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Thermal, Spectroscopic and Antimicrobial Properties of Novel Nickel(II) Complexes with Sulfanilamide and Sulfamerazine Drugs

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Authors' contributions

This work was carried out in collaboration between all authors. Author GP designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author RG managed the analyses of the study. Author NB managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Synthesis and characterisation of metal-based Sulfa drugs have gained much attention in the past few decades, owing to their enhanced therapeutic applications. The present work aims to synthesise novel complexes of Nickel(II) with Sulfanilamide and Sulfamerazine, to prepare new metallodrugs with potential biological activities. The synthesis involves microwave irradiation method that provides a greener way for the synthesis of metallodrugs. Elemental, spectral and thermogravimetric analysis has been carried out to decipher the structural and coordination properties of drug molecules with the metal ion and to interpret the thermal Stability and decomposition behaviour of the complexes. Finally, the microbiological investigations have been done to explore the antibacterial activities of newly formed complexes. The study has been conducted at the Green Chemistry Research Centre, Govt. Dungar College, Bikaner and Ceramic Electrical Research and Development Centre, Bikaner. Effective metal drug coordination was

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confirmed by marked shifts observed in the UV/VIS spectrum of the complexes with respect to the parent drugs. FT-IR spectral studies revealed that sulfanilamide molecule coordinated to the metal ion only through its sulfonamidic nitrogen, whereas sulfamerazine molecule exhibited identity, chelating through its pyrimidic and sulfonamidic nitrogen atoms. Practically unaffected IR bands corresponding to the ligand SO_2 group ruled out any possibility of coordination through O atom. Thermal stability of the complexes was determined through thermogravimetric (TGA) and differential thermogravimetric analysis (DTA). Important thermodynamic and kinetic parameters for their decomposition reactions were hence evaluated using Coats and Redfern integral equation. Antibacterial activities for both the complexes and pure drugs were screened against *E. coli, S. aureus* and *B. subtilis*. Whereas the efficacy of sulfamerazine is substantially enhanced upon metallation, the sulfamerazine complex showed diminished antibacterial properties as compared to its parent drug.

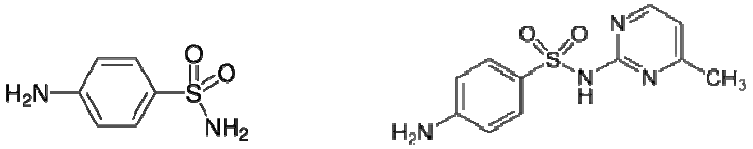
Keywords: Complexes of Ni(II); sulfanilamide; sulfamerazine; microwave synthesis; thermogravimetric analysis; Coats- Redfern integral equation; antibacterial activities.

1. INTRODUCTION

Sulfonamides have known to be the very first chemotherapeutic agents administered clinically in the human biological systems as antibacterial drugs. They are the derivatives of p-amino benzenesulfonamide (Sulfanilamide) [1] and possess their antibacterial action due to the competitive inhibition of the enzyme dihydropteroate synthetase towards the substrate p-aminobenzoate [2]. They are antibiotic medicinal drugs having wide therapeutic and pharmacological importance and are widely used as an antibacterial, antitumor, diuretic, anti-carbonic anhydrase, hypoglycaemic, anti-thyroid and protease inhibitors [3]. With the advancement of medicinal inorganic chemistry, new metal-based compounds known as metallodrugs emerged as advanced therapeutic agents that possessed enhanced pharmacological and toxicological properties. The pharmacological and toxicological properties of such metallodrugs are found to be profoundly modified, as compared to their parent drugs [4]. Owing to the presence of effective donor atoms such as N, O, and S, Sulfanilamide and its derivatives have an excellent ability to form chelates with transition metal ions. The antimicrobial properties of sulfonamides are found to increase variably their coordination with metal ions [5]. These metal-based sulfa drugs are widely used as anticancer agents, antibiotics, antibacterials, antivirals, anti-parasites radiosensitising agents and antidiabetics [6]. In the past few decades, different authors have reported the synthesis and biological studies of various metal complexes of sulfa drugs and their derivatives [7-19], but still, this field meets a big lacuna in terms of detailed structural and biological properties of great many new sulfa drug-metal complexes. Also, it appears that microwave assisted synthesis and thermal properties of many of these complexes have not been meticulously investigated.

In the light of this knowledge, we have initiated keen research to decipher new metal-based sulfa drugs by exploiting the versatile coordinating behaviour of sulfanilamide, and it's unsubstituted derivatives of the types- Sulfapyridine, Sulfadiazine, Sulfamerazine and Sulfamethazine. In continuation with our earlier work of microwave-assisted organic synthesis (MAOS) and structural as well as thermal characterisation of some biologically active Fe(III) based sulpha drugs [20], we are here by describing the green synthesis of Ni(II) based complexes with sulfanilamide and sulfamerazine (Fig. 1).

