s(COO^-)$; in methionine	1388	-	1413
V(M-N)	540, 499	-	-
V(M-O)	403	-	-

Graphical presentation of the selected complexes are mentioned here.

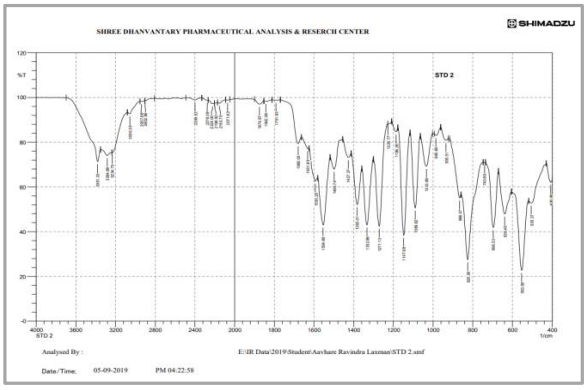


Figure 1. IR spectra of sulfacetamide-Na.

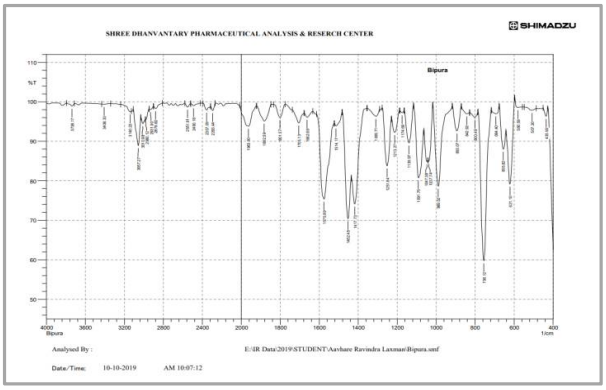


Figure 2. IR spectra of 2,2-bipyridine.

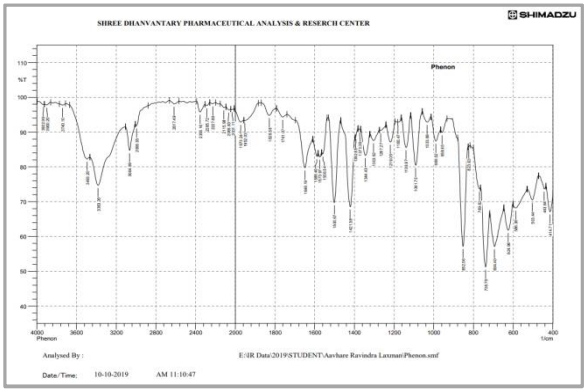


Figure 3. IR spectra of 1,10-phenonthrolene.

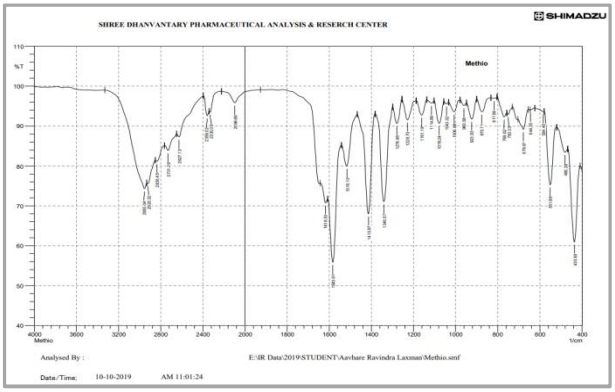


Figure 4. IR spectra of methionine.

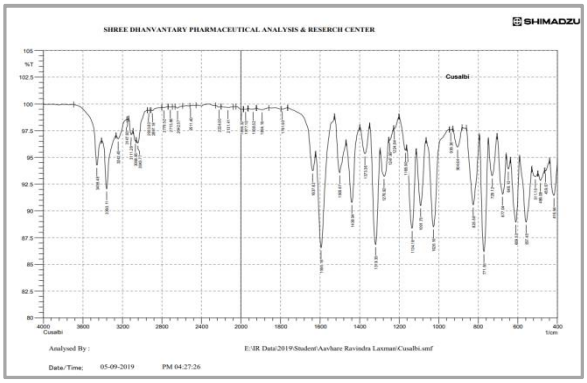


Figure 5. IR spectra of [Cu(sulf)$_2$(BPy)].

