Bulgarian Chemical Communications, Volume 47, Number 3 (pp. 895 – 903) 2015

Synthesis and characterization of some lanthanide metal complexes Ce(III), Gd(III), Nd(III), Tb(III) and Er(III) with sulfasalazine as sulfa drug

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Received December 6, 2013, Revised May 13, 2015

The complexation between lanthanides metal ions like Ce(III), Eu(III), Nd(III) and La(III) with sulfasalazine (H_3suz) produced 1:1 molar ratio (metal : sulfasalazine) as a monodentate via OH group and give general formula: $Na_2[M(Hsuz)(Cl)_3(H_2O)].xH_2O$, where: M= Ce, Eu, Nd and La, x= 2 and 10. The resulted sulfasalazine compounds were assigned by Infrared, ^{1}H-NMR and electronic spectra. Themogravimetric analysis and kinetic thermodynamic parameters have proved the thermal stability feature of sulfasalazine complexes. The anti-microbial activities of the lanthanides metal complexes of sulfasalazine recorded a significant effect against some bacteria and fungi.

Keywords: Sulfasalazine; lanthanide metal ions; complexation; antimicrobial activity

INTRODUCTION

Sulfa drugs have attracted special attention for their therapeutic importance as they were used against a wide spectrum of bacterial ailments [1-9]. Also, some sulfa drugs were used in the treatment of cancer, malaria, leprosy and tuberculosis [4]. The importance of the very interesting features of metal coordinated systems is the concerted spatial arrangement of the ligands around the metal ions [10]. Although the complexes of the sulfa drugs have been investigated in the solid state, relatively was known about their solution chemistry in particular their mixed-ligand complexes [8, 11]. The formation and characterization of binary and mixed-ligand complexes, involving iminodiacetic acid and sulfa drugs as sulfadiazine and sulfadiamidine, were investigated [8, 11, 12]. Sulfasalazine H_3suz (Fig. 1) 2-hydroxy-5-[[4-[(2-pyridinylamino) sulfonyl]phenyl]azo]benzoic acid; is a sulfa drug, a derivative of Mesalazine (5-aminosalicylic acid abbreviated as 5-ASA), used primarily as an anti-inflammatory agent in the treatment of inflammatory bowel diseases as well as rheumatoid arthritis [13-16]. When dealing with the interaction between drugs and metal ions in living systems, a particular interest has been given to the interaction of metal ions with antibiotics, which has been widely used in medicine both towards human beings and animals [17, 18]. In particular the interaction between transition metals and β-lactamic antibiotics such as cephalexin has been recently investigated by several physicochemical and spectroscopic methods, and with detailed biological data [19-22]. Many properties when administered in the form of metallic complexes. Probably the most widely studied cation in this respect is Cu(II), since a host of low-molecular-weight copper complexes have been proven beneficial against several diseases such as tuberculosis, rheumatoid, gastric ulcers, and cancers [23-29] of the complexation of sulfa drugs did not focus on the coordination behavior, but only dealt with the solution state and crystal structures of its metal complexes.

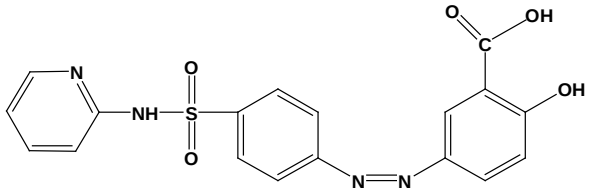

Fig. 1. Sulfasalazine (H_3suz) drug ligand.

The complexation of sulfasalazine (H_3suz) with some of transition metals have been investigated [30]. Three types of complexes, $[Mn(Hsuz)(H_2O)_4].2H_2O$, $[M(Hsuz)(H_2O)_2].xH_2O$ (M= Hg(II), ZrO(II) and VO(II), x=4, 8 and 6, respectively) and $[M(Hsuz)(Cl)(H_2O)_3].xH_2O$ (M=Cr(III) and Y(III), x= 5 and 6, respectively) were obtained and characterized by physicochemical and spectroscopic methods. The IR spectra of the complexes suggest that the sulfasalazine behaves as a monoanionic bidentate ligand. The thermal decomposition of the complexes as well as thermodynamic parameters