Elemental analyses and spectroscopic characterisation (UV/VIS and FT-IR) of the newly formed complexes are herein discussed in this paper to explore the coordination behaviour and relationship of Nickel metal with these ligand



(a) **(b)**

Fig. 1. Chemical structure of Sulfadrugs (a) Sulfanilamide and (b) Sulfamerazine

drugs and to understand the role of metal drug bonding in modifying the biological activity of parent drug molecules. Also since the ease of metal-ligand bond cleavage greatly affects the biological aspects of these metallodrugs in the biological systems, it, therefore, requires a systematic knowledge of thermal stability and decomposition behaviour of these complexes under the influence of varying temperature. The thermal studies (TGA/DTA) were hence conducted for the complexes which also supported the structural findings done through spectroscopic methods. Thermogravimetric data (TGA, DTA and DTG curves) has been utilised to evaluate important kinetic and thermodynamic parameters of Ni(II)-Sulfonamide complexes for their different decomposition stages, using a graphical method of Coats and Redfern [21]. Both the metal drug complexes were also screened for their antibacterial activities against three bacterial strains namely, *Escherichia coli, Staphylococcus aureus and Bacillus subtilis.*

2. MATERIALS AND METHODS

The Nickel salt [$Ni(NO_3)_2.6H_2O$], Sulfa drugs (Sulphanilamide i.e. [4-aminobenzenesulfonamide] and Sulfamerazine i.e. [4-amino-N-(4-methylpyrimidin-2-yl) benzenesulfonamide]) and solvents (acetone and dimethyl sulfoxide) used in the study were of analytical grade (Hi-media). Synthesis of the metal drug complexes mainly involved the preparation of separate solutions of ligand drugs (3 mmol) and metal salt (1 mmol) in acetone solvent, which was finally mixed. The resultant reaction mixture, in each case, was separately subjected to microwave irradiation method as well as conventional heating method.

2.1 Microwave Irradiation Method

In this method, the reaction mixture was irradiated in a microwave reactor for 4- 5 minutes at a medium power level (600W) with occasional shaking [22-26].

2.2 Conventional Method of Synthesis

This method mainly involved heating of the reaction mixture at a temperature of 35°C for 3 hours along with continuous stirring.

The reaction scheme is given as

$$Ni(NO_3)_2.6H_2O + SA \rightarrow [Ni(SA)_2(NO_3)_2] + 6H_2O$$

$$Ni(NO_3)_2.6H_2O + SM \rightarrow [Ni(SM)(NO_3)] + HNO_3 + 6H_2O$$

Where SA represents sulfanilamide and SM represents Sulfamerazine. In both the cases, the reaction proceeded with colour change and was monitored by thin layer chromatography(TLC). The powdery amorphous metallodrug complexes hence precipitated were finally cooled, filtered, washed with doubly distilled water and ethanol and were finally dried in desiccators. Wherein the conventional method yielded 61% and 68%, the green process of microwave synthesis gave 73% and 79% of Sulfanilamide and Sulfamerazine metal complex respectively. Melting points of complexes were experimentally observed and were found to be 175°C and 250°C for sulfanilamide and sulfamerazine Ni(II) complexes respectively. The physicochemical data of both complexes are given in Table 1.

The solid complexes formed were found to be insoluble in water and were soluble in DMSO. The UV/VIS spectra of drugs and their metal complexes were recorded by double beam spectrophotometer of Royal model with quartz cell of 10 mm light path in solvent DMSO within the range 200-1100 nm. FT-IR spectra of the complexes were recorded on Bruker Optic Model Alpha (FT-IR) (Zn-Se Optics, ATR) (4000 - 400 cm^{-1}) using KBr disc at SIL, P.G. Dept. of Chemistry, Govt. Dungar college (NAAC-A-Grade) Bikaner, Rajasthan. Thermal analyses (TGA, DTA and DTG thermograms) of complexes were carried out in an inert nitrogen atmosphere at a heating rate of $10^{o}Cmin^{-1}$, using Mettler Toledo (TGA/DSC IHT/546) STARe system at CERDC, Bikaner. The weight loss was measured from 30°C to 900°C using alumina crucible. The antibacterial studies of drug and complexes were conducted by using nutrient Muller Hinton Agar medium (Himedia). The in-vitro antibacterial assays were performed by disc diffusion- zone inhibition method [27] using bacteria such as *Escherichia coli*, *Staphylococcus aureus* and *Bacillus subtilis*. All the antibacterial testing were carried out with horizontal laminar at BIFR, Bikaner. The inoculated plates were incubated at 37°C and observed after a period of 24 hours. The results (in DMSO) in the form of inhibition zones were measured with an accuracy of 0.5mm and inoculation with only DMSO solvent was also done as a control. The formations of the structure of Ni(II)complexes of Sulfanilamide and Sulfamerazine are shown in Fig. 2(a) and 2(b) respectively.

Table 1. Physico-chemical data of Ni(II) sulfa drug complexes

Compound	BM	Colour	Melting point (°C)		Elemental analysis Calcd (Found) %		
			Expt.	DTA	C	N	H
$[Ni(SA)_2(NO_3)_2]$	3.3	Light Green	175	180	27.25 (27.05)	3.05 (3.01)	15.89 (15.62)
$[Ni(SM)(NO_3)]$	3.2	Pale yellow	250	252	34.23 (34.18)	3.13 (3.11)	18.23 (18.20)

SA= Sulfanilamide, SM=Sulfamerazine, DTA= Differential Thermogravimetric Analysis

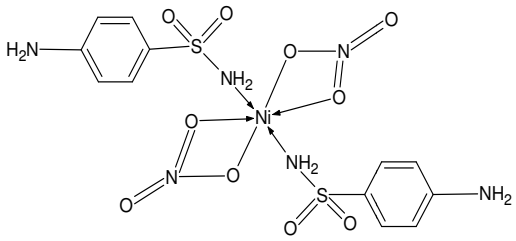


Fig. 2(a). $[Ni(SA)_2(NO_3)_2]$

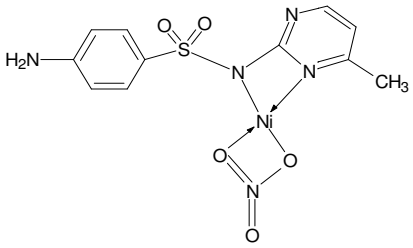


Fig. 2(b). $[Ni(SM)(NO_3)]$

3. RESULTS AND DISCUSSION

3.1 Electronic Spectra

UV/Vis spectra of pure drugs and their nickel(II)complexes were recorded in the wavelength range of 200-1100nm with DMSO as a solvent. The d-d bands of complexes are not well defined and seem to be submerged in the tail of the strong inter ligand transitions or charge transfer bands, that is fairly clear. The recorded spectra and the spectral bands (λ_{max}) are given (200-400 nm) in Fig. 3.