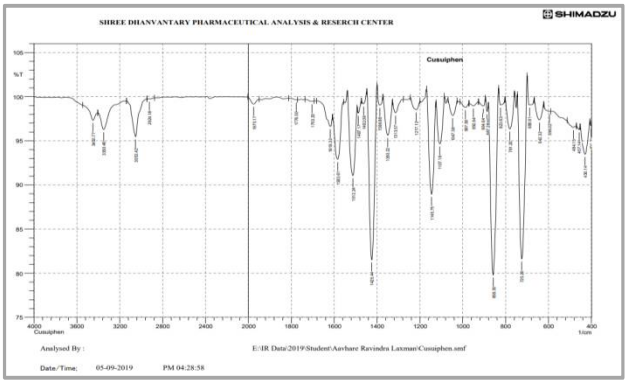


Figure 6. IR spectra of [Cu(sulf)$_2$(Phen)].

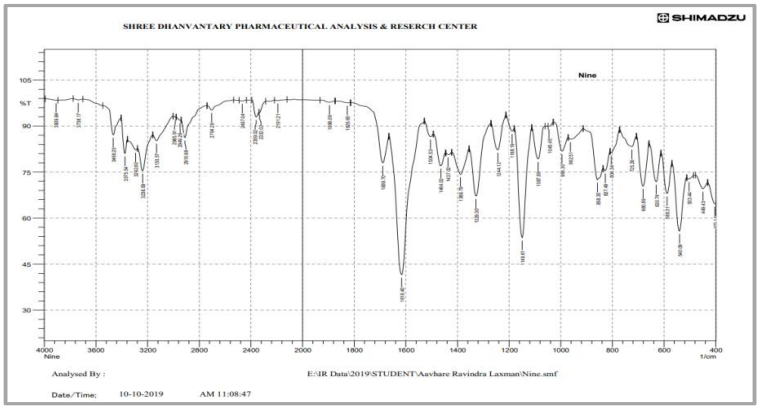


Figure 7. IR spectra of [Cu(sulf)$_2$(Met)].

UV-Visible data: UV/Vis electronic spectra graphs of ligand and complexes are shown in figure 8. UV band of Sulfa-Na-23 6 nm, BPy-203 nm, Phen-220 nm, and met-214 nm may be attributed to $\pi - \pi^*$ transition for that particular ligand.Band of sulfa-Na-265 nm, BPy-256 nm, Phen-255 nm, and Met-256 nm may be assigned due to n-π^* transition which shows slight shifting in complex (Figure 9-13). All complexes which shows λ_{max} in visible range but ligand doesn't appear due to their colourless property. This confirms the complex formation (Figure 14-17).

Thermo gravimetric analysis: Thermogravimetric analysis (TGA) of metal complexes was carried out starting from room temperature 30°C to 600°C under nitrogen atmosphere.

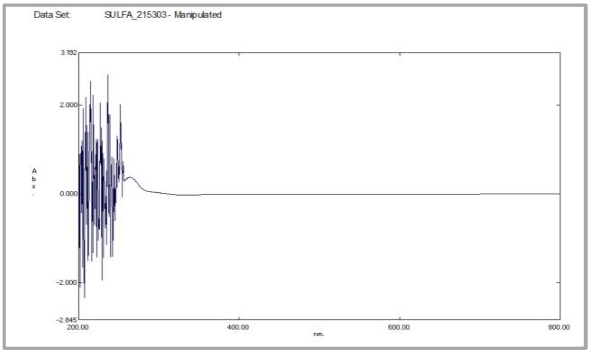


Figure 8. UV/Vis of sulfacetamide-Na.

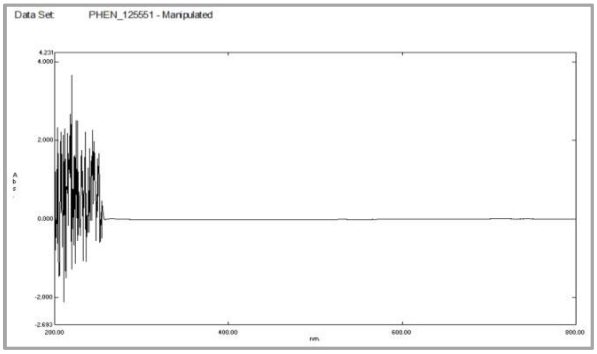


Figure 9. UV/Vis of 1,10-phenonthrolene.