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(E*, ΔH*, ΔS* and ΔG*) were estimated using Coast-Redfern and Horowitz-Metzger equations. In vitro antimicrobial activities of the H_3suz and the complexes were tested. The complexes of sulfasalazine(H_3suz) with some of alkaline-earth metals Mg(II), Ca(II), Sr(II) and Ba(II) have been investigated [31]. Sulfasalazine complexes were synthesized and characterized by spectroscopic tools; Infrared spectra, electronic and mass spectra. The IR spectra of the prepared complexes were suggested that the H_3suz behaves as a bi-dentate through the carboxylic and phenolic groups. The molar conductance measurements gave an idea about the non-electrolytic behavior of the H_3suz complexes. The thermal decomposition processes for metal(II) complexes of H_3suz viz: $[M(Hsuz)(H_2O)_4]$ (where M= Mg(II), Ca(II), Sr(II) or Ba(II)) have been accomplished on the basis of TG/DTG and DTA studies, and the formula conforms to the stoichiometry of the complexes based on elemental analysis. The kinetic analyses of the thermal decomposition were studied using the Coast-Redfern and Horowitz-Metzger equations. The antitumor and antimicrobial activities of the H_3suz and their alkaline-earth metals(II) complexes were evaluated. Sulfasalazine is composed by sulfapyridine (SP) and 5-amino salicylic acid (5-ASA) with a diazo bond linkage. 5-ASA is considered to be the active component in the theraby of inflammatory bowel disease, while SASP and SP are effective in the theraby of rheumatoid disease [32-34]. The complexation behaviour of mesalazine (5-aminosalicylic acid; 5-ASA) towards the transition metal ions namely, Cr(III), Mn(III), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) have been examined by elemental analyses, magnetic measurements, electronic, IR and ^{1}H-NMR. Thermal properties and decomposition kinetics of all complexes are investigated. The interpretation, mathematical analyses and evaluation of kinetic parameters of all thermal decomposition stages have been evaluated using Coast-Redfern equation. The free ligand and its metal complexes have been tested in vitro against *Aspergillus niger* and *Candida albicans* fungi and *Psuseudomonas aeruginosa*, *Escherichia coli*, *Bacillis subtilies* and *Staphylococcus aureus* bacteria in order to assess their anti-microbial activity than the parent 5-ASA drug [35]. Herein, in this work we prepare chelates of Ce(III), Eu(III), Nd(III) and La(III) with Sulfasalazine drug molecule. The solid chelates are characterized using different physico-chemical methods like elemental analyses (C, H, N, S and metal content), IR, UV-vis spectra, ^{1}H-NMR and thermal analyses (TG and DTG). Antimicrobial activity test of the complexes are studied.

EXPERIMENTAL

Physical measurements

Carbon and hydrogen contents were determined using a Perkin-Elmer CHN 2400. The metal content was found gravimetrically by converting the complexes into their corresponding oxides. Infrared spectra were recorded on Bruker FT-IR Spectrophotometer (4000-400 cm^{-1}) in KBr pellets. The UV-vis spectra were studied in the DMSO solvent with a concentration of $1.0x10^{-3}$ M for the H_3suz and their complexes using Jenway 6405 spectrophotometer with 1cm quartz cell, in the range 800-200 nm. Molar conductance of the freshly prepared solutions of H_3suz complexes with $1.0x\ 10^{-3}$ M in DMSO were measured using Jenway 4010 conductivity meter. ^{1}H-NMR spectra were recorded on a Varian Gemini 200 MHz spectrophotometer using DMSO-d6 as solvent. Thermogravimetric analyses (TGA and DTG) were carried out in a dynamic nitrogen atmosphere (30 ml/min) with a heating rate of 10 ^{o}C/min using Shimaduz TGA-50H thermal analyzer.

Antimicrobial activity test

According to [36], the hole well method was applied. The investigated isolates of bacteria were seeded in tubes with nutrient broth (NB). The seeded NB (1 cm^3) was homogenized in the tubes with 9 cm^3 of melted (45 ^{o}C) nutrient agar (NA). The homogeneous suspensions were poured into petri dishes. The holes (diameter, 4 mm) were done in the cool medium. After cooling $2x10^{-3}$ dm^3 of the investigated compounds were applied using a micropipette. After incubation for 24 h in a thermostat at 25-27 ^{o}C, the inhibition (sterile) zone diameters (including disk) were measured and expressed in mm. An inhibition zone diameter of over 7 mm indicates that the tested compounds are active against the bacteria under investigation. The antibacterial activities of the investigated compounds were tested against *Escherichia coli* (Gram –ve), *Bacillus subtilis* (Gram +ve) and antifungal (*Aspergillus niger* and Penicillium activities).

Materials and methods

All chemicals used were of analytical grade where possible and were purchased from Aldrich and Merck companies and sulfasalazine drug was presented from Egyptian international pharmaceutical industrial company (EIPICO). The complexes were prepared by mixing sulfasalazine

(2 mmol) and metal chlorides of Eu(III), Ce(III), Nd(III) and La(III) (1.0 mmol) in mixed solvent MeOH/H_2O (50/50%; 40 cm^3), then pH of the solution was adjusted to 8-9 with 1 M NaOH solution and the reaction mixture was stirred at 60 ^oC for 2 h and left to stand overnight. The precipitated complexes were filtered off, washed with MeOH and H_2O and dried in vacuum at room temperature under anhydrous $CaCl_2$.