The resonance stabilised the structure of Sulfonamides, merges the UV bands of their phenyl and SO_2 groups, in an aqueous medium, to exhibit a single strong absorption band in the region of 265 nm, that is assigned to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions. In DMSO, this single

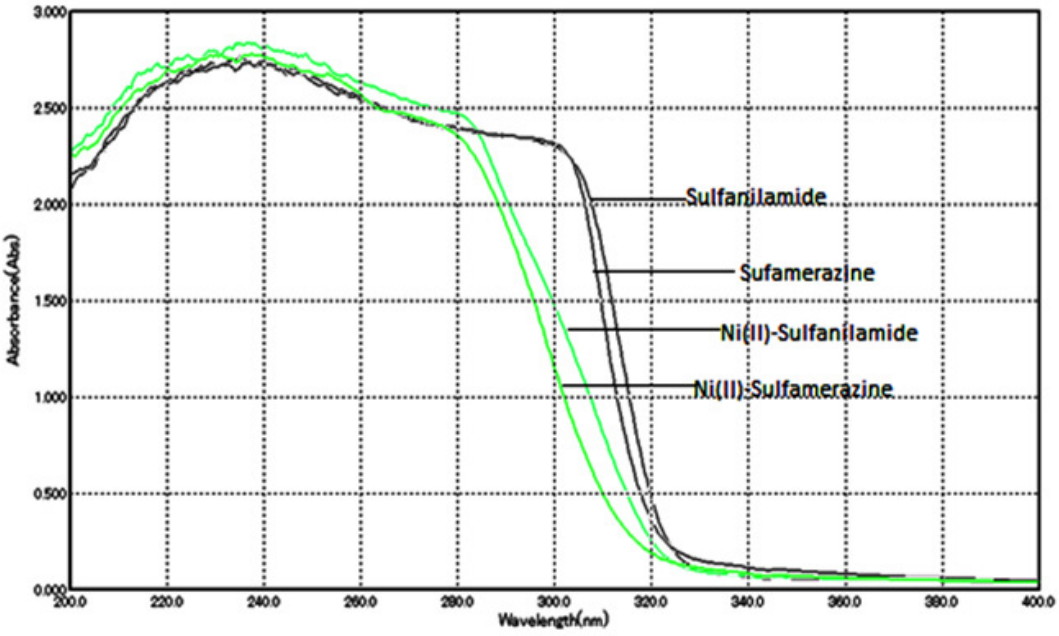


Fig. 3. UV-VIS spectra of Ligands and their Nickel(II) complexes

characteristic band appears around 300 nm. Upon chelation, an appreciable amount of blue shift has been observed for both the complexes, clearly indicating the coordination of sulfonamide ligands with Ni(II) ion in their metal complexes. The substantial decrease in λ_{max} values in metal complexes may be attributed to the decrease of electron delocalisation in the ligand molecule upon coordination with a metal ion. The resonance stabilisation of sulfa drugs is known to be greatly influenced by the electrophilicity or the nucleophilicity of the reaction medium. A reaction medium with high electrophilicity, such as acetone, supports the donor behaviour of this drug molecules to form stable complexes with Ni(II) metal ion.

3.2 FT-IR Analysis

In the present study, the observed vibrational wavenumbers of sulfanilamide and sulfamerazine nickel complexes are compared with those of free drugs. Sulfonamides are potential ligands and can act as monodentate, bidentate or tridentate based on their structures. Hence, the complete IR assignments thus become very important to identify the chelation mode of sulfa drugs with metal ions. The infrared spectrum of the free Sulfanilamide ligand showed two strong bands at 3478 and 3375 cm^{-1} due to the asymmetric and symmetric stretching vibrations of the amino group ($-NH_2$) [28-33]. One medium strong band that appeared at 3267cm^{-1} attributes to the symmetric stretching frequency of the sulfonamide group($-SO_2NH_2$). Similarly, in the case of Sulfamerazine, the two amino bands were observed at 3483 and 3380 cm^{-1}, whereas the substituted sulfonamide group appeared as a single split weak band at 3254 cm^{-1}. Bending vibration band of the primary amino group was shown nearly at 1628 cm^{-1} for sulfanilamide and 1596 cm^{-1} for sulfamerazine (Figs. 4a and 5a).

