Research Article

Antimicrobial and Antioxidant Properties of Sm(III) Complex with β-hydroxyketone and 5-Nitro-1, 10-phenanthroline as Ancillary Ligand

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ABSTRACT

New ternary Sm(III) ion complex, $Sm(HDMPE)_3$.nphen was synthesized by adopting solution precipitation method. The synthesized complex was identified on the basis of various techniques like elemental analysis, ^{1}H-NMR and FT-IR, We studied the antimicrobial and antioxidant properties of the ligand and complex $Sm(HDMPE)_3$. nphen. The in vitro antibacterial activities were studied by using Gram-positive bacteria: *B.subtilis, S.aureus* and gram-negative bacterium: *Escherichia coli.* The antifungal activities were studied by using fungi *C. albicans* and *A.niger.* The antibacterial activities of ligand is poor but better of Sm (III) ion complex $Sm(HDMPE)_3$.nphen than standard drugs ciprofloxacin and fluconazole. The antioxidant activities of the synthesized complex were determined by using DPPH method. The Sm (III) ion complex $Sm(HDMPE)_3$.nphen have poor antioxidant activities.

Keywords: Sm(III) complex, elemental analysis, ^{1}H-NMR, FT-IR, antimicrobial activities, antioxidant activities.

INTRODUCTION

The developing incidence of microbial resistance to at present utilized anti-infection agents represents a serious medical issue. These resistant strains shorten the life expectancy of the medication[1-2]. Infections caused by these microorganisms pose a serious challenge to the medical community and need for an effective therapy has led to a search for novel antibacterial agents[3]. Therefore, there is an urgent need to develop new classes of therapeutic agents to treat microbial infections.

The discovery of the biological ambivalence of oxidative stress, as well as its numerous metabolic, structural, and functional effects, has generated a large number of experimental and clinical investigations concerning the association between hydrogen peroxide metabolism and disease[4]. Increased oxidative stress within mitochondria arising from impaired oxidative metabolism may contribute to greater lipid peroxidation and damage to cell membranes and DNA, activating a cascade of signaling events that further exacerbate the severity of the disease[5]. To prevent oxidation, several kinds of antioxidants are in use for the last few decades and mainly include organic compounds and other metal complexes. In our earlier papers Eu(III), Tb(III) and Sm(III) complexes with β-Hydroxyketones proved excellent antimicrobial agent[6-10]. Keeping this observation in mind and in continuation of our study on exploring the biological profile of complex compounds, we hereby report the synthesis, charatrization, antimicrobial and antioxidant evaluation of novel ternary Sm(III) ion complex "$Sm(HDMPE)_3$.nphen" by using 1-(2-hydroxy-4,6-dimethoxyphenyl)ethanone (HDMPE) as main ligand and 5-Nitro-1, 10-phenanthroline (nphen) as ancillary ligand.

MATERIALS AND METHODS

5-Nitro-1, 10-phenanthroline, $Sm(NO_3)_3 6.H_2O$ (99.9), benzene-1,3-5-triol, dimethyl sulphate, potassium carbonate, xylenol orange and 1,1-Diphenyl-2-picrylhydrazylradical(DPPH) were purchased from Sigma-Aldrich and used as received without additional purification. The microorganisms used in antimicrobial activities were purchased from Institute of Microbial Technology, Sector39-A, Chandigarh, India. Nutrient broth medium, nutrient agar medium, subour and dextrose agar medium and sub our and dextrose broth medium were purchased from Hi-Media Pvt Ltd. The synthesized ligand HDMPE was recrystalized three times with methanol before synthesis of complexes. The elemental analysis was performed using thermo scientific flash 2000 elemental analyzer. The percentage of Sm(III) was estimated by complexometric titration with EDTA. The ^{1}H-NMR spectra were measured on Bruker Avance II 400 spectrometer using tetramethylsilane (TMS) as an internal reference (chemical shift in δ ppm). Infrared spectra were recorded (Perkin Elmer spectrum 400) from 4000–400 cm^{-1} in KBr pellets. Antimicrobial and Antioxidant activities were determined by tube dilution method and DPPH method respectively. All measurements were made at room temperature unless otherwise stated.

