Int. J. Pharm. Investigation, 2019;9(4):158-163 Original Article

Synthesis, Spectral Characterization and Biological Evaluation of Cr(III) Complex with Mixed N,N and O-donor Ligands

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ABSTRACT

Objectives: 2-aminobenzonitrile is used as the starting materials for the synthesis of many biologically active compounds. The main objective of the study was to synthesize, characterization and biological evaluation of a binuclear bridged Cr(III) complex containing 2-aminobenzonitrile (N,N-donor) and octanoate ion (OC) as ligands. **Methods:** This study formulated, the required mole ratio of 2-aminobenzonitrile in methanol and sodium octanoate in ethanol were added to the chromium chloride in methanol followed by microwave irradiation for few seconds after each addition by using microwave oven and the precipitate was filtered off, washed with 1:1 ethanol: water and characterized by various spectral studies and biological significance. **Results:** The resulted complex was investigated by the help of elemental analysis, molar conductance, magnetic moment, electronic spectra, FT-IR, cyclic voltammetry, thermal analysis and powder-XRD techniques. The spectral data's indicates that the geometry of the complex is octahedral. The antimicrobial activities of ligands and their Cr(III) complex were studied by agar-well diffusion method. The free radical scavenging activity of the complex and the ligands has been determined by measuring their interaction with the stable free radical DPPH. DNA-binding properties have been studied by fluorescence-emission method. **Conclusion:** The formulated Cr(III) complex showed moderate and potential activity against the tested bacteria, enhanced activity against the fungi and larger antioxidant activity as compared to the free ligands. The DNA binding study result suggests that the complex strongly binds to DNA.

Key words: 2-aminobenzonitrile, N,N-donor, Antimicrobial, DNA binding.

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DOI: 10.5530/ijpi.2019.4.30

INTRODUCTION

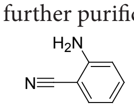
The structure of hybrid inorganic - organic coordination complexes is of high interest in crystal engineering which aims to predict and control the fashion molecules assemble in the solid state.[1-4] In the designing of coordination complexes with unique properties for a wide range of prospective applications including gas storage,[5] antimicrobial,[6] conductive material,[7] luminescent,[8] and magnetic materials.[9] Among the aminobenzonitriles, 2-aminobenzonitrile (ABN) is used for the induction of nitrilase activity in arthrobacter, radio protective agent and starting materials for the synthesis of biologically active compounds.[10,11] 2-aminobenzonitrile is one of the organic ligand in coordination chemistry which can coordinate to the metal ion through different modes *viz.*, monodentate, bidentate or bridging. In general, the biological activities of the metal complexes differ from those of either the ligand or the metal ion itself and increased and/or decreased biological activities are reported for various metal complexes.[12] On the other hand, synthesis of inorganic/organic compounds using microwave irradiation has been a very rapidly developing technique in research area.[13,14] Compared with the conventional method, microwave technique is promising due to its unique effects, such as rapid volumetric heating, higher reaction rates, higher reaction selectivity, higher yields of products and energy saving.

The present study aims at synthesis and spectral characterization of Cr(III) complex with neutral bidentate 2-aminobenzonitrile and anionic monodentate octanoate ion as ligands. The biological activities of the ligands and their complex have also been focused in this study.

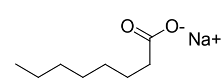
MATERIALS AND METHODS

Materials

2-aminobenzonitrile, sodium octanoate and chromium nitrate were purchased from Alfa Aaser Company and used as such. The organic solvents DMSO, DMF, methanol, ethanol were of AnalaR grade and used as such without further purification.



2-aminobenzonitrile



Sodium octanoate

Methods

Synthesis of Cr(III) complex

2-aminobenzonitrile 0.45g (3.79 mmol) in~ 10 ml methanol and sodium octanoate 1.25g (7.53 mmol) in~ 10 ml ethanol were added to the chromium chloride 1.00g (2.50 mmol) in~10 ml methanol followed by microwave irradiation for a few seconds after each addition by using IFB 25 BG-1S model microwave oven. The consequential precipitate was filtered off, washed with 1:1 ethanol: water mixture and desiccated under vacuum. A green colored complex was obtained with 85.76% yield.

