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Synthesis and antimicrobial activities of sulfonohydrazide-substituted 8-hydroxyquinoline derivative and its oxinates

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Looking at the pharmacological importance of 8-hydroxyquinolines and sulfonamides, in the present study, a novel bi-dentate ligand 4-amino-N'-[(8-hydroxyquinoline-5-yl)methyl] benzenesulfonohydrazide (AHQMBSH) having above both moieties within a single molecular framework was synthesized by the reaction of N-acetamidobenzene sulfonohydrazide with 5-chloromethyl-8-hydroxyquinoline hydrochloride. Its metal(II) oxinates were also prepared with Mn(II), Fe(II), Co(II), Ni(II), Cu(II) and Zn(II) salts. All the above compounds were investigated by physicochemical analyses, thermogravimetric analysis and spectroscopic techniques. Antimicrobial activities for the above prepared compounds were carried out using the agar-plate method against various strains of bacteria (Staphylococcus aureus, Bacillus subtillis, Pseudomonas aerugionsa, Escherichia coli) and fungi (Aspergillus niger and Aspergillus flavous). The results show a significant increase in antimicrobial and antifungal activities of AHQMBSH compared with the parent 8-hydroxyquinoline and sulfonamides. Copyright © 2010 John Wiley & Sons, Ltd.

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Keywords: 8-hydroxyquinoline; sulfonylhydrazide; oxinates; antibacterial and antifungal activity

Introduction

Among the class of hydroxyquinolines, the chemistry of 8hydroxyquinolines (8HQs) has attracted special interest due to their diverse biological properties^[1,2] such as antiamebic,^[3] antiseptic and disinfectant,^[4,5] antimalarial,^[6] antituberculotic,^[7] antidiuretic,^[8] anticancer,^[9,10] antibacterial and antifungal.^[11-13] 8HQ shows remarkable effects similar to the antibiotic, lomofugin, which rapidly and selectively inhibits the RNA synthesis in yeast.^[14] Iron bound to the lipophilic chelator, 8HQ, causes substantial DNA strand breakage of cultured human lung cells.^[15]

8-Hydroxyquinoline-like biological and pharmacological chelating agent-based ligands and chelates are in progress in coordination studies with increasing interest^[16,17] and also in the field of metal extraction.^[18] 8HQs exert the above-mentioned activities, possibly due to their ability to chelate with the metal ions, which essential for metabolism,^[13] where the -OH group of 8HQ acts as an acid, dissociating to $-O^-$. Bivalent cations are bounded by the dissociated acid group and the lone pair of electrons borne by the nitrogen atom. The metal chelates of 8HQs (oxinates) have been reported biologically active due to their lipid solubility and have comparable activity against bacteria and fungi. The activity of oxinates was explained by assuming that these complexes first penetrate the cell wall due to lipid solubility and at the site of action undergo dissociation to 1:1, 8HQ: complex, which then becomes a toxic entity by combining with the metal binding sites of enzymes as well as by blocking the same.[19-22]

In addition to these, the synthetic antibacterial sulfonamides have been well documented since 1935, due to their excellent pharmacological activities, but toxicity and microbial resistance mean that it cannot be used in the treatment of disease.^[13]

Thus, looking at the promising biological activities of sulfonamides and 8-hydroxyquinolines, it was thought interesting to bring these two biologically active moieties within a single molecular framework with a view to studying their additive effects on the chemical and biological properties. Hence, the present study is enriched with progressive findings about the synthesis, characterization and comparative biological study of 4-amino-N'-[(8-hydroxyquinoline-5-yl)methyl]benzene sulfonohydrazide and its M(II) oxinates.

Experimental

Materials and Methods

All the chemicals used, including sulfanilamide, 4aminobenzenesulfonylhydrazide and 8-hydroxyquinoline, were of analytical grade and were purchased from local markets. They were purified by standard methods prior to use.^[23] Nutrientagar and potato dextrose agar were purchased from Hi-media Chemicals, India. Metal(II)-salts (chloride/nitrate/sulfate) of Mn(II), Fe(II), Co(II), Ni(II), Cu(II) and Zn(II) were used in their hydrated form.