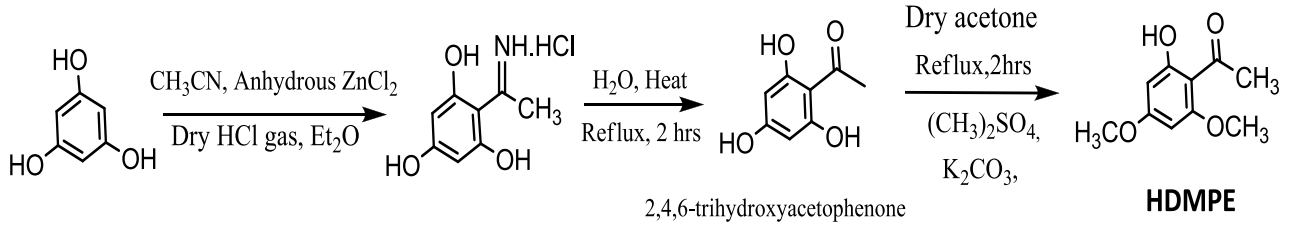
Synthesis

Synthesis of ligand HDMPE

The ligand HDMPE was synthesized by adopting conventional method as per literature[11]andis given in Scheme 1 as follow:

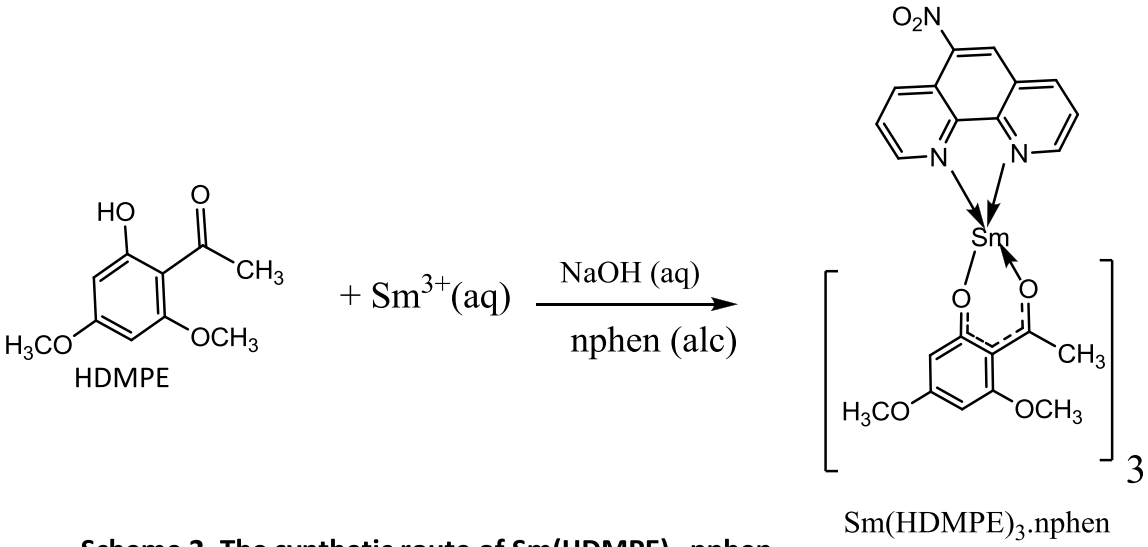
Synthesis of complex Sm(HDMPE)$_3$.nphen

Scheme 2 The complex was synthesized by mixing ethanolic solution of 3 mmol HDMPE ligand, and1 mmol nphen with ethanolic solution of 1 mmol $Sm(NO_3)_3.6H_2O$. Afterwards the pH of mixture was adjusted to 6.5 - 7, using NaOH (0.05 M) solution with constant stirring. This resulted into formation of white precipitates.



Scheme 1. The synthetic route of ligand HDMPE.

These precipitates were stirred for 3 h at about 40°C and then allowed to digest for 1 h. Finally, a suction filter was used to filter precipitates, washed with doubly distilled water and then with ethanol, dried in vacuum oven at 50 °C. The obtained complex was white powder with 83 % yield. The powdered the complex was stored in sample tube in vacuum desiccator.



