Metal Complexes of Sulphadiazine Derivative as Reagent and Evaluation of Antibacterial Activity

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ABSTRACT

Synthesis new organic azo dye 4-amino-*N*-(pyrimidin-2-yl)-3-((4-(*N*-pyrimidin-2-ylsulfamoyl)phenyl)diazenyl) benzenesulfonamide as reagent (SA) and Study some Analytical properties of Co(II) and Ni(II) metals complexes .The azo dye compound and its complexes were characterized by elemental analysis (C.H.N.S), Uv-Vis, FT- IR, ^{1}H-NMR and measurements of molar conductivity. The data show that the complexes of Co(II) and Ni(II) metals have the composition of $[MR]X_2$ type. Octahedral environment is suggested for metal complexes. The synthesized compounds were screened against Escherichia coli, Pseudomonas aeruginosa, and Staphylococcus aureus for antibacterial activity.

**Keywords**: Sulfadiazine, Azo, antibacterial activity and complexes

INTRODUCTION

Azo compounds are class of organic compounds that a very important receiving more attention in most fields of scientific research[1-4]. Azo dyes have widely applications in many fields such as industrial, coloring fiber[5], photo electronic applications [6]sensitive chromogenic regent[7] as well as there are important biological agents [8] and they possess important biological activities such as antitumor, anticancer [9-12], antiinflammatory[13], Schistosomicidal agents[14], antibacterial[15], antituberculotic[16], fungicidal[17],antihistamines[18]. In this respect an attempt has been made to synthesize and characterize a new azo reagent derived from sulfadiazine. The complex of this reagent with some metal ions has also been studied spectral characterization and analytical study.

MATERIALS AND METHOD

All reagents, compounds and solvents were obtained from Fluka company, The Merck company and BDH company. The melting points of compounds measured by a Electro thermal melting point apparatus 9300. Elemental analyses (C.H.N.S) by Micro analytical unit of 1108 C.H.N.S Elemental analyzer. F.T.I.R. spectra were measured by using discs of KBr in the range (4000-400) cm^{-1}on F.T.I.R. Shimaduz model 8300. While the UV-Vis. Spectra measured on Shimaduz model 1650PC in ethanol .^{1}H-NMR spectra were performed using a Bruker Advance 400 MHz Spectrometer. Molar conductance were measured in DMF as solvent by using a Alpha Digital conductivity apparatus model 800. By using pH-meter Hanna measurements of pH were carried out. The metal content of the complex was measured by using atomic absorption technique by Perkin-Elmer model 2280.

Preparation of the reagent (SA)