In both the metallodrug complexes (Figs. 4b and 5b), it was observed that the position of amino bands ($-NH_2$) was completely unaffected, thereby clearly indicating non-coordination of this group of the ligand with a metal ion. In the sulfanilamide complex, although the sulfonamide symmetric stretching band is only slightly perturbed and appears almost at the same position as the ligand, the bending vibrational bands of an amide group, shown by the pure drug at 1572 cm^{-1} is substantially shifted to lower wavenumber and

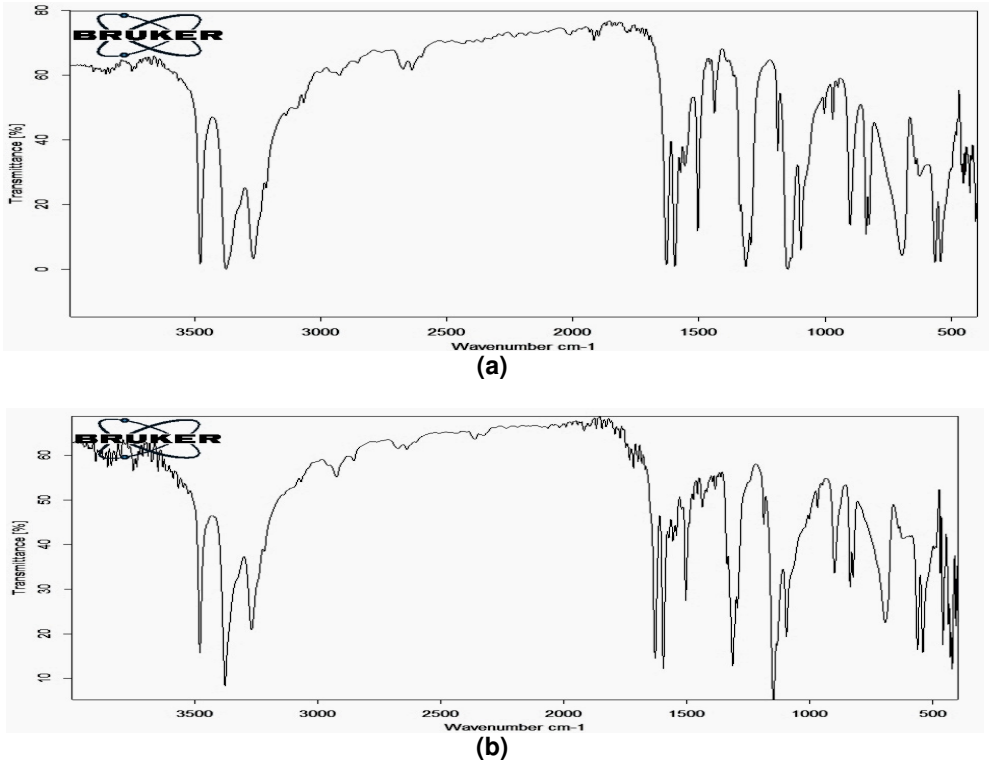


Fig. 4. Experimental FT-IR spectra of (a) Sulfanilamide, (b) Ni(II)-Sulfanilamide complex

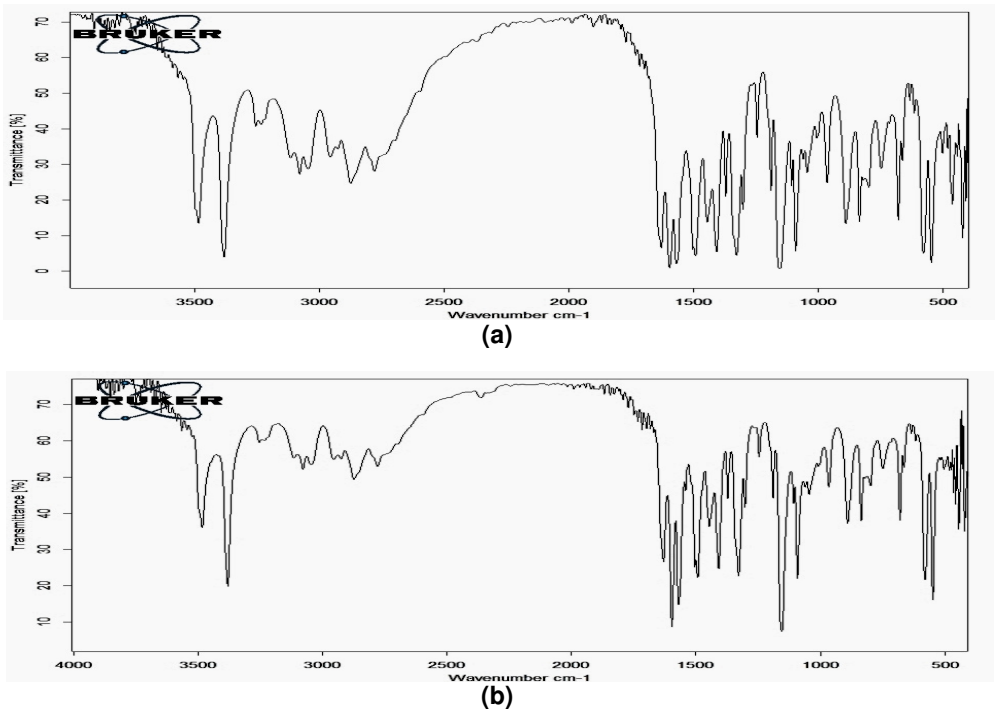


Fig. 5. Experimental FT-IR spectra of (a) Sulfamerazine and (b) Ni(II)-Sulfamerazine complex