Scheme 2. The synthetic route of Sm(HDMPE)$_3$.nphen

Biological activity

Antimicrobial activity

The assay was carried out on the synthesized ligand HDMPE and their corresponding Sm(III) ion complex 'Sm(HDMPE)$_3$.nphen' using tube dilution method[12]. The following bacteria were used for *in vitro* antibacterial activities, Gram-positive bacteria: *B.subtilis, S.aureus* and gram-negative bacterium: *Escherichia coli.* The following fungi were used for antifungal activity *C.albicans* and *A.niger.* The standard drugs ciprofloxacin and fluconazole[13] have also tested for their antibacterial and antifungal activity at the same concentration under the same condition as that of the tested HDMPE and Sm(HDMPE)$_3$.nphen. The dilutions of synthesized complex as well as standard drugs have been prepared in double strength nutrient broth I.P and sabouraud dextrose broth I.P media for bacteria and fungi respectively[14]. The standard, ligand and complex were dissolved in DMSO to give concentration of 100 µg/mL. The incubation period for HDMPE and Sm(HDMPE)$_3$.nphen were 24 h at 37 °C for bacteria, 48 h at 37°C for *C.albicans* and 7 days at 25 °C for*A.niger* respectively. The zone of inhibitions of the antimicrobial activity has been recorded in terms of minimum inhibitory concentration (MIC).

Antioxidant activity

The antioxidant activities of the synthesized ligand HDMPE and complex Sm(HDMPE)$_3$.nphen were determined by using DPPH method[15]. When DPPH reacts with antioxidant HDMPE and complex 'Sm(HDMPE)$_3$.nphen, it shows a significant absorption decrease at 517 nm. Methanol was used as a solvent for preparation of various concentrations (25, 50, 75, and 100) µg/ml of the materials. After a 30 minutes incubation period at room temperature, the absorbance was read against a blank at 517 nm. Tests were carried out in triplicate and ascorbic acid was used as a standard antioxidant. The DPPH scavenging activity is expressed as IC_{50}, whose concentration is sufficient to obtain 50% of maximum scavenging activity. Standard curve is plotted for different concentration of ascorbic acid, ligand and

complex. Scavenging of DPPH free radical was calculated as:

DPPH scavenging activity (%) = [(Ac-At) / Ac] $\times$ 100

Where, Ac is the absorbance of the control reaction and At is the absorbance of the test sample.

RESULTS AND DISCUSSION

Solubility

The complex $Sm(HDMPE)_3$.nphen was stable under atmospheric condition. The complex $Sm(HDMPE)_3$.nphen was found to be soluble in dimethylsulfoxide, dimethyl formamide, chloroform and acetone, sparingly soluble in methanol and ethanol but insoluble in benzene and hexane.

Elemental analysis, ^{1}H-NMR and IR Spectra

The elemental analysis data for HDMPE ($C_{10}H_{12}O_4$) were found (calculated) % C, 60.87 (61.22); H, 6.14 (6.16); O, 32.19 (32.61) IR (KBr) cm^{-1} 3430 (b), 3099 (m), 3005 (w), 2943 (w), 2847 (w), 1640 (s), 1538 (s), 1457 (m), 1366 (s), 1324 (m), 1270(s), 1221 (s), 1207 (s), 1112 (m), 1079 (m), 1045 (w), 896 (m), 835 (m), 658 (m), 594 (s). ^{1}HNMR (400 MHz, DMSO): d 2.52 (s, 3H, CH3), 3.83 (s, 6H, OCH3), 6.02 (s, 2H, Ar-H), 13.84 (s, 1H, OH).

The elemental analysis data for $Sm(HDMPE)_3$.nphen ($C_{42}H_{40}O_{14}N_3Sm$) was found (calculated) % C, 52.32 (52.48); H, 4.17 (4.19); N, 4.29 (4.37); O, 23.32 (23.38); Sm, 15.42 (15.64). IR(KBr):cm^{-1} 2934 (m), 2454 (m), 2326 (w), 1617 (m), 1587 (s), 1562 (s), 1486 (s), 1372 (s), 1325 (m), 1236 (s), 1211 (m), 1142 (m), 1127 (s), 1056 (m), 907 (m), 874 (s), 841 (m), 823 (s), 787 (m), 769 (s), 682 (s), 621 (m), 585 (m), 432 (m).^{1}HNMR (400 MHz, DMSO): d 2.49 (bs, 9H, CH3), 3.47 (bs, 18H, OCH3), 6.22 (bs, 6H, Ar-H),7.66 (d, H, nphen), 7.90 (d, H, nphen), 8.36 (d, H, nphen), 8.67 (s, H, nphen), 8.90 (d, H, nphen), 9.06 (d, H, nphen), 9.12 (d, H, nphen).