The organic azo dye (SA) was synthesized according to the general procedure [19] sulfadiazine (1.5 gm, 0.006 mol) was dissolved in (2 ml) concentrated HCl and (10 ml) D.W. The solution was cooled at (0-5 ^{0}C) in ice-bath. Then a solution of (NaNO$_2$) sodium nitrite (0.006 mol) dissolved in (4 ml) of D.W. was cooled at (0-5 ^{0}C) in ice-bath. This solution was added a drop wise to the solution with stirring at the same temperature. Then sulfadiazine (1.5 gm, 0.006 mol) dissolved in (3%) NaOH cooled below (5°C) was added a drop wise to the solution of diazonium chloride and stirred for (30 min). The solution leaving overnight, the solution was acidified with dilute HCl until pH = 5. The precipitate was filtered off, and recrystallized twice from hot ethanol, and dried in a vacuum desicator.
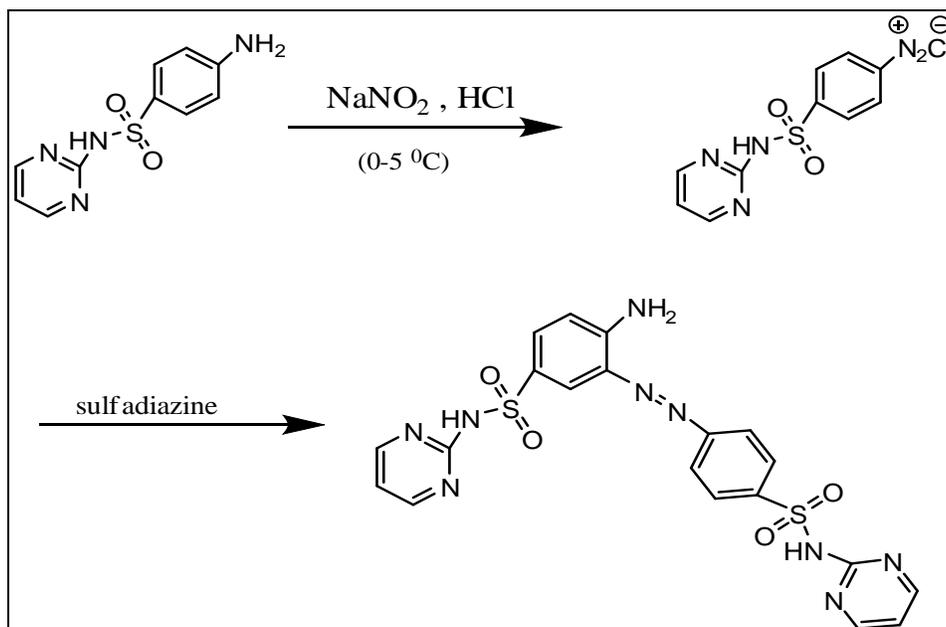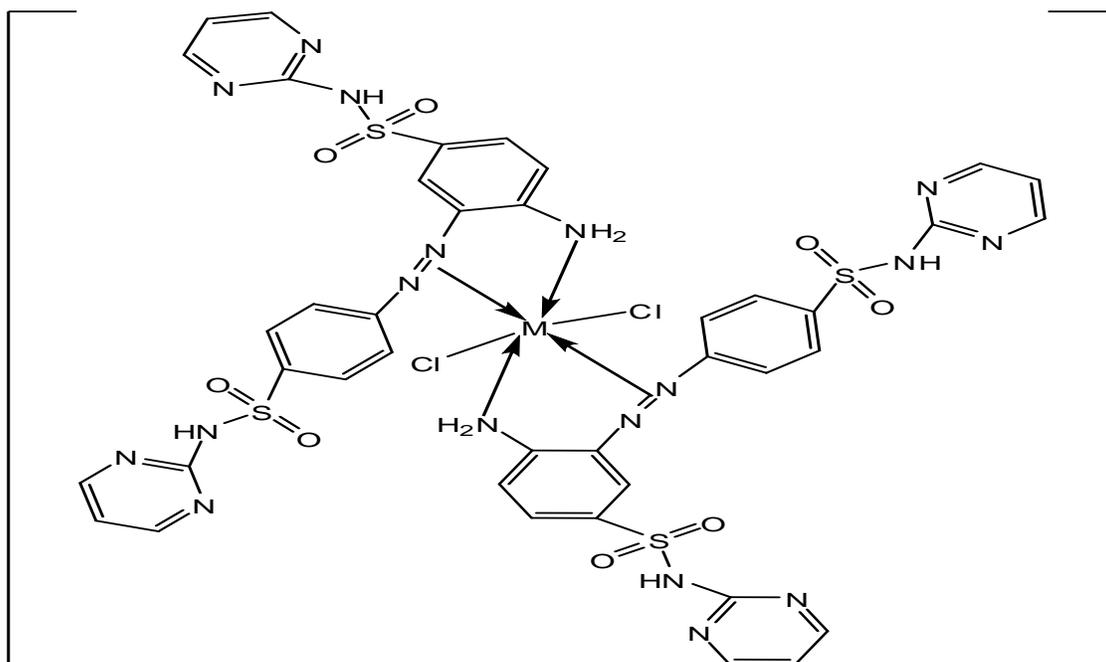
Scheme 1

Scheme 2:The suggested geometry of chelete complexes M = Co(II), Ni(II)

Preparation of metal complexes

The complexes were prepared by the mixing of 50 ml ethanolic solution of the salts (CoCl$_2$.6H$_2$O and NiCl$_2$.6H$_2$O) with the 50 ml of ethanolic solution of azo reagent (SA) in (1:2) (metal : reagent) ratio. The resulting mixture was refluxed for (2 hrs). The precipitation was collected by filtration, washed several times with ethanol and dried under vacuum and recrystallized with ethanol several times.