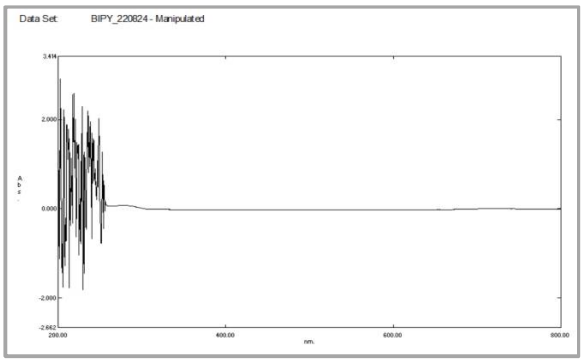


Figure 10. UV/Vis spectra of 2,2-bipyridine.

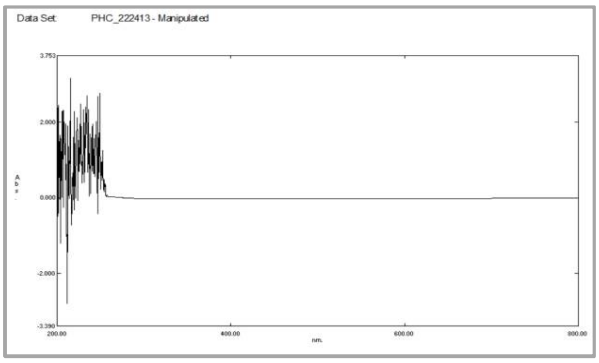


Figure 11. UV/Vis spectra of [Cu(sulf)$_2$(Phen)].

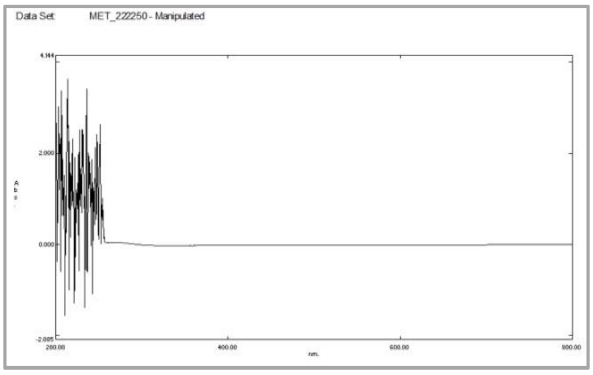


Figure 12. UV/Vis spectra of [Cu(sulf)$_2$(met)].

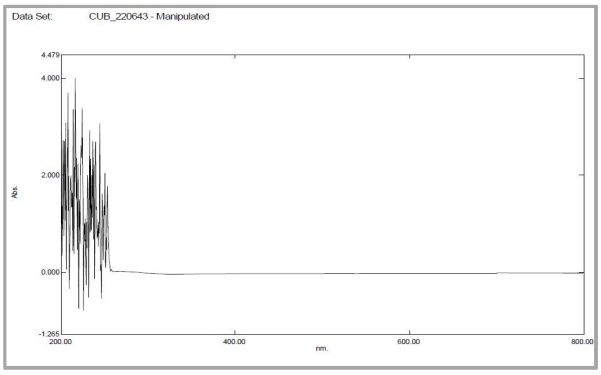


Figure 13. UV/Vis spectra of [Cu(sulf)$_2$(BPy)].

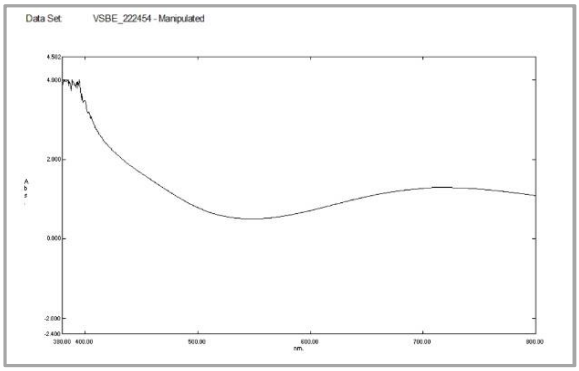


Figure 14. Vis spectra of[Cu(sulf)$_2$(BPy)].