RESULTS AND DISCUSSION

The elemental analysis (CHN) agrees quite well with the speculated structure of the colored sulfasalazine complexes (Table 1). The prepared complexes have brown color. They are thermally stable above >250 ^oC, soluble in DMSO and DMF. The conductivity values measured in DMSO at room temperature are located in the range of non-electrolytes [37] for Ce(III), Eu(III), Nd(III) and La(III)/H_3suz complexes while complexes behaves as 1:1 non-electrolytes. The interpretation concerning decreasing of conductivity values back to the deprotonation of both OH of carboxylic and OH of phenolic groups for the sulfasalazine ligand. This assumption proves that free ligand acts in a bidentate fashion via carboxylic and phenolic groups and also attributed to the participation of carboxylic group as a monodentate chelate.

Infrared spectra

The infrared spectra of sulfasalazine and its complexes exhibited with the main coordination bands which reveal the mode of bonding and are summarized in Table 2. Concerning the sulfasalazine complex, the most important region in the infrared spectra of all complexes and the H_3suz free ligand (~1700-1300 cm^{-1}) is selected and assigned in Table 2 as follows; In contrast to the assignments data of sulfasalazine, Ce(III), Eu(III), Nd(III) and La(III) complexes show no absorption band at 1677 cm^{-1}, characteristic to the ν(C=O) vibration of the carboxylic group (in case of free H_3suz ligand), that is indicative of the involvement of the carboxylic group in the coordination with metal ion. The peaks at 1655 cm^{-1} (vs) Ce(III)/Hsuz, 1652 cm^{-1} (vs) for Eu(III)/Hsuz, 1649 cm^{-1} (s) for Nd(III)/Hsuz, 1654 cm^{-1} (vs) for La(III)/Hsuz complexes, respectively, are absent in the spectrum data of the free H_3suz and can be assigned to the asymmetric stretching vibration of the carboxylate group, ν_{as}(COO-). The spectra of $Na_2[M(Hsuz)(Cl)_3(H_2O)].xH_2O$ (M= Ce(III), Eu(III) Nd(III) and La(III), x= 2 and 10 respectively) complexes also have medium to strong intensity band in the range of 1437-1456 cm^{-1}. This band is absent in spectrum of H_3suz and interpretive to the symmetric vibration of the ν_s(COO-) group. Deacon and Phillips [38] studied the criteria that can be used to distinguish between the three binding states of the carboxylate complexes. These criteria are: (i) ν >200cm^{-1} (where $\nu = [\nu_{as}(COO^-) - \nu_s(COO^-)]$), this relation is found in case of unidentate carboxylato complexes, (ii) bidentate or chelating carboxylato complexes exhibit ν significantly smaller than ionic values (ν <100 cm^{-1}) and finally (iii) bridging complexes show ν comparable to ionic values (ν ~150 cm^{-1}). The observed ν for all the sulfasalazine complexes is > 200 cm^{-1} which confirms a unidentate interaction of the carboxylate group.

Table 1. Elemental analyses and physical data of suzH and its complexes

Complexes	Mwt	Color	Content ((calculated) found)					Am
			% C	% H	% N	% Cl	% M	Ω^{-1} cm^{-1} mol^{-1}
Ce(III)	698.5	Brown	(30.11) 30.26	(2.79) 2.79	(7.39) 7.19	(14.03) 14.44	(18.49) 18.31	9.2
Eu(III)	854.5	Brown	(24.97) 25.63	(4.08) 4.52	(6.13) 6.40	(11.64) 12.60	(16.63) 17.95	5.9
Nd(III)	702.5	Brown	(29.95) 30.56	(2.78) 4.92	(7.35) 7.38	(13.96) 15.23	(18.93) 20.82	8.7
La(III)	697.5	Brown	(30.16) 30.73	(2.80) 2.83	(7.40) 8.43	(14.06) 15.73	(18.36) 19.57	6.8

Table 2. Main IR data of the suzH and its metal complexes

Compound	V(O-H)	V(C-O)	δ (OH)	V_{as}(COO)	V_s(COO)	ΔV(COO)	V(M-O)
H_3suz	--	1281	1393	1625	1427	--	--
Ce(III)	3430	1239	1374	1655	1449	206	529
Eu(III)	3383	1239	1378	1652	1437	215	538-458
Nd(III)	3423	1240	1380	1649	1441	208	439
La(III)	3422	1240	1382	1654	1456	198	411