RESULTS AND DISCUSSION

The study analytical data for the azo reagent (SA) and complexes with some physical properties are shown in Table(1). The analytical data of the complexes correspond well with the general formula $[MR]X_2$ where R=(SA), M= Co(II) and Ni(II).

Table 1: Analytical data and physical properties of the reagent (SA) and complexes.

No.	Compound color	m.P °C	Yield%	Molecular formula	Found (Calc.)%				
					C	H	N	S	M
1	R=(SA) Reddish brown	255-257	88	$C_{20}H_{17}N_9O_4S_2$	45.587 (46.96)	3.218 (3.35)	24.0225 (24.64)	12.17 (12.54)	-
2	Co-SA Dark purple	262-264	80	$C_{40}H_{34}N_{18}O_8S_2Cl_2Co$	34.301 (34.82)	2.331 (2.48)	17.969 (18.27)	9.121 (9.29)	5.97 (4.27)
3	Ni-SA brown	186-188	85	$C_{40}H_{34}N_{18}O_8SCl_2Ni$	34.438 (34.82)	2.335 (2.48)	17.912 (18.27)	9.144 (9.30)	3.981 (4.25)

Absorption spectra

In aqueous ethanolic solution 50% (V/V) was studied for the synthesized complexes showed the absorption spectra was a bath chromic shift ranging about (70-90 nm). The absorption spectra of reagent (SA) and Co(II) and Ni(II) chelate complexes is shown in Fig   (1-3).
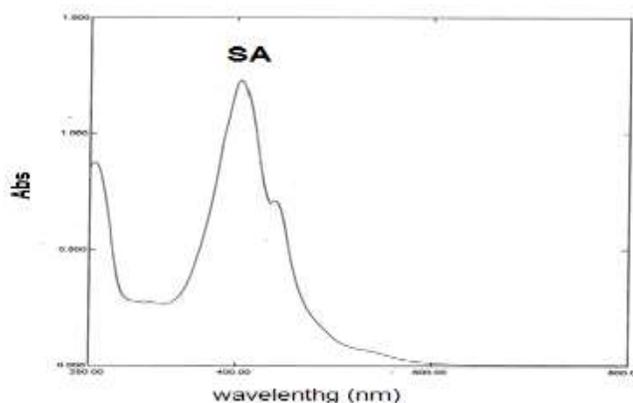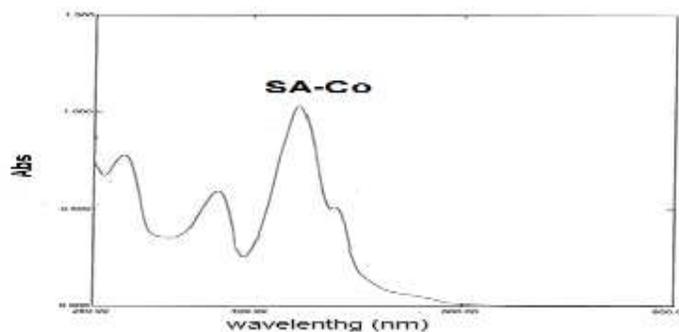

Figure 1: The absorbance spectra of free Reagent (SA)

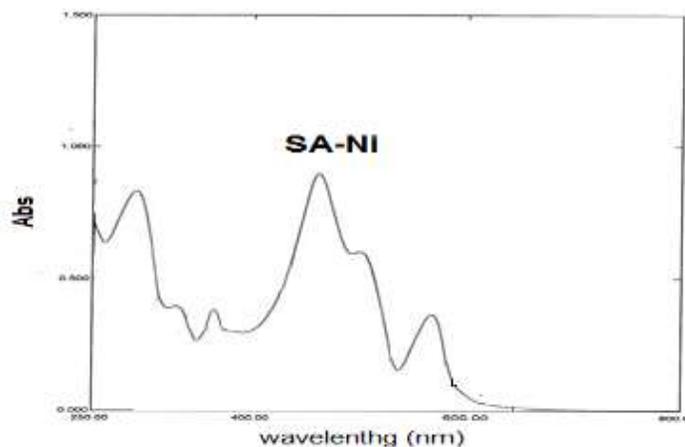**Figure 2:The absorbance spectra of Co(II) complex with(SA)**