Instrumentations

CHN elemental analyses were performed using Thermo Finnegan make, Flash EA1112 Series CHNS(O) analyzer. The molar conductivity measurement was conducted using 10^{-3}M solutions of the metal complex in acetonitrile with Systronic Conductivity Bridge (model number-304) at 30°C. The electronic spectrum of the Cr(III) complex was recorded on Varian, Cary 5000 model UV Spectrophotometer. Infra-red spectra for the complexes and the ligands were recorded on a Perkin Elmer, Spectrum RX-I, FT-IR spectrometer in KBr discs at room temperature. The cyclic voltammogram of the complex was taken in acetonitrile medium using Princeton make (MC-Tech, Applied Research) equipment. Tetraethylammoniumbromide was used as the supporting electrolyte. The thermogravimetric analysis of the complex was carried out using Perkin Elmer Diamond TGA/DTA Instrument. The powder X-ray diffraction analysis of the complex was recorded on a Rigaku model X-ray Diffractometer.

Biological activities

Antimicrobial activity

The free ligands and their Cr(III) complex were tested for *in-vitro* antimicrobial activity by the well diffusion method using agar nutrient as the medium. The antibacterial and the antifungal activities of the ligands and the Cr(III) complex was evaluated by well diffusion method against the strains, cultured on potato dextrose agar as medium. The stock solution (10^{-2}M) was prepared by dissolving the compounds in DMSO and the solutions were successively diluted at different concentration (µg/ml). According to the typical procedure a well was made on the agar medium inoculated with the micro-organisms. The well was filled with the test solution using a micropipette and the plate was incubated for 24 hr for bacteria and 72 hr for fungi at 35°C. At the end of the period, inhibition zones formed on the medium were evaluated in millimeters (mm) and diameter.[15]

Antioxidant activity

Evaluation of antioxidant activity stock solution (1 mg/ml) was diluted to final concentrations of 10–500 µg/ml. Ethanolic DPPH solution (1 ml, 0.3 mmol) was added to the sample solutions in DMSO (3 ml) at different concentrations (10–500 µg/ml).[16] The mixture was shaken energetically and acceptable to stand at room temperature for 30 min. The absorbance was then measured at 517 nm in a UV-Vis Spectrophotometer. The lower absorbance of the reaction mixture indicates higher free radical scavenging activity. Ethanol was used as the solvent and ascorbic acid as the standard. The DPPH radical scavenging activity is designed by the following equation:

$$\text{DPPH Scavenging effect (\%)} = \frac{A_o - A_1}{A_o} \times 100$$

Where Ao is the absorbance of the control reaction and A_1 is the absorbance in the presence of the samples or standard.

DNA binding studies

The DNA binding experiments involving interaction of the Cr(III) complex and the ligands with calf thymus *CT*-DNA were conducted in Tris buffer containing HCl (0.01 M) adjusted to pH 7.2 with hydrochloric acid. The *CT*-DNA was dissolved in Tris-HCl buffer and was dialyzed against the same buffer overnight. Solutions of *CT*-DNA gave the ratios of UV absorbance at 260 and 280 nm above 1.8, demonstrating that the DNA was adequately free of protein. DNA concentration per nucleotide was determined by absorption spectroscopy using the molar absorption coefficient 6600dm^3 mol^{-1} cm^{-1} at 260 nm. The stock solutions were stored at 4°C and used within 4 days.[17] For fluorescence-quenching experiments, DNA was pre-treated with ethidium bromide (EtBr) for 30 min. The Cr(III) complex then added to this mixture and their effect on the emission intensity was measured. Samples were excited at 450 nm and emission was observed between 500 nm and 800 nm.

RESULTS

Selection of ligands

Metal complexes with a variety of organic chelating ligand are also of current interest due to their biological activities. These include anti-inflammatory and anticonvulsant properties, cytotoxicity and antiviral activity. The 2-aminobenzonitrile and octanoate ion are also organic ligands. These ligands can bind as neutral ligands or as anionic ligands in monodentate, bi dentate or bridging manner. The required mole ratio of 2-aminobenzonitrile in methanol and sodium octanoate in ethanol were added to the chromium chloride in methanol followed by microwave irradiation for few seconds after each addition by using microwave oven and the precipitate is filtered off, washed with 1:1 ethanol: water and characterized by elemental analysis, molar conductance, magnetic moment, electronic spectra, FT- IR, cyclic voltammetry, thermal analysis and powder-XRD techniques. The spectral data's indicates that the geometry of the complex is octahedral. The antimicrobial activities of ligands and their Cr(III) complex were studied by agar - well diffusion method. The free radical scavenging activity of the complex and the ligands has been determined by measuring their interaction with the stable free radical DPPH. DNA-binding properties have been studied by fluorescence-emission method.