A board diffuse band of strong to medium strong intensity in the 3500-3350 cm^{-1} region may be assigned to the OH stretching vibration for the coordinated and uncoordinated water molecules in the H_3suz complexes. It is note-worthy to say that when the media of precipitation is sodium hydroxide, this means that the sodium salt of sulfasalazine is formed so, the stretching vibration band of ν (OH) of carboxylic group. As is also difficult distinction between the ν (OH) phenolic group of sulfasalazine and the stretching vibrational bands of water molecules because of the overlapping values, and appear in one place. To ascertain the involvement of ν (OH) of phenolic group of sulfasalazine in the coordination process to the followed by the stretching vibration bands of ν (C-O) in all sulfasalazine complexes, examination of the H_3suz complexes found that the ν (C-O) shifted to lower wave number from 1281 cm^{-1} in case of free ligand to 1239 to 1240 cm^{-1} in case of their complexes. This result indicates that the phenolic group participated in the complexation and the H_3suz ligand acted as bidentate. The lower shift of δ(OH) from 1393 cm^{-1} in the free H_3suz ligand to 1374-1382 cm^{-1} in their complexes is another factor confirming the involvement of OH phenolic group in the coordination process. The presence of ν(M-O) stretching vibrations at two bands: 538-458 cm^{-1} for Eu(III)/Hsuz and one band: 529 cm^{-1} for Ce(III)/Hsuz, 439 cm^{-1} for Nd(III)/Hsuz and 411 cm^{-1} for La(III)/Hsuz, supports coordination by H_3suz ligand as a bidentate monoanionic chelating agent via OH of carboxylic and phenolic groups [39].

Electronic spectra

The electronic spectra of the free H_3suz and their metal complexes were measured and listed in Table 3.

Table 3. Electronic spectral data of the sulfasalazine metal complexes

Compound	λ_{max} (nm)	Assignment
Ce (III)	226, 246, 260, 268,308, 332, 389 427, 601, 701, 787	π- π* trans n- π* trans
Eu(III)	226, 248, 259, 270, 296, 332 597, 704	π- π* trans n- π* trans
Nd(III)	228, 269, 298, 332 403, 427, 591	π- π* trans n - π* trans
La(III)	215, 227, 231, 245, 251, 262, 270, 306, 332 428, 591	π- π* trans n- π* trans

There are some absorption peaks at ranged from 215-390 nm (225, 280, 290, 360, 390 nm) and at 415 nm, which are assigned to π- π* and n-π* transitions within the organic moiety of sulfasalazine ligand. On the other hand, there are two absorption ranges at 215-389 nm and 403-787 nm, due to π-π* and n-π* transitions, respectively, within the H_3suz complexes. The electronic absorption spectra of all H_3suz complexes show a bathochromic shift comparable to free ligand within n-π* transition region [40-45]. This shift attributed to the place of complexation and the change in the electronic configuration for the H_3suz complexes resulted.

^{1}H-NMR spectra

The ^{1}H-NMR spectra presented the persuasive confirmation of the coordination modes. Thus, the ^{1}H-NMR spectra of complexes (Fig. 2) on comparing with those of spectrum of the free sulfasalazine indicate that, H_3suz ligand acts as bidentate ligand through the phenolic OH group and carboxylic OH group. ^{1}H-NMR spectra of complexes were carried out in DMSO-d_6 as a solvent, the data obtained are in agreement with the suggested coordination through the carboxylic and phenolic groups by absence of the signals of two protons which exist in the free ligand about δ= 11.00 and 5.00 ppm, respectively, and due to different chemical environments the signals of aromatic protons at 6.00–8.00 ppm are present with decreasing intensities.

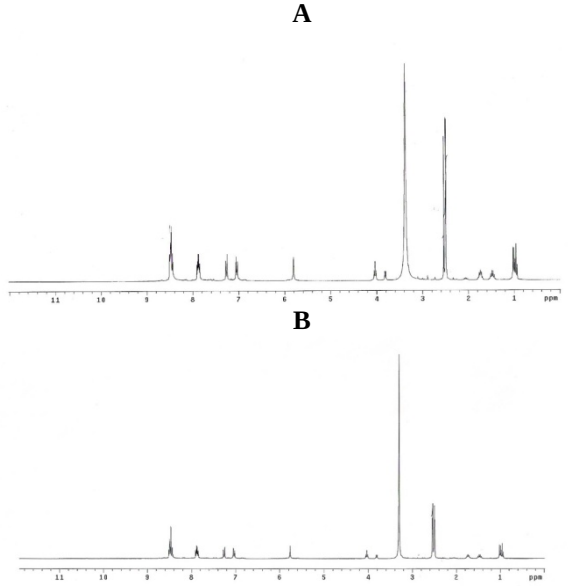


Fig. 2. ^{1}H-NMR spectra of (A) Eu(III)/Hsuz and (B) Nd(III)/Hsuz complexes

Thermal analysis

The thermal decomposition curves (TG/DTG and DTA) are given in Fig. 3, while the TG weight loss data, DTG and DTA peak temperatures are