Figure 3:The absorbance spectra of Ni(II) complex with(SA)

Effect of PH

The effect pH of the absorbance values of the complexes were studied in the 50%(v/v) ethanolic by changing the pH value of the solution and the results are shown in Table 2 , where demonstrated that the best absorbance of Co(II) and Ni(II) (SA) system is in the range (7.5-8.5). The reagent formed a stable complex with metal ions at same pH.

Metal: Reagent ratio

Ratios (metal: reagent) of complexes were measured by molar ratio method at fixed pH , concentration and wavelengths of maximum absorption. The results are given in Table 2, the reagent was found to form (2 : 1) chelates with all metal ions.

Calculation of the metal complexes stability constant

Stability constants of complexes are obtained spectrophotometrically by measuring the absorbance of solutions of reagent (SA) and metal mixture at wavelength (λmax) and pH values. The degree of formation of the complexes is obtained according to the relationship[20], $\beta = (1 - \alpha) / (4\alpha 3c2)$, and $\alpha = (Am - As)/Am$, where As and Am are the absorbance's of the partially and fully formed complexes respectively at optimum concentration. The calculated β and Log β values for the synthesized complexes are shown in Table (2).

Table 2: metal: reagent stability constant value (β), molar conductivity, optimal concentration and wave length

No.	Metal ions color	PH	wave length (λ_{max})nm	molar conc. x 10^{-5} M	β $L^2.mol^{-2}$	log β	Molar conduc. $S.mol^{-1}.cm^2$
1	Co-SA brwon–red	7	490	2.6	$613*10^{10}$	12.787	73.23
2	Ni-SA Green	6.5	470	1.7	$511*10^{10}$	12.708	66.91

Infrared spectra

Selected IR absorption of the ligand and its complexes are given in Table 3.

In order to clarify the mode of bonding and the effect of the reagent(SA) to the metal ion of the complexes, the FT- IR spectra of the free reagent and the metal complexes were studied and assigned based on carful comparison of their spectra with that of the free reagent. The bands in the region 3388-3348 cm^{-1} due to stretching mode of ν (NH$_2$) group and at 3290 cm^{-1} due to stretching of ν (NH) sulfonamide, 1624-1590 cm^{-1} due to ν (C=N) group of pyrimidine ring which is remains in the same region in free reagent and in complexes. The ν(N=N) stretching vibration appears at 1480 cm^{-1} in the free reagent spectra. This band appearing at (1490 – 1484 cm^{-1}) with different shape in the spectra of complexes. Both band shifted and reduced intensity due to complex formation. The spectrum of free reagent show two absorption bands at 1335 and 1160 cm^{-1} due to symmetrical and asymmetrical of ν(SO$_2$)) sulfonamide. These bands are stable in position and intensity in both reagent and its metal complexes. New weak bands in the region 465 and 435 cm^{-1} were observed in the spectra of metal complexes. These bands were not present in the spectrum of reagent, and they due to ν (M─N).

3-6.^{1}H-NMR spectrum, (δ ppm), (DMSO-d6):

((1<u>H</u>) (-NH) $_{sulfonamide}$ 11.256), (CH=N) pyrimidine 8.494), (Ar-<u>H</u>) 7.266 -7.967), ((2H) (NH$_2$) 7.047).