appears at 1564 cm^{-1}. Also, the wagging sulfonamide band that appears at 626cm^{-1} in the pure drug is diminished in its nickel complex. This confirms the chelation of sulfanilamide ligand in its Ni(II) complex is through sulfonamide group via N atom. Similarly, in the case of sulfamerazine complex, the only amide band that is exhibited in the pure drug is highly diminished. Also, the bending vibrational band for amide δ(-NH-) (observed at 1006 cm^{-1} in the ligand) is missing in case of its metal complex, confirming the chelation of sulfamerazine to the metal ion via deprotonated sulfonamidic N atom. The sulfonyl group appeared as three distinct bands with wavenumbers 1314, 1147 and 563 cm^{-1} in sulfanilamide and at 1328, 1154 and 579 cm^{-1} in sulfamerazine. In case of both the complexes it was observed that the sulfonyl peaks are completely unaffected and appeared exactly at the same frequency as their parent drugs. This observation rules out any role of the sulfonyl group in coordination with a metal ion. In the nickel complex of sulfamerazine two new bands are observed in the region 1541and 616 cm^{-1}, not present in the IR spectrum of pure drug. These new bands correspond to the M-N bond with pyrimidinic N atom. Both complexes [34] exhibit two bands around 1750 and 1780 cm^{-1}corresponding to the presence of bidentate nitrate groups.

Thus in Ni(II-)Sulfanilamide complex the coordination of drug molecule with the metal is only through sufonamidic N atom and hence it exhibits a monodentate behaviour. However, in the case of Ni(II)-Sulfamerazine complex, the drug molecule exhibits bidentate behaviour by chelating to the metal ion via pyrimidinic and deprotonated sulfonamidic N atom. In both the cases vibrational frequencies corresponding to ν(M-O) and ν(M-N) were shown at 470, 429 cm^{-1} and at 472, 430 cm^{-1} for sulfanilamide and sulfamerazine nickel complex respectively.

3.3 Thermal Analysis

Thermograms, showing a mass loss with temperature, ranging from 30- 900°C were recorded for both the complexes along with their DTA and DTG curves. Any possibility of the presence of lattice water in both the complexes was ruled out by the absence of any mass loss till 150°C.

3.3.1 Ni(II)-Sulfanilamide complex $[Ni(SA)_2(NO_3)_2]$

The TGA, DTG and DTA thermograms for the metal complex are shown in Fig. 6. The data support a three-stage decomposition process

starting from 30℃ to 600℃. The complex remained practically stable till 170℃, where after it started melting at nearly 180℃, which corresponds to the experimental m.pt. of Ni(II)-Sulfanilamide complex at 175℃. This state change was clearly demarcated by a sharp endothermic peak that is observed in the DTA curve of a complex. Subsequently, the complex underwent slow decomposition after 270℃ showing the first step of endothermic degradation, with maximum mass loss observed at 295℃ (DTG curve). This decomposition may be attributed to the loss of aminophenyl moiety from the ligand, observing a net loss of 17.46% (calcd. 16.67%). In the second stage, the fragmented metal drug complex decomposed within a range of 320-380℃. Estimated mass loss of 28.51% (calcd. 28.57%) for this endothermic stage corresponds to the removal of two nitrate groups. The final decomposition step (390℃- 600℃), accompanied by a mass loss of76.01% (calcd. 76.80%), shows a broad exothermic peak indicating the final breakdown of the complex to yield a dark blackish residue of

Table 2. Important infrared frequencies (cm^{-1}) of drugs and their metal complexes

Funtional groups		Sulfanilamide (SA)	$[Ni(SA)_2(NO_3)_2]$	Sulfamerazine (SM)	$[Ni(SM)(NO_3)]$
Aromatic amino group (NH_2)	$\nu_{asym}(NH_2)$	3478	3478	3483	3483
	$\nu_{sym}(NH_2)$	3375	3375	3380	3380
	$\delta(NH_2)$	1628	1628	1596	1596
Amido group (-NH-)	$\nu_{asym}(NH)$	-	-	3252, 3232	3254, -
	$\nu_{sym}(NH)$	3267	3267	-	-
	$\delta(NH)$	1572	1564	1569	-
	$\omega(NH)$	626	-	-	-
($-SO_2-N$) Moiety	$\nu_{asym}(SO_2)$	1314	1313	1328	1328
	$\nu_{sym}(SO_2)$	1147	1148	1154	1154
	$\delta(SO_2)$	563	563	579	579
Nitrate group NO_3 ($\nu_1+\nu_4$)		-	1750, 1780	-	1747, 1780
Pyrimidic					
$\nu(M-N)$		-	-	-	616
$\nu(M-O)$		-	470	-	472
$\nu(M-N)$		-	429	-	430

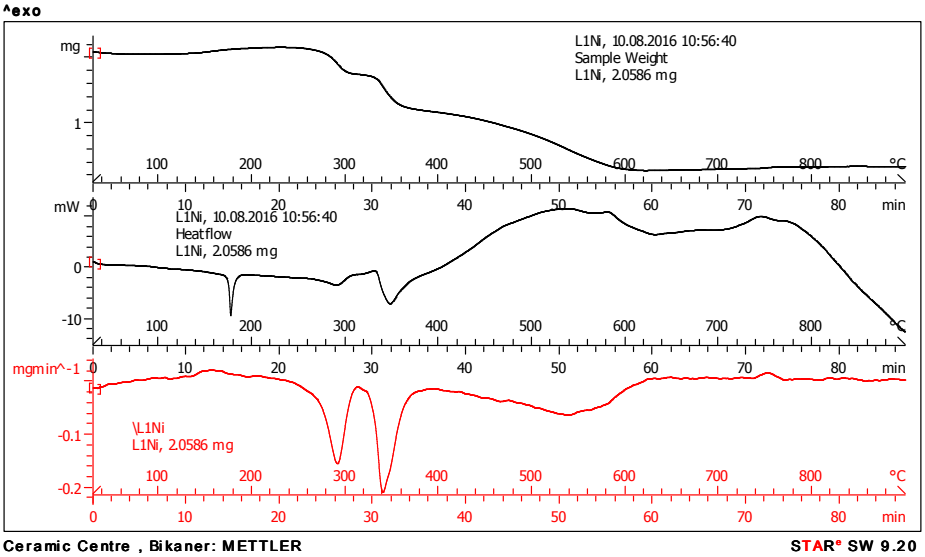


Fig. 6. Thermogravimetric analysis (TGA), Differential thermogravimetric analysis (DTA) and Derivative thermogravimetric (DTG) curves for Ni(II)-Sulfanilamide complex