existed in Table 4. The results showed that the complexes lost its hydration water below 573 K, within the temperature range 573-653 K the coordinated water molecules were liberated. The anhydrous complexes displayed the decomposition of the organic ligand within the temperature range 673-1073 K leading to metal oxide. The metal contents were calculated from the residual contents and were found to be in good agreement with the results of elemental analysis. $Na_2[Ce(suzH)(Cl)_3(H_2O)].2H_2O$ complex was thermally decomposed in three successive decomposition steps within 327-1073 K, the first decomposition step (obs= 5.0%, calc= 5.4%) within the temperature range 327-519 K, may be attributed to the liberation of the two hydrated water molecules. The second decomposition step found within the temperature range 519-768 K (obs= 45.6%, calc= 45.3%), which are reasonably accounted for by the removal of ($3C_2H_2$+2HCN+SO_2+1.5Cl_2+0.5O). The rest of sulfasalazine molecule was removed on the third step within the temperature range 768-1073 K (obs= 27.9%, calc= 27.4%). The decomposition of the ligand molecule ended with a final oxide residue of $CeO_{1.5}$.

The TG curve of $Na_2[Eu(suzH)(Cl)_3(H_2O)].10H_2O$ complex indicates that the mass change begins at 352 K and continues up to 814 K. the first mass loss corresponds to the liberation of the three hydrated water molecules (obs= 7.9%, calc= 8.0%). The second decomposition step occurs in the range 600-814 K and corresponds to the loss of ($2C_2H_2$+SO_2+2HCN+2HCl+5.5H_2O+O_2) (obs= 43.2%, calc= 43.7%). The final decomposition step occurs in the range 814-1073 K and corresponds to the loss of ($5C_2H_2$+HCl+N_2+2CO) (obs= 29.2%, calc= 29.3%). DTG profile shows three endothermic peaks, the first at 352 K corresponds to the melting of the complex, while the second at 600 K corresponds to the dehydration and decomposition of the complex. The third board endothermic peak corresponds to the final decomposition of the organic ligand to the $EuO_{1.5}$.

To make sure about the proposed formula and structure for the Nd complex, thermo gravimetric (TG) and differential thermo gravimetric (DTG) was carried out for this complex under N_2 flow. The thermal decomposition for $Na_2[Nd(suzH)(Cl)_3(H_2O)].2H_2O$ complex occurs in three steps. The first degradation step take place in the range of 298-344 K and it is corresponds to the elimination of $2H_2O$ molecules due to weight loss (obs, =5.8% and calc=5.4%).

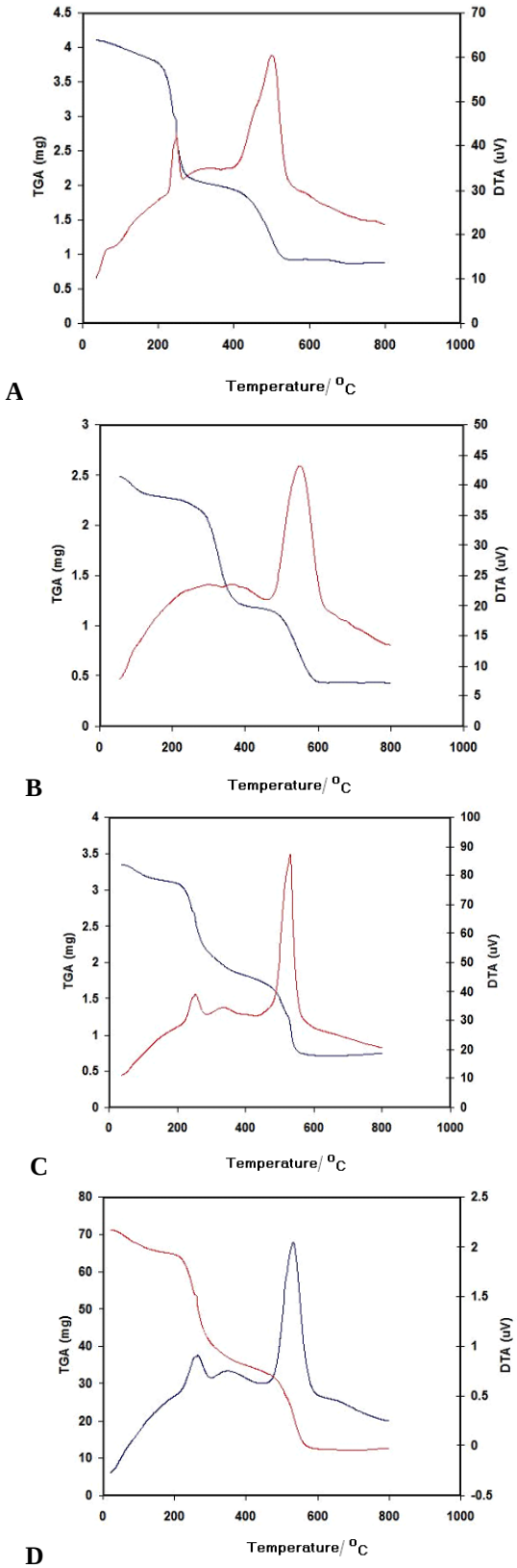


Fig. 3. TG and DTG curves of (A): Ce-sulfasalazine, (B): Eu-sulfasalazine, (C): Nd- sulfasalazine and (D): La-sulfasalazine