Table 3: Characteristic IR absorption bands of the reagent (SA) and its complexes in cm^{-1} units (KBr disk)

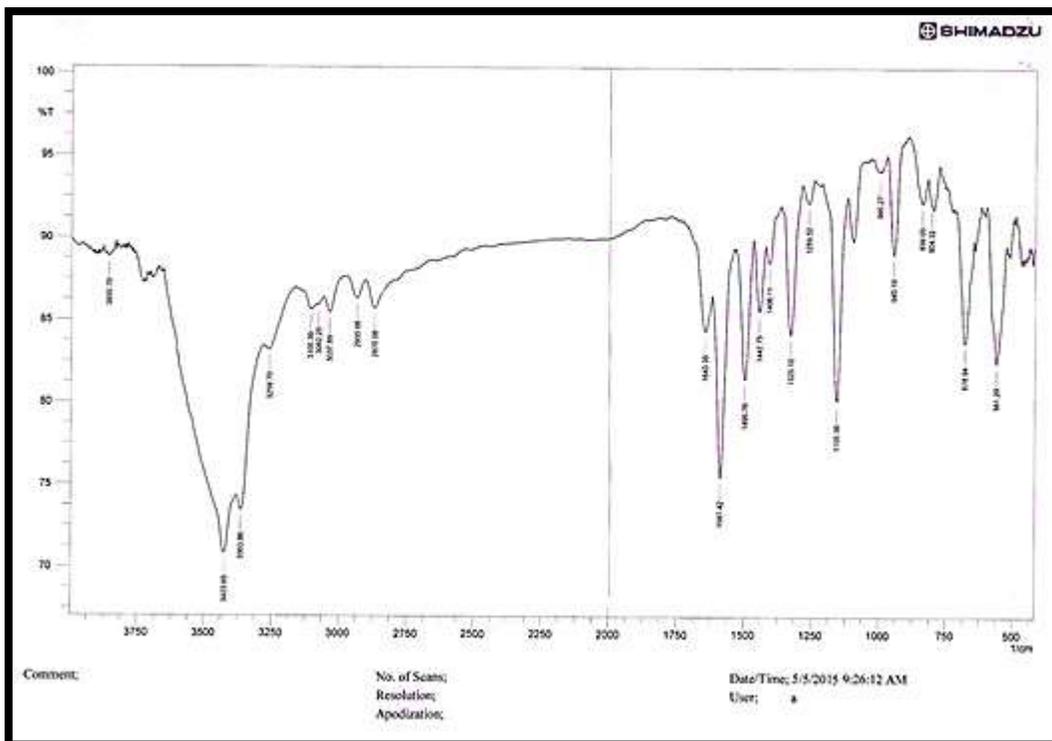| No.	Compound	ν (NH$_2$)	ν (NH)	ν (C=N)	ν (N=N)	ν (SO$_2$)	ν (M-N)
1	R=(SA)	(3388-3348)	3290	1598	1480	1335 1160	-
2	Co-SA	(3371-3338)	3280	1624	1489	1317 1149	435
3	Ni-SA	(3420-3378)	3285	1590	1494	1330 1180	465

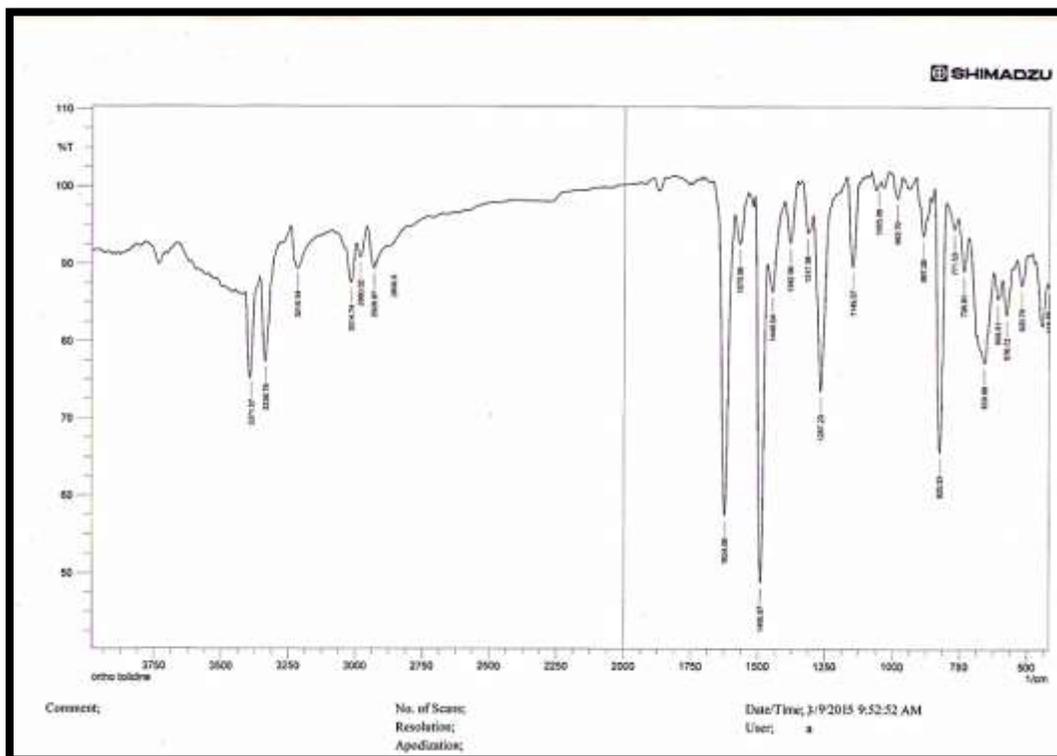**Figure 4: FT-IR Spectrum of (SA) reagent**