Characterization of free ligands and their Complex

Elemental analysis and molar conductance

In Table 1, the elemental analysis results (C, H, N) and the molar conductance value of the prepared complex.

Electronic spectra and Magnetic moment

In Figure 1, The electronic spectrum of Cr(III) complex exhibits three absorption bands at 540 nm, 390 nm and 280 nm for the electronic Spectrum of Cr(III) complexe. The magnetic moment at room température is 3.31 B.M.

FT-IR Spectra

In Figure 2a, 2b, the FT-IR spectra of 2- aminobenzonitrile shows in characteristic absorption bands in the 3453 cm^{-1}, 3366 cm^{-1} and 2206 cm^{-1} region, assignable to asymmetric, symmetric stretching frequencies of $\nu(NH_2)$ and ν (C≡N) respectively.[18] A small band noticed at 3076 cm^{-1} is due to ν(CH) aryl. Aromatic ν(C= C) stretching vibration is seen as a sharp peak at 1570 cm^{-1}. The octanoate ion shows ν(C–O) at 1207 cm^{-1} and the carbonyl group ν(C=O) noticed at 1605 cm^{-1}.

Table 1: Elemental analysis and molar conductance.

Complex	% of elements found			Λm (Ω^{-1}cm^2 mol^{-1})
	Carbon	Hydrogen	Nitrogen	
Cr(III) Complex	68.91	8.13	6.15	65.92

Cyclic voltammetry of Cr(III) complex

In Figure 3, the Cr(III) complex exhibits a reduction peak at Epc = 0.6V with the corresponding oxidation peak at Epa= 1.3V and the scan rate of 50mV/s.

Thermogravimetric analysis

In Figure 4, Thermogravimetric analysis of Cr(III) complex of 2-aminobenzonitrile and octanoate ion shows two significant temperature transitions of weight loss with common and specific stages, termed as two stages of thermal degradation. The TGA plateau of the complex shows that the endothermic peak at 160°C and 280°C.

Powder X-ray diffraction technique

In Figure 5, the Powder X-ray diffractogram of the Cr(III) complex was recorded in the range of 5° to 80° 2θ values. The XRD pattern indicates that the prepared complexes have well defined crystalline patterns, with various degrees of crystallinity. In the complex, the trend of the curves decreases from maximum to minimum intensity indicating amorphous nature of the complex.

Biological activity

Antibacterial activity

The free ligands and their Cr(III) complex were evaluated against the bacteria *staphylococcus aureus, streptococcus*, *Escherichia coli, Klebsiella pneumonia, P. aeruginosa, salmonella typhi* and *Enterobacter* at different concentration by using agar-well diffusion method. The results are given in the Table 2.

Antifungal activity

The synthesized Cr(III) complex and the free ligands were evaluated against the fungi, *viz., C.albicans, Aspergillus Niger* and *Aspergillus Flavus* at different concentrations by agar-well diffusion method. The results are given in the Table 3.

Antioxidantal activity (Radical Scavenging Activity)

The 2,2″-diphenyl-1-picrylhydrazyl (DPPH) radical assay provides an easy and rapid way to evaluate the antiradical activities of antioxidants. Determination of the reaction kinetic types DPPHH is a product of the reaction between DPPH and an antioxidant.

The reversibility of the reaction is evaluated by adding DPPHH at the end of the reaction. If there is an increase in the percentage of remaining DPPH• at the plateau, the reaction is reversible, otherwise it is a complete reaction.

DPPH was used as stable free radical electron accepts or hydrogen radical to become a stable diamagnetic molecule. DPPH is a stable free radical containing an odd electron in its structure and usually used for detection of the radical scavenging activity in chemical analysis. The reduction capability of DPPH radicals was determined by decrease in its absorbance at 517 nm induced by antioxidants. The graph was plotted with percentage scavenging effects on the y-axis and concentration (µg/mL.) on the x-axis is given in Figure 7.