The second step fall in the range 523-803 K which is assigned to loss of ($3C_2H_2$+2HCN+SO_2+Cl_2+0.5O) with a weight loss

(obs=38.7% and calc=39.0%). The final step fall in 803 K was accompanied by mass loss (obs=32.1% and calc=31.9%) which is assigned to loss of ($4C_2H_2+N_2+2CO+0.5Cl_2$). The ($NdO_{1.5}$) is the final product remains stable till 1073 K.

The $Na_2[La(suzH)(Cl)_3(H_2O)].2H_2O$ complex was thermally decomposed in three successive decomposition steps with in the temperature range 352-1073 K. the first decomposition step (obs= 6.0%, calc= 5.4%) within the temperature range 352-600 K, may be attributed to the liberation of two hydrated water molecules.

The second decomposition steps found within the temperature range 534-803 K (obs= 35.5%, calc= 35.5%) which corresponds to loss of ($2C_2H_2+2HCN+SO_2+Cl_2+0.5O$). The rest of sulfasalazine molecule was removed on the final step within the temperature range 803-1073 K and corresponds to loss of ($2.5C_2H_2+N_2+$ 2CO+HCl) (obs= 27%, calc= 27.3%). The decomposition of the ligand molecule ended with a final oxide residue of $LaO_{1.5}$ contaminated carbon atoms.

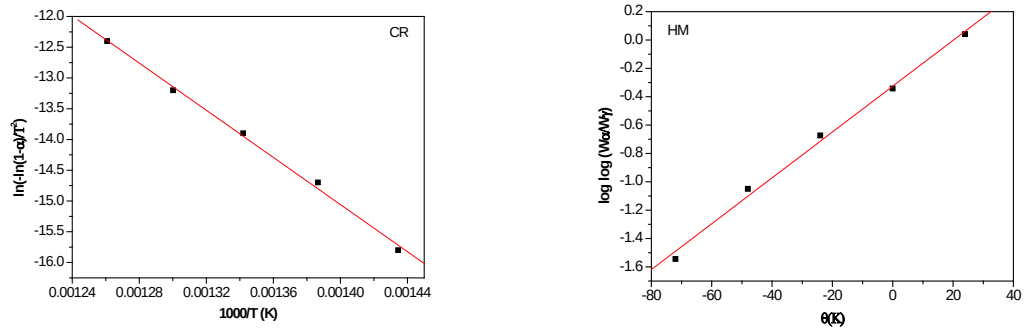
In the present investigation, the general thermal behaviors of the sulfasalazine complexes in terms of stability ranges, peak temperatures and values of kinetic parameters, are shown in Table 5 and Fig. 4. The kinetic and thermo dynamic parameters have been evaluated using the Coats-Redfern and Horowitz-Metzger equations [46, 47]. The entropy of activation, ΔS^*, was calculated. The enthalpy activation, ΔH^*, and Gibbs free energy, ΔG^*, were calculated from; $\Delta H^* = E^* - RT$ and $\Delta G^* = \Delta H^* - T\Delta S^*$, respectively. The thermodynamic behavior of the all complexes of sulfasalazine with some lanthanide(III) metal ions is non-spontaneously (more ordered) reactions (ΔS is negative value), endothermic reactions ($\Delta H>0$) and endergonic ($\Delta G >0$) during the reactions. The thermodynamic data obtained with the two methods are in harmony with each other. The correlation coefficients of the Arrhenius plots of the thermal decomposition steps were found to lie in the range ~ 0.99, showing a good fit with linear function. It is clear that the thermal decomposition process of all sulfasalazine complexes is non-spontaneous, i.e., the complexes are thermally stable.

Structure of the sulfasalazine complexes

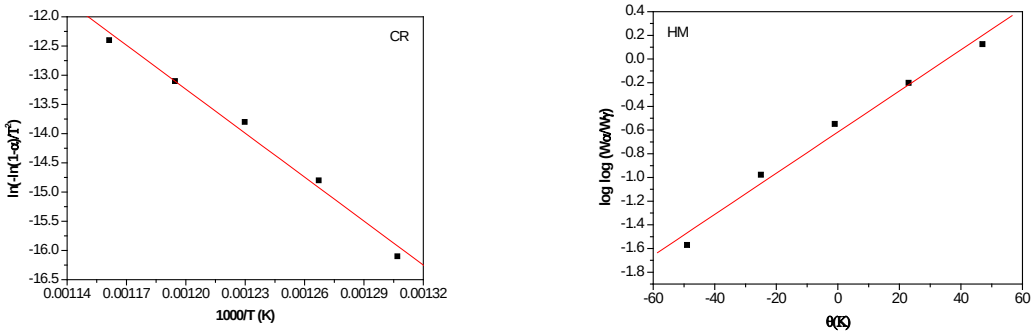
Finally on the basis of the above studies, the suggested structures of the sulfasalazine complexes can be represented in Fig. 5.