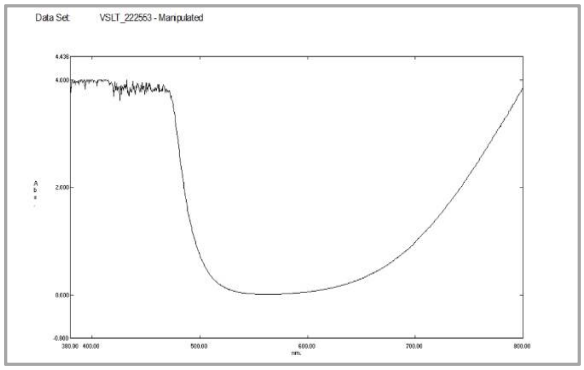


Figure 15. Vis spectra of $CuCl_2 2H_2O$ salt.

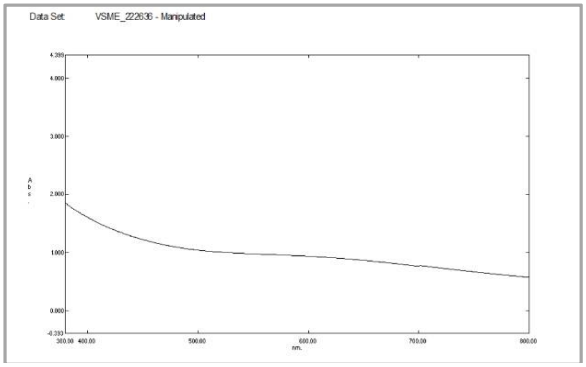
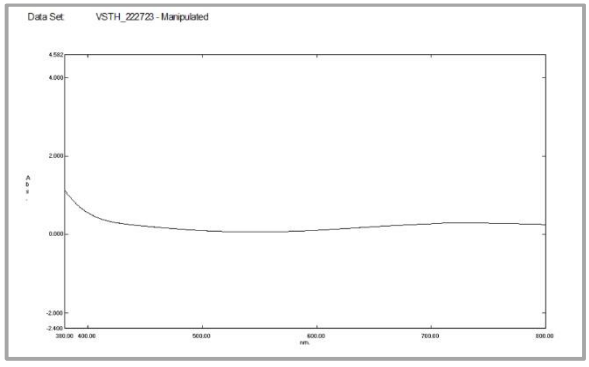


Figure 16. Vis spectra of [Cu(sulf)$_2$(phen)].



Fuigure 17. Vis spectra of [Cu(sulf)$_2$(met)].

[Cu(sulf-Na)$_2$(Phen)]; At near 300°C, 37.8% mass loss indicates the continuous loss, which can be considered for one chlorine, one water molecule, and one molecule of sulfacetamide-Na, subsequent 23.3% mass loss of 1,10-phenanthroline (Figure 18). The remaining % of mass loss may be considered for sulfacetamide-Na and metal oxide.

Thermal decomposition of complex [Cu(sulf-Na)$_2$(BPy)] at 100°C shows 2.4% loss of mass then curve move slightly downside with decomposition (1.2 % + 3.9 % =5.1%) then its shows high mass of loss 35.6%. 2.4% mass loss is considered for 1 mole of a water molecule. 5.1% loss of mass can be considered of chlorine in coordinated form. Further decomposition 35.6% loss of mass should be 1 mole of sulfacetamide-Na and remaining mass percentage of 2, 2-BPy and metal oxide (Figure 19).

TGA data of [Cu(sulf-Na)$_2$(met)] shows a decomposition of one molecule of water and chlorine starting from 50°C to 180°C with 7.7% of mass loss. 23.3% of mass loss can be considered for methionine and then continue falling plot shows decomposition of one molecule of sulfacetamide-Na with 30% mass loss. The remaining mass should be one molecule of sulfacetamide-Na metal oxide (Figure 20).