NiO. Thereafter the mass remained constant till 900℃ confirming complete decomposition of the complex.

3.3.2 Ni(II)-Sulfamerazine complex [Ni(SM)(NO_3)]

As shown in Fig. 7, the sulfamerazine complex seems to follow a slow but steady degradation process including three stages of decomposition. Almost like the sulfanilamide complex, this complex also remained stable and underwent decomposition only after its melting point which was observed at 252°C (except. m.pt. 250°C). The DTA thermogram indicates a small yet very clear endothermic peak for the melting point. The complex thereafter exhibited an immediate decomposition, between a range of 250°C - 320°C, corresponding to the loss of amino-phenyl and methylene fragments, involving a mass loss of 27.59% (calcd. 28.36%). The second stage of decomposition (330°C - 440°C) observed a very small mass change and was quite diminished, observing a total mass loss of 22.64% (calcd. 18.75%) due to loss of nitrate group. The final decomposition exhibited a broad exothermic curve between 450°C - 640°C with a total mass loss of 65.35% (calcd. 64.10%) attributing to the formation of the final dark residual solid of NiO.

3.4 Evaluation of Kinetic Parameters

The kinetics of a heterogeneous solid state reaction occurring in non -isothermal conditions can be expressed by using Arrhenius equation:

$$\frac{d\alpha}{dT} = \frac{A}{\beta} e^{-\frac{E}{RT}} . f(\alpha) \quad (1)$$

where *A* is the pre-exponential factor or the frequency factor, *E* is the activation energy of the reaction, *β* is the linear heating rate in °C/min, *T* is the temperature, *R* is the universal gas constant, $f(\alpha)$ is the conversion function dependent on the reaction mechanism, and α is the extent of reaction which can be calculated from TGA/ DTA data as;

$$\alpha = \frac{m_o - m_t}{m_o - m_f} \quad (2)$$

where m_o, m_t and m_f are the masses of the sample at the beginning of the reaction, at a particular temperature and the end of reaction, respectively. Kinetic parameters for a given process can be evaluated by using non-isothermal rate laws [35]. Model fitting methods involve various reaction models that may be used to derive temperature curves and hence to determine the order of reaction, activation energy and frequency factors.

In the present study, Coats and Redfern integral equations are used for determining kinetic parameters for all the steps of decomposition. For selecting the final order of each reaction, a comparison of linearity between plots having varying orders of the reaction was done. Coats and Redfern method can be expressed as the following relationship;

$$ln\left[\frac{-ln(1-\alpha)}{T^2}\right] = ln\left[\frac{AR}{\beta E}\left(1-\frac{2RT}{E}\right)\right] - \frac{E}{RT} \quad for\ n = 1 \quad (3)$$

$$ln\left[\frac{1-(1-\alpha)^{1-n}}{T^2(1-n)}\right] = ln\left[\frac{AR}{\beta E}\left(1-\frac{2RT}{E}\right)\right] - \frac{E}{RT} \quad for\ n \neq 1 \quad (4)$$

where *n* is the order of reaction. In the present studies, the heating rate *β* is taken to be 10°C/min.

A plot of $ln\left[\frac{-ln(1-\alpha)}{T^2}\right]$ vs $1/T$ for n = 1 and $ln\left[\frac{1-(1-\alpha)^{1-n}}{T^2(1-n)}\right]$ vs $1/T$ for n = 0, 1/2, 3/2 etc., yields the value of activation energy *E* from the slope and the value of frequency factor *A* from the intercept. Fig. 8 shows Coats Redfern plot for the second stage of decomposition of both complexes.

Applying different values of *n* equations (3) and (4) were plotted as mentioned above for both the metal drug complexes. The final linear plot with the best correlation coefficient was selected to get the correct value of *n*, for all the stages of decomposition.

3.5 Evaluation of Thermodynamic Parameters

The thermodynamic parameter, ΔS entropy of activation was calculated using;

$$\Delta S = R\ ln\left[\frac{Ah}{kT_{max}}\right]$$

where T_{max} is the DTG peak temperature and *h* and *k* are Planck and Boltzmann constants respectively. Enthalpy of reaction ΔH and Gibbs free energy ΔG were calculated by standard thermodynamic relations;

$$\Delta H = E - RT$$
$$\Delta G = \Delta H - T\Delta S$$

The calculated thermoanalytical, kinetic and thermodynamic parameters are listed in Table 4 and 5. The experimental data suggest that both the sulfanilamide and sulfamerazine complexes of Nickel(II)show almost the same decomposition behaviour in three stages. Both the complexes acquire good stability at a lower temperature and undergo decomposition only after melting, which is immediately followed by decomposition in three distinct steps. The solid product of decomposition in both cases was a stable blackish green residue of NiO which no longer decomposed till 900°C. In both the complexes, the activation energy (*E*) for the last step is the lowest, indicating the presence of less stable and weaker bonding interaction in the fragmented complex. The higher activation energy (*E*) for the first two steps attributes to the decomposition of ligand moiety and cleavage of strongly bonded nitrate group. A similar trend is followed by the frequency factor (*A*) and enthalpy of activation (ΔH) for all the steps of thermal degradation. The negative values of the entropy of activation(ΔS) suggest that the activated complex has a more ordered structure than the reactants. Also the positive values of (ΔG), Gibbs free energy indicate that the thermal decomposition processes are slower than normal and are highly non-spontaneous for both the complexes.

