Research Article

Study of Biological Properties of Sm(III) Complex with β-Hydroxyketone and Biquinoline as Ancillary ligand

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ABSTRACT

New ternary Sm(III) ion complex, Sm $(HDMPE)_3$.biq 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 spectroscopy. We studied the antimicrobial and antioxidant properties of the ligand and complex Sm $(HDMPE)_3$. biq. 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 $(HDMPE)_3$.biq 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 $(HDMPE)_3$.biq have poor antioxidant activities.

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

INTRODUCTION

One of the key objectives of inorganic and organic medicinal chemistry is to design and synthesize molecules that exhibit potent therapeutic effects[1]. Rapid and continuous evolution of resistance to currently used antimicrobial medications produces a serious challenge to the medical researchers[2-3]. Therefore, there is an essential requirement for the advancement of new antimicrobial agents with potent activity against drug resistant microorganisms. Oxidative stress is involved in the generation of potentially harmful free radicals which play a pivotal role in the pathogenesis of various diseases including rheumatoid arthritis, neurodegenerative diseases, atherosclerosis, age-related degeneration, neurodegenration and cancer initiation[4-5]. To prevent oxidation, different types of antioxidants are in utilized throughout the previous couple of decades and principally include natural organic molecules and other metal complexes. For this reason, large-scale investigation of inorganic compounds with potential radical-scavenging effects is receiving high attention in health research.

Literature reports show that there are limited studies reported on the pharmacological activity of inorganic complexes[6]. Complex compounds are considered to be among the most important group of therapeutic leads in medicinal chemistry due to their preparative accessibility, structural variety and wide biological profile. In our earlier papers Eu(III), Tb(III) and Sm(III) complexes with β-Hydroxyketones proved excellent antimicrobial agent[7-11]. Searching for new complex derivatives possessing antioxidant and antimicrobial activity, we have synthesized a new ternary Sm(III) ion complex "Sm$(HDMPE)_3$.biq" by using 1-(2-hydroxy-4,6-dimethoxyphenyl) ethanone (HDMPE) as main ligand and biquinoline (biq) as ancillary ligand. The synthesized complex was characterized by various techniques like elemental analysis, ^{1}H-NMR and FT-IR spectroscopy. Also, here the ligand and complex is probed for their antimicrobial properties as well as antioxidant properties.

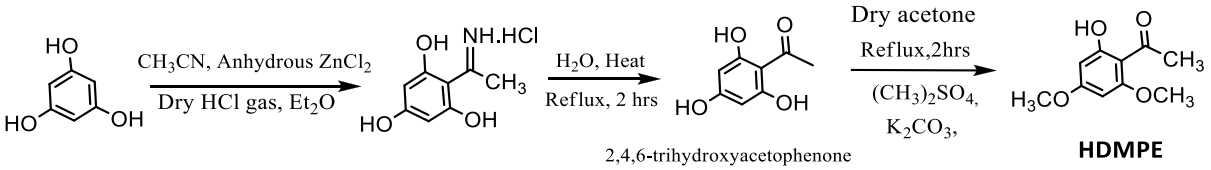
MATERIALS AND METHODS

Biquinoline, $Sm(NO_3)_3 6.H_2O$ (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 subour 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 tetramethyl silane (TMS) as an internal reference (chemical shift in δ ppm). Infrared spectra were recorded (Perkin Elmer spectrum 400) from 4000–400 cm^{-1}inKBr 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 1-(2-hydroxy-4,6-dimethoxyphenyl)ethan-1-one (HDMPE)

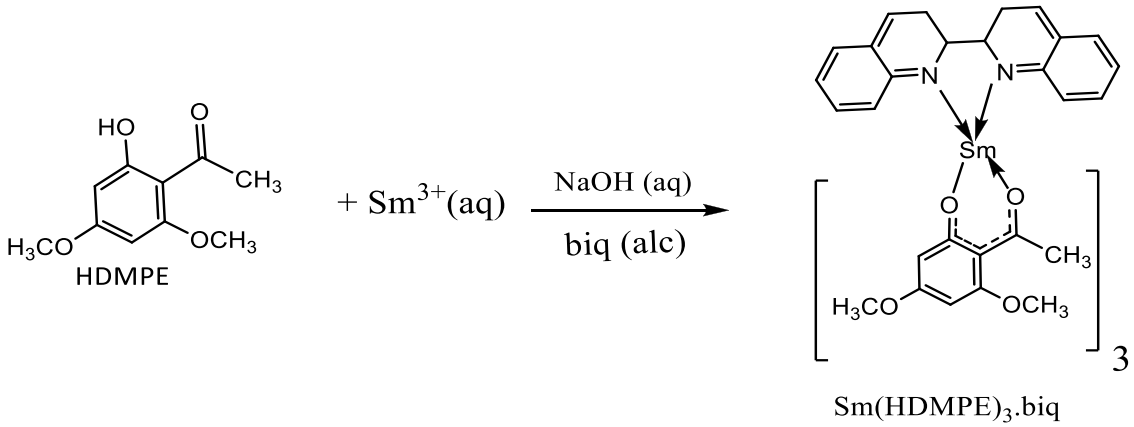
The ligand HDMPE was synthesized by adopting conventional method as per literature[12]andis given in Scheme 1 as follow:



Scheme 1. The synthetic route of ligand HDMPE.