DNA Binding – Emission study

In Figure 8, the binding of Cr(III) complex to *CT*-DNA can be studied by competitive binding experiments. Ethidium bromide (EB) is known to show fluorescence when bound to DNA, due to its strong intercalation between the adjacent DNA base pair. The fluorescent light is quenched

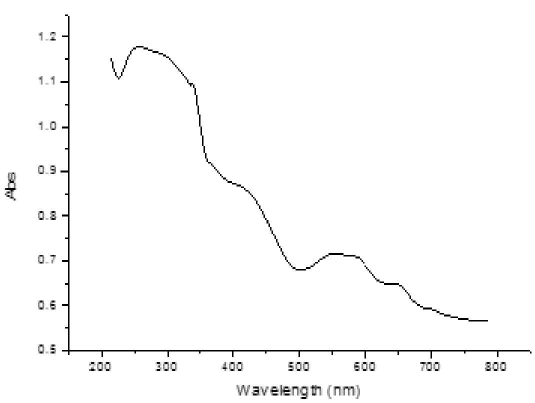


Figure 1: Electronic spectrum of Cr(III) complex.

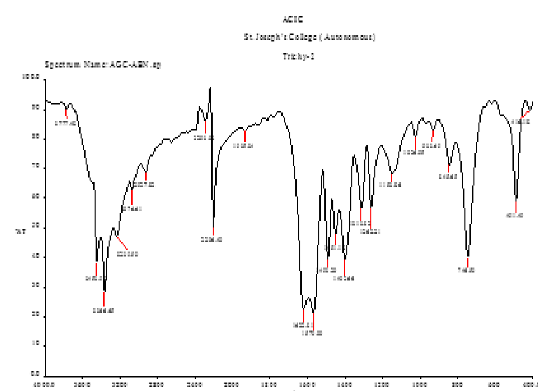


Figure 2a: FT IR Spectrum of 2-aminobenzonitrile.

Table 2: Antibacterial activity of the ligands and complex.

S. No	Ligand/ Complexes	Conc. µg/ml	Zone of inhibition in diameter (mm)						
			S. aureus	*Streptococcus*	*E. coli*	*Klebsiella*	*P. aeruginosa*	S. typhi	Entero bacter
1	2-ABN	50	04	05	06	11	14	10	11
		100	09	12	11	16	21	16	18
2	NaOC	50	04	05	05	04	11	03	05
		100	08	18	07	09	17	04	21
3	Cr(III) Complex	50	10	15	04	06	04	05	04
		100	21	29	10	09	11	08	08

05-10 Resistant; 11-16 Moderate; 16-21 Highly activity; 21-30 Enhanced activity

Table 3: Antifungal activity of the ligands and complex.

S. No	Ligands/ Complexes	Conc. µg/ml	Zone of Inhibition in diameter (mm)		
			C. albicans	*Aspergillus Niger*	*Aspergillus Flavus*
1	2-ABN	50	05	04	03
		100	07	05	05
2	NaOC	50	04	03	04
		100	05	05	05
3	Cr(III) Complex	50	05	04	03
		100	07	05	15

05-10 Resistant; 11-16 Moderate; 16-21 Highly activity; 21-30 Enhanced activity

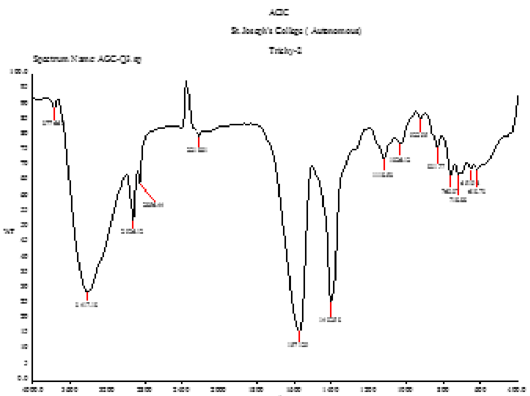


Figure 2b: FT IR Spectrum of Sodium octanoate.