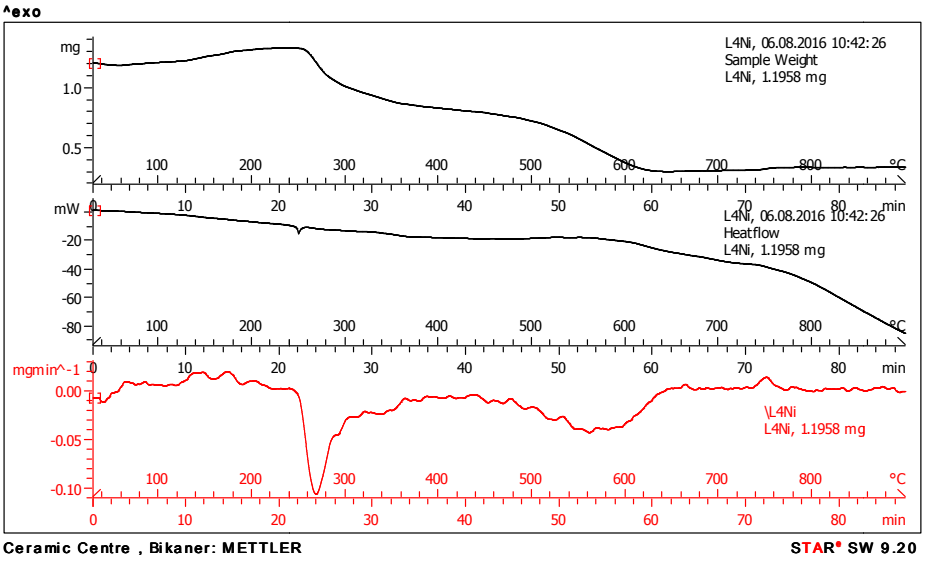


Fig. 7. Thermogravimetric analysis (TGA), Differential thermogravimetric analysis (DTA) and Derivative thermogravimetric (DTG) curves for Ni(II)-Sulfamerazine complex

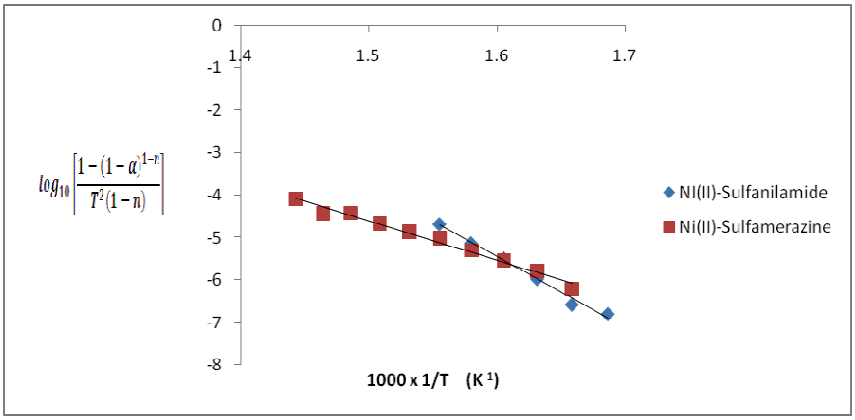


Fig. 8. Coats Redfern plot for second stage of decomposition for both the complexes

Table 3. Thermoanalytic data along with kinetic parameters

Complex	Decomp. Steps	Temp. range (°C)	Weight loss per step (%) obsd (calcd)	DTG_{max} (°C)	Order of reaction n	Activation energy (kJ/mol) E	Frequency factor (sec^{-1}) A	Correlation coefficient R^2
$[Ni(SA)_2(NO_3)_2]$	Decomp. Stage 1	240-310	17.46 (16.67)	290	1.0	201.95	$4.58x10^{16}$	0.988
	Decomp. Stage 2	320-380	40.99 (40.48)	343	1.5	321.69	$2.48x\ 10^{20}$	0.989
	Decomp. Stage 3	390-610	85.85 (86.19)	540	1.0	85.43	$1.13\ x\ 10^{3}$	0.993
$[Ni(SM)(NO_3)]$	Decomp. Stage 1	250-320	27.55 (28.36)	270	2.5	292.13	$1.22x10^{26}$	0.993
	Decomp. Stage 2	330-430	43.67 (41.79)	340	3.0	166.62	$1.00x\ 10^{12}$	0.988
	Decomp. Stage 3	440-640	80.61 (79.10)	570	1.0	120.86	$1.08\ x\ 10^{5}$	0.995