"The above elemental analytical data indicate the stoichiometry of the ternary complex $Sm(HDMPE)_3$.nphen to be 3:1:1 (HDMPE: Sm: nphen). The ^{1}H-NMR spectrum of the ligand HDMPE showed singlet at δ 13.84 due to phenolic proton which disappeared in the complex $Sm(HDMPE)_3$.nphen was indicating that ligand is coordinated with Sm(III) ion through the oxygen atom of phenolic OH group of the ligand HDMPE. The FT-IR spectra of ligand HDMPE exhibits abroad absorption band at 3430 cm^{-1} assigned to ν(O-H) stretching vibration[7,8,16] which disappeared in the IR spectra of complex the $Sm(HDMPE)_3$.nphen. The ligand also displays the intense C=O stretching vibration band at 1640 cm^{-1}, which was red shifted 23 cm^{-1} in complex the $Sm(HDMPE)_3$.nphen, indicating that phenolic and carbonyl group of HDMPE participated in coordination with Sm(III) ion[9]. The strong absorption band at 1587 cm^{-1} in complex the $Sm(HDMPE)_3$.nphen assigned to C=N stretching vibration, provided good evidence that the nitrogen atoms of nphen were coordinating with the Sm(III) ion[10,17]. The strong absorption band at 1562 cm^{-1} in complex the $Sm(HDMPE)_3$.nphen assigned to N=O stretching vibration. The peak for Ph-O vibration of the ligand HDMPE present at 1270 cm^{-1} showed a red shift of 34 cm^{-1} in the complex $Sm(HDMPE)_3$.nphen, indicating that the phenolic group is involved in coordination with the Sm(III) ion. The appearance of absorption bands at 585 cm^{-1} and at 432 cm^{-1} in the complex $Sm(HDMPE)_3$.nphen was assigned to ν(Sm-N) and ν(Sm-O)[10, 18] respectively, which affirms that the nitrogen atoms of the nphen and oxygen atoms of the ligand HDMPE participated in coordination with the Sm(III) ion. Finally, it can be concluded from the FT-IR and ^{1}H-NMR spectra of the ligand HDMPE and complex $Sm(HDMPE)_3$.nphen, that the coordination of Sm(III) was through the oxygen atoms of phenolic and carbonyl group of ligand HDMPE and nitrogen atoms of the nphen.

Antimicrobial activity

The synthesized ligand HDMPE and $Sm(HDMPE)_3$.nphen were evaluated for their *in vitro* antimicrobial activity as tabulated in Table 1 and presented as bar diagram Figure 1. The antimicrobial activity has been investigated by taking ciprofloxacin and fluconazole[13] as standard drugs for antibacterial and antifungal activity respectively. The results revealed that the ligand HDMPE was having insignificant antimicrobial activity against bacterial and fungal strains, while $Sm(HDMPE)_3$.nphen showed moderate to good activity compared to the standard antibiotics and showed excellent activity against *S.aurius.* Moreover, it was interesting to note that $Sm(HDMPE)_3$.nphen proved to be better than the standard ciprofloxacin against *S. aureus*. Further it was noticed that complex was excellently active in case of *C.albicans,* while moderately active in case of *A.niger.* Moreover, it was interesting to note that $Sm(HDMPE)_3$.nphen proved to be better than the standard fluconazole against *C. albicans.* The increase in antimicrobial activity of the complex may be due to the presence of Sm (III) ion coordinated with the donor atom of the ligand which leads to the π- electron delocalization over the chelate rings[19].

Table 2: Minimum inhibitory concentration of HDMPE and $Sm(HDMPE)_3$.nphen

Compound	Minimum Inhibitory Concentration (µM/mL)				
	B. subtillis	*S.aureus*	*E.coli*	*C.albicans*	*A.niger*
HDMPE	31.8	31.8	31.8	31.8	63.7
$Sm(HDMPE)_3$.nphen	13.53	6.76	13.53	6.76	13.53
Standard.	8.71[a]	8.71[a]	8.71[a]	10.09[b]	10.09[b]

[a]Ciprofloxacin[b] Fluconazole

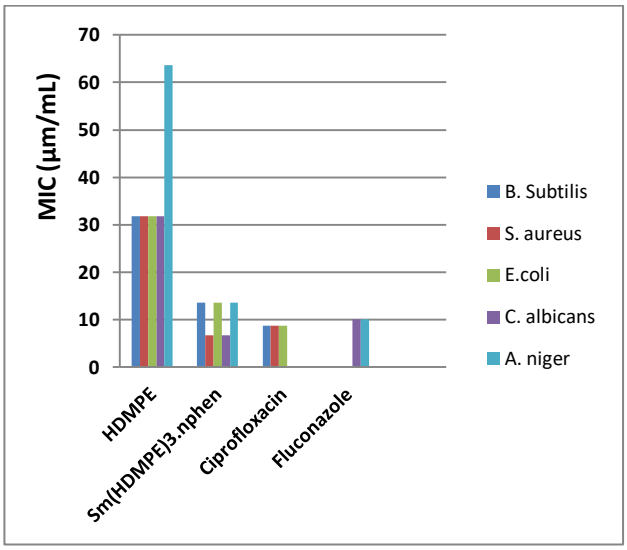


Figure 1: Bar diagram showing the antimicrobial activities of HDMPE and $Sm(HDMPE)_3$.nphen with respect to standard drugs.