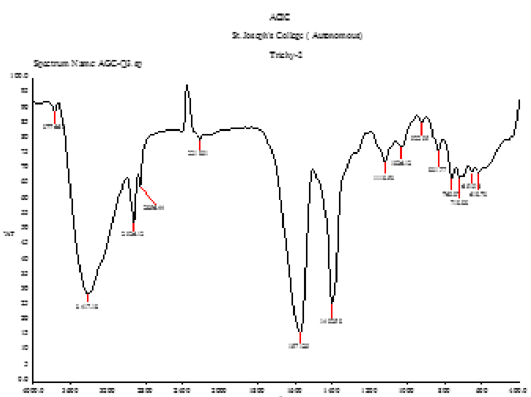


Figure 2c: FT IR Spectrum of Cr(III) complex

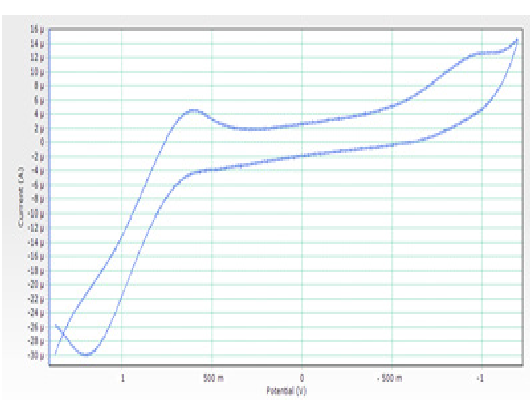


Figure 3: Cyclic voltammogram of Cr(III) complex.

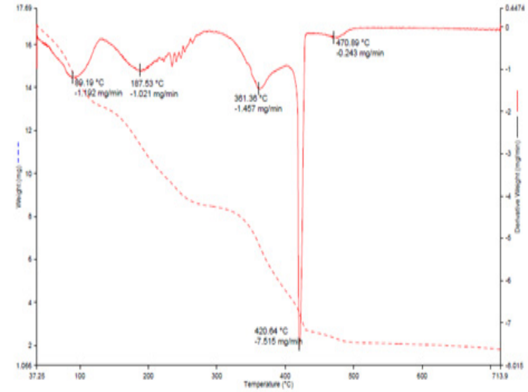


Figure 4: Thermogram of Cr(III) complex.

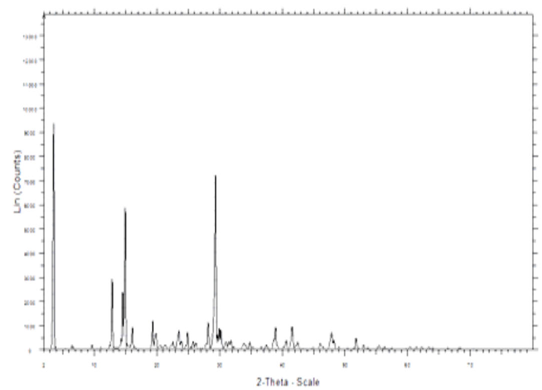


Figure 5: X-Ray Diffractogram of Cr(III) complex.

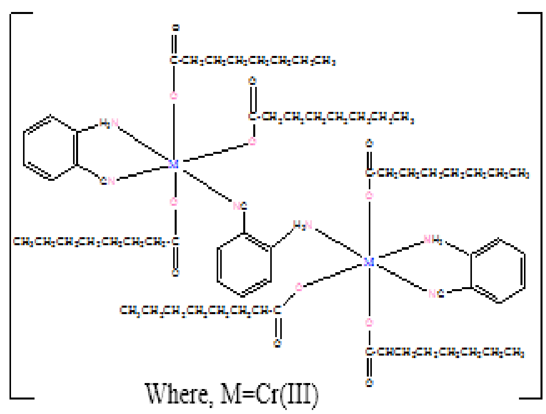


Figure 6: Octahedral dimeric structure of Cr(III) complex.

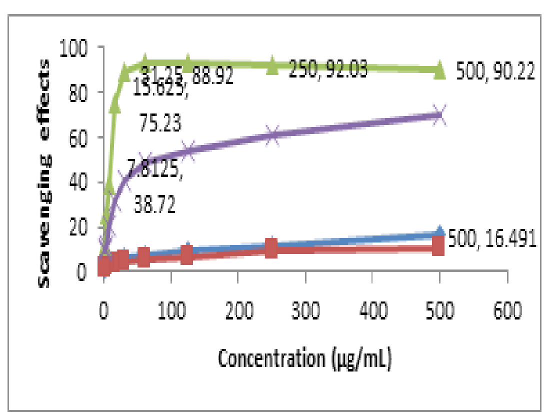


Figure 7: Antioxidant activity of ABN, NaOC, Cr(III) complex and Vitamin C.