Table 4. Thermoanalytic data and thermodyanamic parameters

Complex	Decomp. steps	Temp. range (°C)	Entropy of activation (J/Kmol) ΔS	Enthalpy of activation (kJ/mol) ΔH	Gibb's free energy (kJ/mol) ΔG
$[Ni(SA)_2(NO_3)_2]$	Decomp. Stage 1	240-310	68.75	197.26	158.55
	Decomp. Stage 2	320-380	139.58	316.57	230.59
	Decomp. Stage 3	390-610	-194.80	78.67	237.04
$[Ni(SM)(NO_3)]$	Decomp. Stage 1	250-320	249.49	287.62	152.15
	Decomp. Stage 2	330-430	-21.25	161.52	174.55
	Decomp. Stage 3	440-640	-157.20	113.85	246.37

3.6 Biological Activity

Both the complexes along with their parent drugs were tested for antibacterial activities against the cultures of *E.coli, S.aureus and B.subtilis*. It has been known that the free amino group present in the sulfadrugs is responsible for their antimicrobial properties [36,37]. In the present study it was found that, whereas Ni(II)-Sulfamerazine complex showed no significant antibacterial activity, the Ni(II)-Sulfanilamide complex proved to be promisingly effective against all the three strains. Especially in the case of *S.aureus*, it showed prominently enhanced antibacterial activity.

Maximum zones of inhibition shown by both the metallodrugs as well as their parent drugs have been presented in Table 2 and Fig. 4.

Table 5. Antibacterial activity of sulfa drugs and synthesised compounds

Complexes (100 ppm)	Zone of inhibition (in mm)		
	E. coli	*S. aureus*	*B. subtilis*
Sulfanilamide (SA)	6	0	6
$[Ni(SA)_2(NO_3)_2]$	8	6	7
Sulfamerazine(SM)	6	14	12
$[Ni(SM)(NO_3)]$	0	6	0

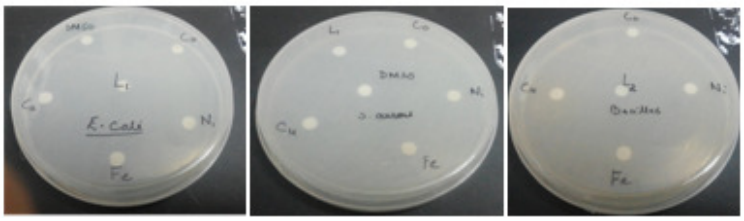


Fig. 9. Biological activity of Sulfanilamide and its Nickel(II) complex

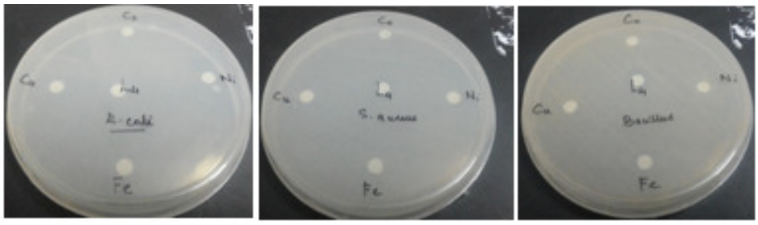


Fig. 10. Biological activity of Sulfamerazine and its Nickel(II) complex

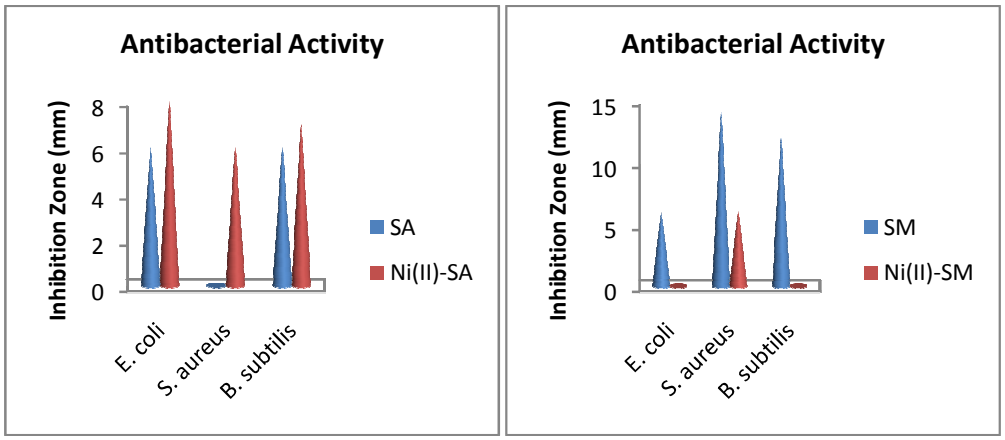


Fig. 11. Comparative study of biological activity shown by drugs and their Nickel(II) complexes

4. CONCLUSIONS

In the present study, Ni(II) complexes of sulfanilamide and sulfamerazine were synthesised and characterised by elemental analysis, spectral studies, antibacterial activities and thermal gravimetric analyses. Initial confirmation of co-ordination of drug molecules with the metal ion was provided by UV/VIS spectral analyses.On the basis of FT-IR and thermal decomposition data, both Sulfanilamide and Sulfamerazine drugs were found to behave as monodentate and bidentate ligands, facilitating six coordinating octahedral and four co-ordinating square planar geometry in their nickel (II) complexes respectively. Biological studies for determining the antimicrobial activities of the complexes were carried against of *E.coli*, *S.aureus* and *B.subtilis*. TGA and DTA studies of both the complexes ruled out the presence of any molecule of water of crystallisation. Thermal degradation followed a three-step decomposition for both the complexes followed by formation of a final blackish green residue of metal oxide. The kinetic parameters were evaluated for all three decomposition stages by using Coats and Redfern integral method for thermal decomposition under non-isothermal conditions. Standard relations were used for the determination of Thermodynamic parameters.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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