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Silica gel F254 thin-layer chromatographic plates of size 20×20 cm were purchased from the E. Merck (India) Limited, Mumbai and used for purity evaluation. The elemental analyses (C, H, N and S) were performed with a model Elemental Vario EL C, H, N elemental analyzer. The infrared spectra (FT-IR) were obtained from KBr pellets in the range 4000-400 cm⁻¹ with a Perkin Elmer spectrum GX spectrophotometer (FT-IR) instrument. The ¹H NMR and ¹³C NMR Attached Proton Test (APT) spectra were recorded on a Bruker (400 MHz) instrument using DMSO d_6 as solvent as well as an internal reference standard. The mass (ESI-MS) spectrum of 4-amino-N'-[(8-hydroxyquinoline-5yl)methyl]benzenesulfonohydrazide (AHQMBSH) was recorded on a Shimadzu LC-MS 2010 eV mass spectrophotometer in acetonitrile. Diffuse electronic spectra were recorded on a Beckman DK-2A spectrophotometer using MgO as a reference. Magnetic moments were determined by the Gouy method with mercury tetrathiocyaneto-cobaltate(II), [HgCo(NCS)₄] as calibrant (χ_g = 1644 \times 10⁻⁶ cgs units at 20 $^\circ$ C), by Citizen Balance (at room temperature). The diamagnetic correction was made using Pascal's constant.^[24] The thermogravimetric analyses studies were carried out with a model Perkin Elmer thermogravimetry analyzer at a heating rate of 10°C min⁻¹ in air. The metal contents of the complexes were analyzed by EDTA titration after decomposing the organic matter with HClO₄, H₂SO₄ and HNO₃ (1:1.5:2.5) mixture.^[25] The melting point of AHQMBSH was checked by standard open capillary method and is uncorrected.

The 4-acetamidobenzenesulfonylhydrazide^[26] and 5chloromethyl-8-hydroxyquinoline hydrochloride (CMHQ)^[4] were prepared and used as starting materials for the synthesis of novel ligand AHQMBSH by slight modification of the method reported in the literature^[27] while metal(II) complexes of AHQMBSH were synthesized by a subsequently reported method.^[28]

The outline of synthesis of AHQMBSH and its M(II) oxinates is shown in Scheme 1. The physicochemical parameters of metal(II) oxinates are summarized in Table 1.

Synthesis of ligand: AHQMBSH

To the mixture of 4-acetamidobenzenesulfonylhydrazide (5.87 g, 25.6 mmol) and triethylamine (8.18 g, 80.8 mmol) in dry pyridine (40 ml), CMHQ (6.2 g, 26.9 mmol) was added with continuous stirring. The contents were refluxed for 70 min. The completion of the reaction was confirmed by TLC using CHCl₃ : CH₃OH (80 : 20) mixture as the mobile phase (R_f 0.45). The excess of pyridine was distilled off and the residue was poured into the ice-cold water to yield a dark orange product which was filtered and washed with hot water and ethyl acetate and then dried over a vacuum desiccator (7.6 g).

It was further hydrolyzed by refluxing with 0.2 M hydrochloric acid solution (50 ml) for 45 min. The reaction mixture was then cooled, poured into ice-cold water and neutralized with saturated Na₂CO₃ solution to yield a dark green product, which was filtered off, washed with boiling water followed by ethyl acetate and recrystallized from acetonitrile to afford dark green crystals, then dried in a vacuum oven. The formation of the product was confirmed by TLC using CHCl₃:CH₃OH (80:20) mixture as the mobile phase (R_f 0.53). Yield: 4.5 g, (51%). Decomposed at 241°C; ESI-MS: 344.02 *m/z* (M⁺ peak).