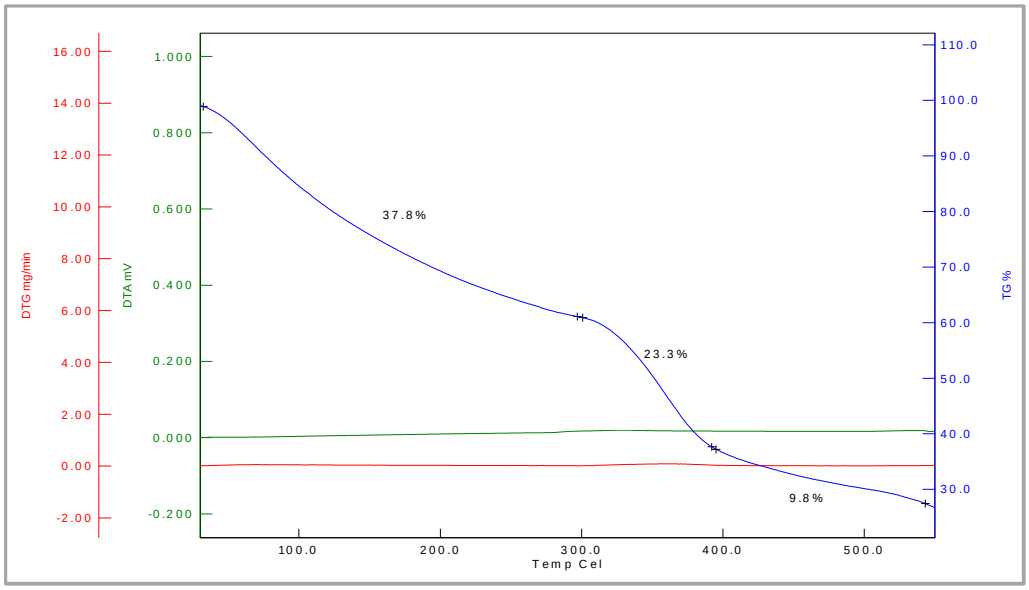


Figure 18. Thermo gravimetric analysis of [Cu(sulf-Na)$_2$(phen)].

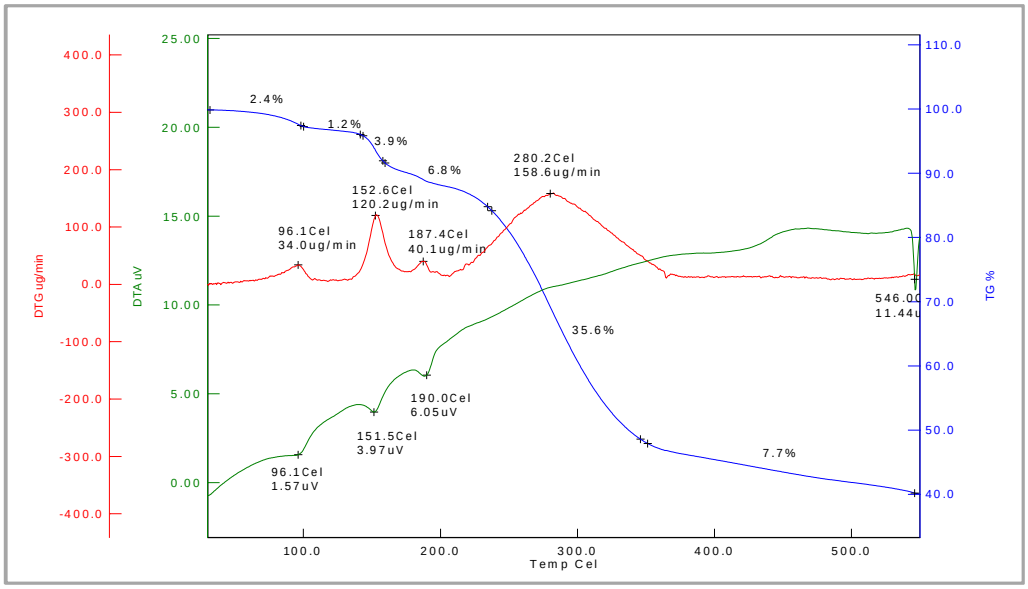


Figure 19. Thermo gravimetric analysis of [Cu(sulf-Na)2(BPy)].