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

Scheme 2 The complex was synthesized by mixing ethanolic solution of 3 mmol HDMPE ligand, and1 mmolbiq 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. These precipitates were stirred for 3 h at about 40°Cand 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 81 % yield. The powdered the complex was stored in sample tube in vacuum desiccator.



Scheme 2. The synthetic route and structure of Sm(HDMPE)$_3$.biq.

Biological activity

Antimicrobial activity

The assay was carried out on the synthesized ligand HDMPE and their corresponding Sm(III) ion complex'Sm(HDMPE)$_3$.biq' using tube dilution method[13]. 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[14] 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)$_3$.biq. The dilutions of synthesized complex as well as standard drugs have been prepared in double strength nutrient broth I.P and sabour aud dextrose broth I.P media for bacteria and fungi respectively[15]. The standard, ligand and complex were dissolved in DMSO to give concentration of 100µg/mL. The incubation period for HDMPE and Sm(HDMPE)$_3$.biqwere 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)$_3$.biq were determined by using DPPH method[16]. When DPPH reacts with antioxidant HDMPE and complex 'Sm(HDMPE)$_3$.biq' 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:

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

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

RESULTS AND DISCUSSION

Solubility

The complex $Sm(HDMPE)_3$.biq was stable under atmospheric condition. The complex $Sm(HDMPE)_3$.biq was found to be soluble in dimethylsulfoxide, dimethylformamide, 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 $Sm(HDMPE)_3$.biq ($C_{48}H_{45}O_{12}N_2Sm$) was found (calculated) % C, 57.86 (58.06); H, 4.48 (4.57); N, 2.77 (2.82); O, 19.21 (19.34); Sm, 16.81 (15.14). IR (KBr):cm^{-1}2921 (w),2462 (m), 2321 (w), 1618 (m), 1589 (s), 1484 (s), 1376 (s), 1332(m), 1243 (s), 1214 (m), 1145 (m), 1129 (s), 1058 (m), 903 (m), 870 (s), 843 (m), 828 (s), 783 (m), 766(s), 688 (s), 623 (m), 588 (m), 436 (m). ^{1}HNMR (400 MHz, DMSO): d 2.63 (bs, 9H, CH3), 3.48 (bs, 18H, OCH3), 6.23 (bs, 6H, Ar-H), 7.56 (d, 2H, biq), 7.78 (d, 2H, biq), 8.12 (d, 2H, biq), 8.27 (d, 2H, biq), 8.54 (d, 2H, biq), 8.89 (d, 2H, biq).

The above elemental analytical data indicate the stoichiometry of the ternary complex $Sm(HDMPE)_3$.biqto be 3:1:1 (HDMPE: Sm: biq). The ^{1}H-NMR spectrum of the ligand HDMPE showed singlet at δ 13.84 due to phenolic proton which disappeared in the complex $Sm(HDMPE)_3$.biq was indicating that ligand is coordinated with Sm(III) ion through the oxygen atom of phenolic OH group ofthe ligand HDMPE. The FT-IR spectra of ligand HDMPE exhibits abroad absorption band at 3430 cm^{-1} assigned to ν(O-H) stretching vibration[8, 9, 17] which disappeared in the IR spectra of complex the $Sm(HDMPE)_3$.biq. The ligand also displays the intense C=O stretching vibration band at 1640 cm^{-1}, which was red shifted 22 cm^{-1} in complex the $Sm(HDMPE)_3$.biq, indicating that phenolic and carbonyl group of HDMPE participated in coordination with Sm(III) ion[10].The strong absorption band at 1589 cm^{-1} in complex the $Sm(HDMPE)_3$.biqassigned to C=N stretching vibration, provided good evidence that the nitrogen atoms of biq were coordinating with the Sm(III) ion[11,18]. The peak for Ph-O vibration of the ligand HDMPE present at 1270 cm^{-1}showed a red shift of 27cm^{-1}in the complex $Sm(HDMPE)_3$.biq, indicating that the phenolic group is involved in coordination with the Sm(III) ion. The appearance of absorption bands at 588$cm^{-1}$and at 436 cm^{-1}in the complex $Sm(HDMPE)_3$.biqwas assigned to ν(Sm-N) and ν(Sm-O)[11,19]respectively, which affirms that the nitrogen atoms of the biq 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 $Sm(HDMPE)_3$.biq,that the coordination of Sm(III) was through the oxygen atoms of phenolic and carbonyl group of ligand HDMPE and nitrogen atoms of the biq.