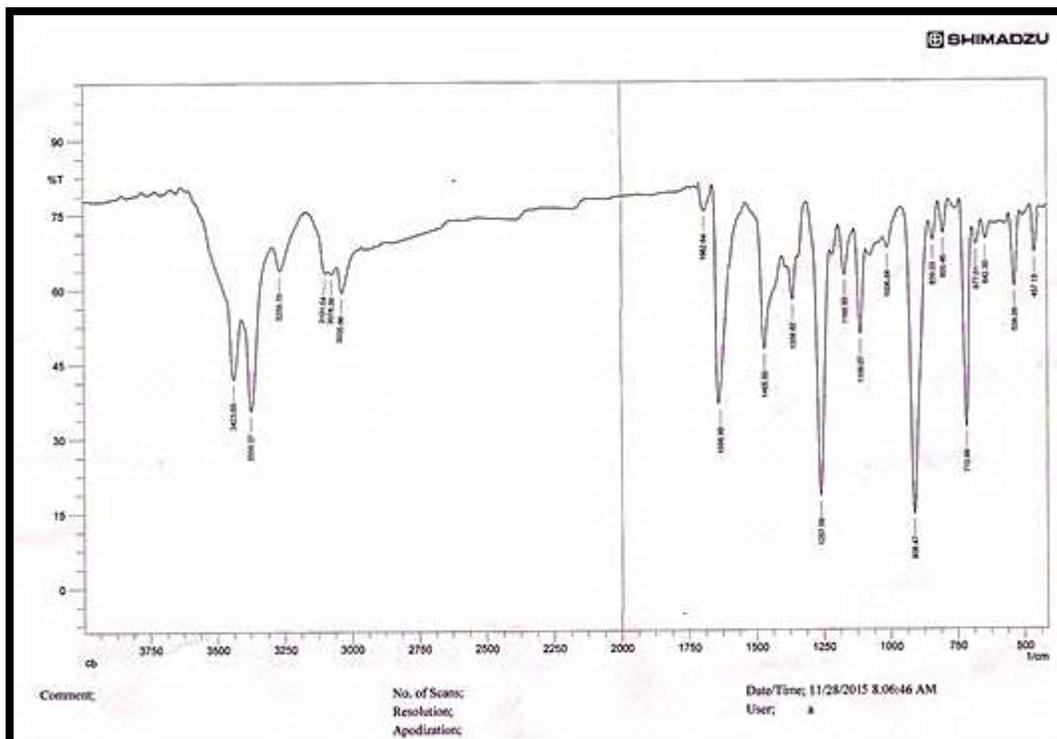**Figure 5: FT-IR Spectrum of Co(II) complex with (SA) reagent**