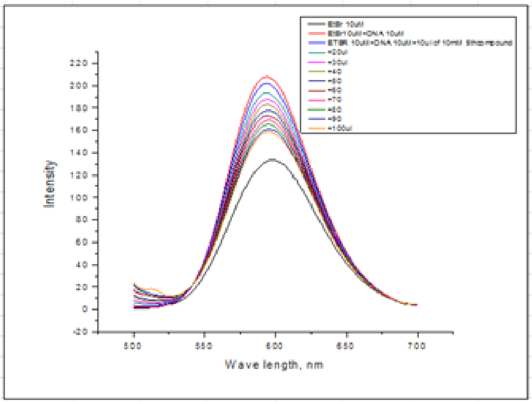


Figure 8: Emission spectrum of EtBr bound to DNA in the absence and presence of Cr(III) complex.

by the addition of a second molecule. The quenching extent of fluorescence of ethidium bromide binding to DNA is used to determine the extent of binding between the second molecule and DNA. The addition of the complex to DNA pretreated with ethidium bromide causes appreciable reduction in the emission intensity, indicating the replacement of the ethidium bromide fluorophore by the complex results in a decrease of the binding constant of the ethidium to the DNA.

DISCUSSION

The elemental analysis and metal estimation of the complex led to the formula $[Cr_2(OC)_6(ABN)_3]$. The percentages of carbon, hydrogen and nitrogen in the complex were found to be 68.91 (69.01), 8.13(8.26) and 6.15(6.37) respectively. The experimental values are in good agreement with the theoretical values (given in the parentheses). The low electrical conductivity value indicates that the chromium complex is non-electrolytic nature (1:0) type, confirming its molecular formula $[Cr_2(OC)_6(ABN)_3]$.[19]The electronic spectrum of Cr(III) complex exhibits three absorption bands at 540 nm, 390 nm and 280 nm, which are assignable to the transitions, ${}^4A_{2g} \rightarrow {}^4T_{2g}(\nu_1)$, ${}^4A_{2g} \rightarrow {}^4T_{2g}(F)(\nu_2)$ and ${}^4A_{2g} \rightarrow {}^4T_{1g}(P)(\nu_3)$, respectively. The electronic spectrum of the chromium complex reported here is in reasonable agreement with those in literature.[20,21] The magnetic moment at room temperature is 3.31 B.M which corresponds to the expected value for octahedral geometry and involving d^2sp^3 hybridisation in the Cr(III) metal ion. The observed magnetic moments are slightly less than the spin-only value probably due to the weak antiferromagnetic coupling of the spins of neighbouring Cr(III) through the ABN bridge in the possible dimeric complex and this lends support to the inference made from analytical data.[22]

In Figure 2c, FT IR spectra of 2-aminobenzonitrile and octanoate ion ligands were compared with Cr(III) complex. The band(s) are broadened at 3417 cm^{-1} and the nitrile group of the ABN underwent at 2228 cm^{-1} after complexation, indicating the coordination of amino nitrogen and nitrile group to the metal atom. In free octanoate ion the ν(C-O) stretching at 1207 cm^{-1} get shifted to the frequencies of 1118 cm^{-1} in complex, which indicates the monodentate coordination of the octanoate ion through oxygen atom. Thus, the IR spectral data suggest that the ABN is bound to the metal ion through the amino nitrogen and cyano nitrogen and OC is bound through the oxygen donor atom.[23]

The peak separation of cyclic voltammetry (ΔEp) of the couple is 0.7V. With increasing scan rates, the ΔEp value also increases giving more evidence of quasi-reversible one electron transfer process Cr(III)/Cr(II) couple.[24] The difference between forward and backward peak potentials can provide a rough evaluation of the degree of the reversibility. The ratio of cathodic to anodic peak height is less than one. However, the peak current increases with the increase of the square root of the scan rates.