Antioxidant activities

In DPPH free radical scavenging activity, antioxidant reacting with stable free radical 2,2-diphenyl-2-picrylhydrazyl (DPPH) produced colorless 2,2-diphenyl-2-picrylhydrazyl. The absorbance decreased, after receiving hydrogen radical. The DPPH scavenging activity is expressed as IC_{50}. The IC_{50} value of ligand and $Sm(HDMPE)_3$.nphen were calculated from the graph plotted as inhibition percentage against concentration of HDMPE and $Sm(HDMPE)_3$.nphen as shown in Table 2 and Figure 2. The results show that ligand HDMPE and complex showed poor activity as compared to standard ascorbic acid (IC_{50}= 43.78µg/ml).

Table 2: Percentage inhibition and IC_{50} values of DPPH radical scavenging activity of synthesized HDMPE and $Sm(HDMPE)_3$.nphen.

Compound	Concentration (µg/mL)				
	25	50	75	100	IC_{50}
HDMPE	23.12	43.02	60.08	80.83	60.42
$Sm(HDMPE)_3$.nphen	23.03	45.12	66.32	85.43	56.54
Ascorbic acid	34.02	56.22	76.12	92.01	43.78

CONCLUSION

In this work, one new ternary Sm(III) complex, $Sm(HDMPE)_3$.nphen have been synthesized which is further characterized through various techniques like elemental analysis, FT-IR, ^{1}H-NMR spectroscopy. Variation in FT-IR and NMR spectra of free ligand (HDMPE) and evolved complex have indicated that oxygen atoms of both phenolic as well ascarbonyl group of prime ligand and nitrogen atoms of ancillary ligand (nphen) were effectively coordinated to Sm(III)ion. This evolved complex has showcased excellent *in vitro* antimicrobial against *S.aureus* and *C.albicans* but poor antioxidant profile as compared to standard ascorbic acid (IC_{50}= 43.78µg/ml).

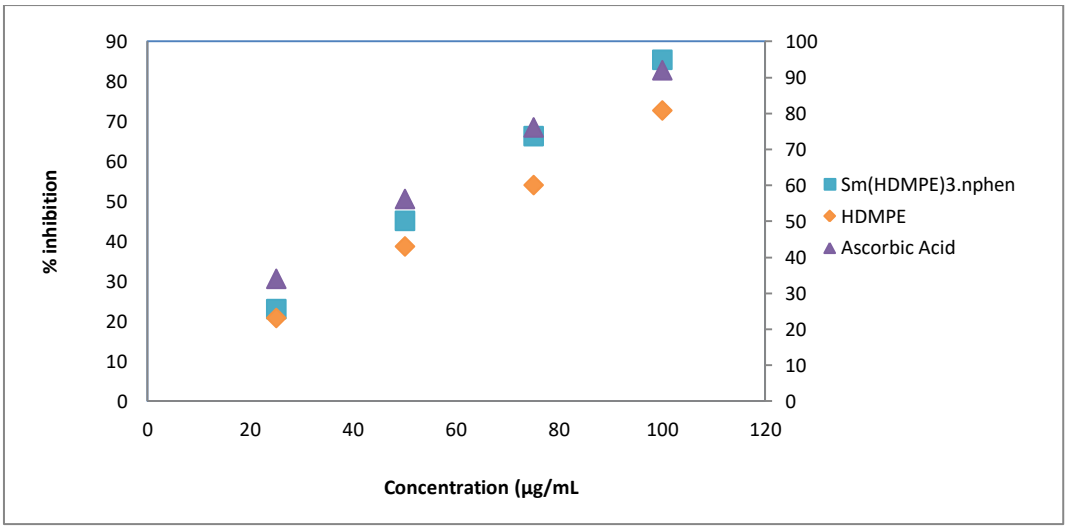


Figure 2: Percentage inhibition of HDMPE and $Sm(HDMPE)_3$.nphen with respect to standard ascorbic acid.

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