Table 4. Thermal data of sulfasalazine and its complexes

Compound	Step	Temp range (°C)	DTG peak (°C)	TG weight		Assignments
				Calc	Found	
Ce(III)	1	50-150	54.59	5.4	5.0	$2H_2O$
	2	200-250	246.73	45.3	45.0	$3C_2H_2+2HCN+SO_2+1.5Cl_2+0.5O$
	3	260-500	495.97	27.4	27.9	$4C_2H_2+N_2+2CO$ $CeO_{1.5}+Na_2O$
Eu(III)	1	40-180	80	8.0	7.9	$3H_2O$
	2	200-330	327.43	43.7	43.2	$2C_2H_2+SO_2+2HCN+2HCl+5.5H_2O+O_2$
	3	350-800	541.82	29.3	29.2	$5C_2H_2+N_2+2CO+HCl$ $EuO_{1.5}+Na_2O$
Nd(III)	1	30-150	71.50	5.4	5.8	$2H_2O$
	2	200-450	250	39.0	38.7	$3C_2H_2+2HCN+SO_2+Cl_2+0.5O$
	3	500-800	530	31.9	32.1	$4C_2H_2+0.5Cl_2+N_2+2CO$ $NdO_{1.5}+Na_2O$
La(III)	1	50-150	62.36	5.4	6.0	$2H_2O$
	2	200-250	261	35.5	35.5	$2C_2H_2+2HCN+SO_2+Cl_2+0.5O$
	3	560-800	530	27.3	27.0	$2.5C_2H_2+N_2+2CO+0.5Cl_2$ $LaO_{1.5}+Na_2O$



Ce(III) complex



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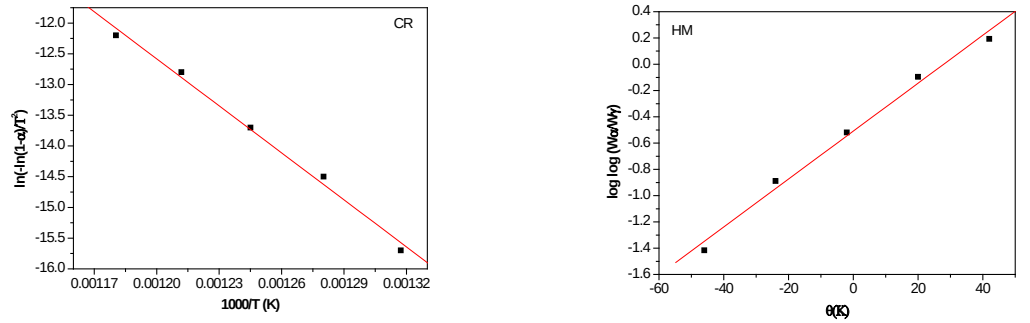
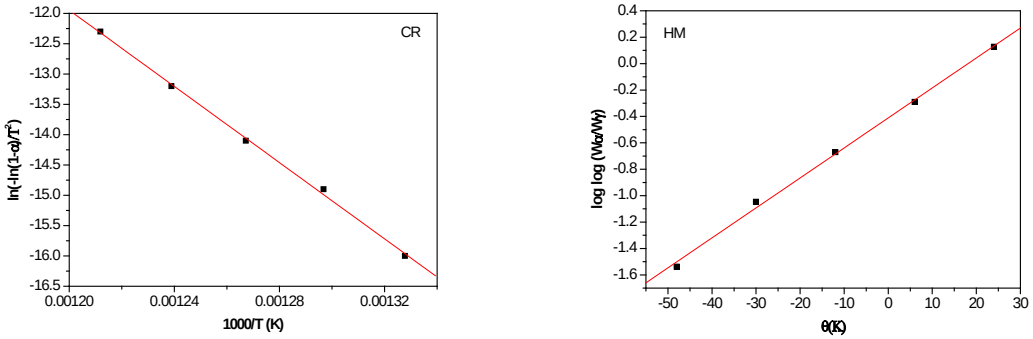


La(III) complex



Nd(III) complex

Fig. 4. Coat-Redfern (CR) and Horowitz and Metzger (HM) curves for sulfasalazine complexes