The TGA plateau of the complexes shows that these complex exhibits no mass loss up to 100°C, indicating the absence of coordinated water and a high thermal stability of the complexes. The weight loss at 160°C in TGA curves of complexes is termed the first stage of thermal degradation. In this case, the present weight loss is in the range of (46.57- 49.82%), which may be attributed to the decomposition of less stable 2-aminobenzonitrile. The onset of second step decomposition occurs at 280°C, which gives the loss of octanoate ion (18.02 - 25.88%) bonding with the metal complexes. The experimental values are in full agreement with the percent weight calculated on the basis of stoichiometry proposed for the complex.[25]

The powder XRD patterns of the synthesized Cr(III) complex show sharp crystalline peaks indicating their crystalline phase. The average crystallite size (d_{XRD}) of the complexes was calculated using Scherer's formula. The prepared complexes had an average crystallite size of 45 nm indicating its nanocrystalline in nature.[26,27]

Suggested structure of the Complex

The proposed structure of complex based on the above mentioned physico-chemical and the spectral (elemental analysis, molar conductance, magnetic moment, electronic, FT-IR spectra, cyclic voltammetry, thermal analysis and powder XRD technique) studies, the tentative structures proposed for the complex is shown in Figure 6.

The antibacterial activity of the complex shows enhanced activity against *Staphylococcus aureus, streptococcus* and moderately active against the rest of the organisms. The increased activity of the metal complexes can be explained on the basis of chelation theory.[28] It is known that chelation tends to make the ligand act as powerful and potent bactericidal agents, killing more number of bacteria than the ligand.

The antifungal activity of the complex shows enhanced activity against the tested fungi. A comparative study of zone of inhibition diameter values of the ligands and their complex indicate that the metal complex has a better fungicidal activity than the free ligands. This is probably due to the greater lipophilic nature of the complexes. It is evident from the data that this activity significantly increases on coordination.[29]

The metal complex showed enhance activity as a radical scavenger compared with ascorbic acid, these results were in good agreement with previous metal complexes studies where the ligand has the antioxidant activity and it is expected that the metal moiety will increase its activity.[30,31]

In the DNA binding study, the classical Stern-Volmer equation: Io/I = 1 + Ksvr, where Io and I are the fluorescence intensities in the absence and the presence of complex respectively. Ksv is a linear Stern–Volmer quenching constant, r is the ratio of the total concentration of complex to that of DNA. The quenching plots illustrate that the quenching of ethidium bromide bound to DNA by the complex are in good agreement with the linear Stern-Volmer equation, which also indicates that the complex binds to DNA. In the plot of I_0/I versus $C_{Complex}/C_{DNA}$, K is given by the ratio of the slope to intercept. The K values for Cr(III) is 5.47. The data suggest that the interaction of Cr(III) complex with DNA is strongest, which is consistent with the above absorption spectral results. K values indicate that the interaction of the complex with DNA is a intercalative mode.[32]

CONCLUSION

In the present study, our efforts were to synthesize and characterize the Cr(III) metal complex with 2-aminobenzonitrile and octanoate ion as ligands. The new complex was synthesized using microwave irradiation. The synthesized metal complex were characterized by various physicochemical and spectral analyses. Based on the analytical, molar conductance, spectral and magnetic moment, octahedral geometry has been suggested for the Cr(III) complex. The synthesized complex was tested for antimicrobial activities. The metal complex has significant antimicrobial and antioxidantal activities as compared to the free ligands. The effectiveness of the DNA binding of the complexes is being confirmed by means of change in intensity of emission in the case of emission spectral studies.

ACKNOWLEDGEMENT

The authors thank the Management and the Principal of Thanthai Hans Roever College (Autonomous), Perambalur, Tamil Nadu, India for permitting them to carry out this work. The authors are also thankful the Heads, SAIF, IIT Madras , IIT-Roorkee, IIT-Bombay and the Director, STIC, Cochin for providing the spectral data.

CONFLICT OF INTEREST

The authors declare that there is no conflict of Interest.

ABBREVIATIONS

ABN: 2- aminobenzonitrile; **NaOC:** Sodium benzoate.

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Cite this article: Govindharaju R, Muruganantham N, Balasubramaniyan S, Palanivelan L, Jayalakshmi B, Rajalakshmi K, Ramachandramoorthy T. Synthesis, Spectral Characterization and Biological Evaluation of Cr(III) Complex with Mixed N,N and O-donor Ligands. Int. J. Pharm. Investigation. 2019;9(4):158-63.