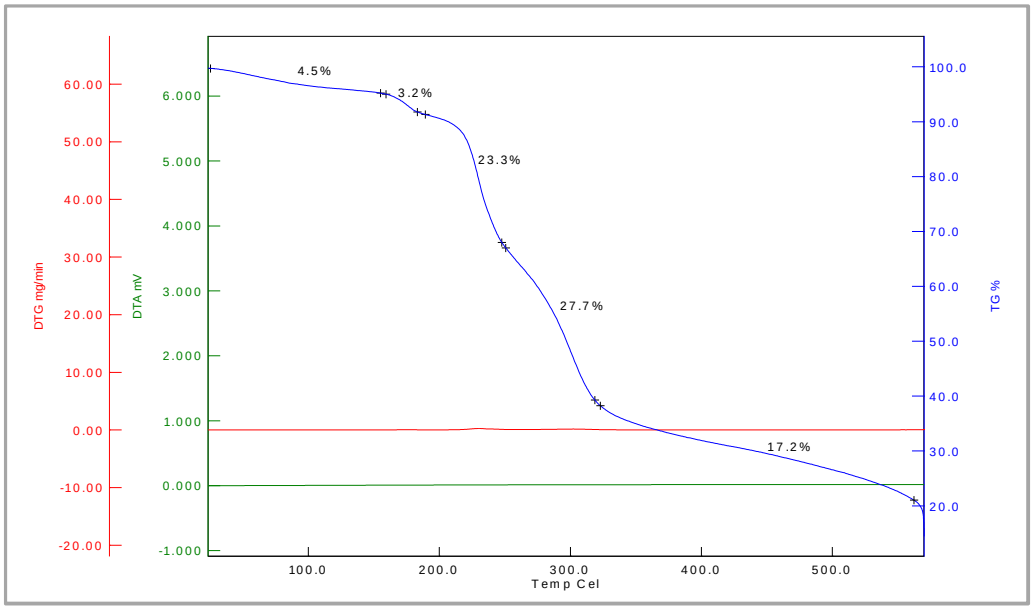


Figure 20. Thermo gravimetric analysis of [Cu(sulf-Na)$_2$(Met)].

APPLICATION

Antimicrobial activity of complexes: The result of antimicrobial activity testing of the sulfacetamide-Na and its complexes are presented in table 3. Sulfacetamide-Na and its Complexes were tested on *E. coli* (gram-negative), C*andida albicans* (yeast), and *Staphylococcus aureus* (gram positive).

In this table activities of complexes are more than sulfacetamide-Na. The activity of [Cu(sulfa)$_2$(Phen)] is higher on yeast (*candida Albicans*), which shows 40 mm inhibition zone diameter and 14 mm, 25 mm for *E.coli* and *Staphylococcus aureus*, respectively. Inhibition zone of [Cu(sulfa)$_2$(BPy)] is 13, 25 and 20 mm of *E.coli, Candida albicans* and *Staphylococcus aureus* respectively which is lesser then [Cu(sulfa)$_2$(Phen)] but higher than [Cu(sulfa)$_2$(meth)]. As compare

to sulfacetamide-Na, its complexes show the better result on gram-positive, gram-negative bacteria, and yeast. [Cu(sulfa)$_2$(met)] is less effective as compared to other complexes due to secondary ligand methionine (amino acid), which is less effective on bacteria.

Table 3. Inhibition zone diameter mm

Bacteria	Concentration	[Cu(sulfa)$_2$ (BPy)]	[Cu(sulfa)$_2$(Phen)]	[Cu(sulfa)$_2$(meth)]	Sulfa-Na
E.*Coli*	1.0 mg mL^{-1}	13	14	10	8
Candida albicans	1.0 mg mL^{-1}	25	40	14	14
Staphylococcus aureus	1.0 mg mL^{-1}	20	25	14	14

CONCLUSION

Sulfacetamide-Na is antibacterial and antibiotic drug which is mono dentate ligand can easily bind with metal ion due to its NH_2 group. 2, 2-bipyridine and 1,10-phenonthrolene both has nitrogen atom which show basic nature there for its easily can form mixed ligand complex with another molecule. Here complexes show more antibacterial activity then its ligands. Antibacterial tests shows mixed ligand complex [Cu(sulfa)$_2$(Phen)]is more effective on gram positive, gram negative bacteria and yeast as compare to other[Cu(sulf)$_2$(BPy)] and [Cu(sulfa)$_2$(met)] complexes. Methionine is not too much effective in antibacterial tests.

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