Antimicrobial activity

The synthesized ligand HDMPE and $Sm(HDMPE)_3$.biqwere 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[14] 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 $Sm(HDMPE)_3$.biq showed moderate to good activity compared to the standard antibiotics and showed excellent activity against *S.aurius.* Moreover, it was interesting to note that $Sm(HDMPE)_3$.biqproved to be better than the standard ciprofloxacin against *S. aurius*. Further it was noticed that complex was excellently active in case of *C.albicans, while* moderately active in case of *A.niger.* 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[20].

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 $Sm(HDMPE)_3$.biq were calculated from the graph plotted as inhibition percentage against concentration of HDMPE and $Sm(HDMPE)_3$.biq as shown in Table 1 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 1: Minimum inhibitory concentration of HDMPE and $Sm(HDMPE)_3$.biq

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
$Sm(HDMPE)_3$.biq	12.59	**6.29**	12.59	**6.29**	12.59
Standard.	8.71[a]	8.71[a]	8.71[a]	10.09[b]	10.09[b]

[a] Ciprofloxacin [b] Fluconazole

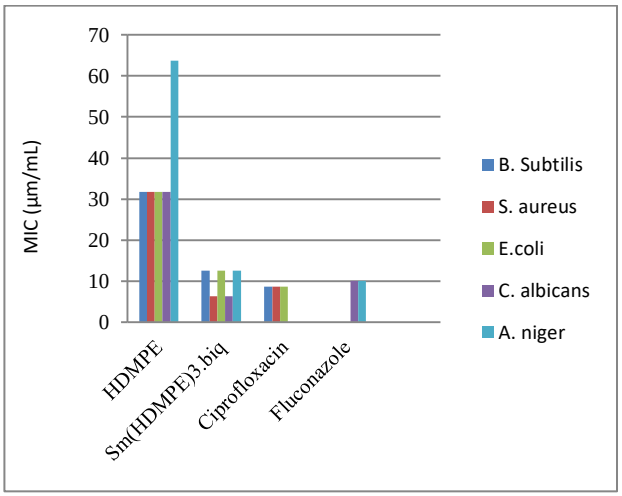


Figure 1: Bar diagram showing the antimicrobial activities of HDMPE and $Sm(HDMPE)_3$.biq with respect to standard drugs.

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

Compound	Concentration (µg/mL)				
	25	50	75	100	IC_{50}
HDMPE	23.12	43.02	60.08	80.83	60.42
$Sm(HDMPE)_3$.biq	22.07	44.02	64.27	81.24	58.85
Ascorbic acid	34.02	56.22	76.12	92.01	43.78

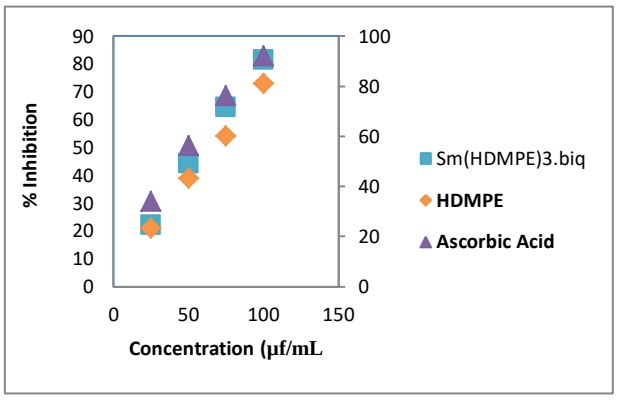


Figure 2: Percentage inhibition of HDMPE and $Sm(HDMPE)_3$.biq with respect to standard ascorbic acid.

CONCLUSION

In this work, one new ternary Sm(III) complex, $Sm(HDMPE)_3$.biq have been synthesized which is further characterized through various techniques like elemental analysis, FT-IR, ^{1}H-NMR spectroscopy. Differences in FT-IR and NMR spectra of free ligand (HDMPE) and complex have indicated that oxygen atoms of both phenolic as well as carbonyl group of main ligand (HDMPE) and nitrogen atoms of ancillary ligand (biq) were effectively coordinated to Sm(III)ion. This evolved complex has showed 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).

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