Table 5. Thermodynamic parameters of the thermal decomposition of sulfasalazine complexes

Thermodynamic Parameters	Methods CR	Methods HM	Complexes
r	0.99836	0.99732	
E*	1.59E+05	1.83E+05	
A	6.17E+08	2.56E+10	
ΔS*	-	-	Ce(III)
	8.45E+01	5.35E+01	
ΔH*	1.53E+05	1.77E+05	
ΔG*	2.18E+05	2.18E+05	
r	0.99408	0.99172	
E*	2.09E+05	2.20E+05	
A	1.33E+11	1.39E+12	
ΔS*	-	-	Eu(III)
	4.03E+01	2.08E+01	
ΔH*	2.02E+05	2.14E+05	
ΔG*	2.35E+05	2.31E+05	
r	0.99645	0.99536	
E*	2.12E+05	2.26E+05	
A	4.29E+11	5.13E+12	
ΔS*	-	-	La(III)
	3.05E+01	9.86E+00	
ΔH*	2.05E+05	2.20E+05	
ΔG*	2.30E+05	2.28E+05	
r	0.99926	0.99885	
E*	2.61E+05	2.79E+05	
A	1.22E+15	2.06E+16	Nd(III)
ΔS*	3.57E+01	5.92E+01	
ΔH*	2.55E+05	2.72E+05	
ΔG*	2.26E+05	2.25E+05	

Antimicrobial activity

The results of antimicrobial activities (bacteria and fungi) in vitro of sulfasalazine ligand and their complexes Table 6 and Fig. 6, show that, the $Na_2[La(suzH)Cl_3(H_2O)].2H_2O$ test complex have high activities against A. niger>B. subtilis>pencillium. On the other hand, Ce(III), Eu(III) and Nd(III) sulfasalazine complexes have antimicrobial activities against B. subtilis and pencillium These results clearly obviously that, some metal ions after complexation give the sensitive nature for the ligand against some bacteria and fungi.

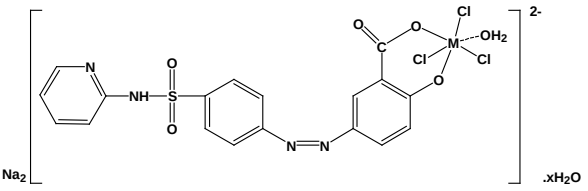


Fig 5. Mode of chelation of sulfasalazine complexes, where M= Ce(III), Eu(III), Nd(III) and La(III); X= 2 and 10.

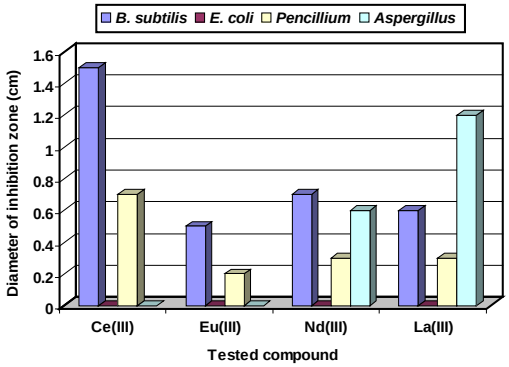


Fig. 6. Microbial test for sulfasalazine complexes

Table 6. Antimicrobial activity of sulfasalazine complexes.

Tested compounds	Diameter of inhibition zone (cm)			
	B. subtilis	E. col	P.rotatum	A.niger
Ce(III)	1.5	0	0.7	0
Eu(III)	0.5	0	0.2	0
Nd(III)	0.7	0	0.3	0.6
La(III)	0.6	0	0.3	1.2

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СИНТЕЗА И ОХАРАКТЕРИЗИРАНЕ НА НЯКОИ КОМПЛЕКСИ НА ЛАНТАНИДИТЕ Ce(III), Gd(III), Nd(III), Tb(III) И Er(III) СЪС СУЛФАСАЛАЗИН КАТО СУЛФА-ЛЕКАРСТВА

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Постъпила на 6 декември, 2013 г.; Коригирана на 13 май, 2015 г.

(емюзеР)

Комплексообразуването между йони на лантанидите (напр.Ce(III), Eu(III), Nd(III) и La(III)) със сулфасалазин (H_3suz) дава комплекси с моларно съотношение 1:1 (метал : сулфасалазин) като монодендатичрез хидроксилна група и с обща формула$Na_2[M(Hsuz)(Cl)_3(H_2O)].xH_2O$, където M= Ce, Eu, Nd иLa, x = 2 и 10. Получените съединения за охарактеризирани с инфрачервени, ^{1}H-NMR и електронни спектри. Доказана е тяхната термична стабилност чрез термогравиметричен анализ, термодинамични и кинетични изследвания Тези комплексни съединения на лантанидите със сулфалазина показват анти-микробна активност спрямо някои бактерии и гъбички.