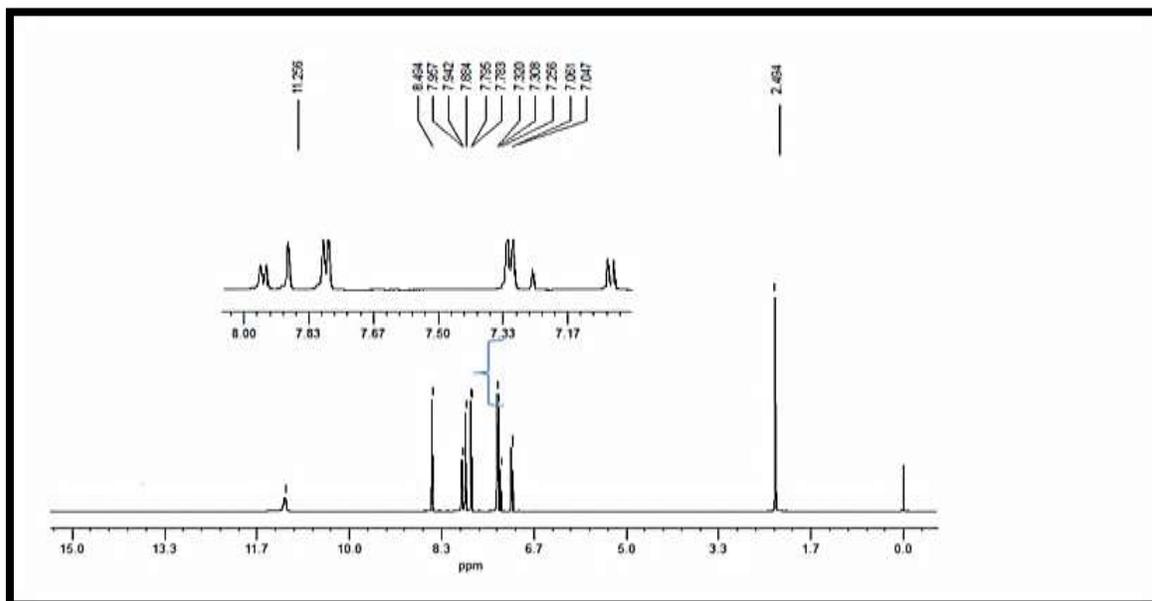**Figure 6: FT-IR Spectrum of Ni(II) complex with (SA) reagent**

Figure 7:^{1}H-NMR Spectrum of (SA) reagent

Antibacterial activity test

Azo reagent (SA) and complexes were screened for antibacterial activity against Escherichia coli, Pseudomonas aeruginosa, and Staphylococcus aureus in Muller Hinton agar [21] by measuring the inhibition zone in (mm). Each bacteria isolated was inoculated on to the Muller-Hinton Agar

[sterilize in autoclave] by dipping a cotton swab in to the suspension and streaking over the surface of the agar plates. Then, in the solidified medium, four holes were made (6 mm). These holes were filled with (0.5 ml) of the prepared compounds ((300 µg/ µL) of the compound dissolved in 1ml of DMSO solvent). These plates were incubated at 37 ^{0}C and measured of zone inhibition after 48 hours. The results are presented in Table 4.

Table 4 Antibacterial activities of compounds SA, Co- SA and Ni- SA.

Comp. No.	Escherichia Coli		Staphylococcus aureus		Pseudomonas aeruginosa	
	Zone of inhibition (mm)	% Inhibition	Zone of inhibition (mm)	% Inhibition	Zone of inhibition (mm)	% Inhibition
SA	50	250	25	132.5	34	133.33
Co- SA	35	175	35	185.5	0	0
Ni- SA	30	150	0	0	35	116.67

When we show the data of (inhibition zone %) of all compounds in Table 4 we observe some important results: The first that all compounds showed good activity against Escherichia coli, SA and Co- SA compounds showed good activity against Staphylococcus aureus, and SA and Ni- SA compounds showed good activity against Pseudomonas aeruginosa.

CONCLUSION

In this paper report the synthesis, characterization and spectroscopy study of new azo reagent derived from sulfadiazine and its complex with Co(II) and Ni(II) metal ions. The isolated complex was characterized by available techniques. The aryl azo reagent (SA) behaves as a bidentate chelating agent and coordinating through the N atom of sulfadiazine and another nitrogen atom of azo group which is to form five-membered metals ring. The coordination of the metal ions Co(II) and Ni(II) with reagent(SA) are to give hexa coordinated show octahedral stereochemistry.

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