Scheme 1. Proposed route for the synthesis of AHQMBSH and $[M(AHQMBSH)_2(H_2O)_2].$

Synthesis of Metal(II) Oxinates: M(II)(AHQMBSH)₂; M = Mn(II), Fe(II), Co(II), Ni(II), Cu(II), Zn(II)

A warm solution of metal(II) salt (2.5 mmol) in 50% aqueous formic acid (2.5 ml) was added drop by drop with continuous stirring to previously warmed solution of AHQMBSH (5 mmol, 2 equivs) in 20% aqueous formic acid solution (20 ml). With the proper adjustment of the pH (~8.5) with 50% NH₄OH, the resultant mixture was further digested in a water bath for 4–5 h and centrifuged. The suspended solid complex was allowed to settle and collected by filtration, washed with sufficient quantity of distilled water and then with a little hot ethanol and acetonitrile, then dried in vacuum desiccators over anhydrous calcium chloride. The yield was 80–90%.

Results and Discussion

5-Chloromethyl-8-hydroxyquinoline hydrochloride was prepared by chloromethylation of 8-hydroxyquinoline. Considerable difficulties were faced to obtain high purity of CMHQ even after washing the crude CMHQ with concentrated hydrochloric acid and acetone. This might be due to incomplete removal of 8-hydroxyquinoline. Another difficulty was the possibility of substitution reaction during the crystallization with protic solvent. The use of inorganic base catalyst was avoided, such as sodium/potassium bicarbonate, sodium/potassium hydrogen carbonate and sodium hydroxide, as it either leads to a slow reaction or may give 5-hydroxymethyl-8-hydroxyquinoline in quantitative yield.^[4] To overcome these difficulties, triethylamine (TEA) was used as scavenger while reacting CMHQ with

Table 1. Physicochemical parameter of the AHQMBSH ligand and M(II)(AHQMBSH) ₂ complexes											
Compounds	Molecular weight	Color	Yield (%)	m.p.ª (°C)	Elemental analysis, % found (required)				//	F. (kcal	
(empirical formula)					С	Н	Ν	S	Metal	(calcd)	mol^{-1})
AHQMBSH (C ₁₆ H ₁₆ N ₄ O ₃ S)	344.39	Dark green	63.5	241	55.82	4.66	16.31	9.33	-	-	12
					(55.80)	(4.68)	(16.27)	(9.31)			
$[Mn(AHQMBSH)_2(H_2O)_2](C_{32}H_{34}MnN_8O_8S_2)$	777.73	Brown	87	>300	49.40	4.43	14.38	8.28	7.14	5.58	7.5
					(49.42)	(4.41)	(14.41)	(8.25)	(7.06)	(5.92)	
[Fe(AHQMBSH) ₂ (H ₂ O) ₂] (C ₃₂ H ₃₄ FeN ₈ O ₈ S ₂)	778.64	Dark brown	84	>300	49.39	4.39	14.41	8.21	7.08	5.28	8.6
					(49.36)	(4.40)	(14.39)	(8.24)	(7.17)	(4.90)	
$[Co(AHQMBSH)_2(H_2O)_2](C_{32}H_{34}CoN_8O_8S_2)$	781.72	Dark green	88	>300	49.14	4.41	14.30	8.23	7.48	4.86	8.5
					(49.17)	(4.38)	(14.33)	(8.20)	(7.54)	(3.87)	
[Ni(AHQMBSH) ₂ (H ₂ O) ₂] (C ₃₂ H ₃₄ NiN ₈ O ₈ S ₂)	781.48	Dark red	91	287	49.21	4.37	14.37	8.18	7.64	3.27	8.9
					(49.18)	(4.39)	(14.34)	(8.21)	(7.51)	(2.83)	
$[Cu(AHQMBSH)_2(H_2O)](C_{32}H_{32}CuN_8O_7S_2)$	768.32	Dark green	89	>300	49.99	4.18	14.61	8.33	8.30	1.86	8.4
		-			(50.02)	(4.20)	(14.58)	(8.35)	(8.27)	(1.73)	
$[Zn(AHQMBSH)_2(H_2O)_2](C_{32}H_{34}ZnN_8O_8S_2)$	788.20	Dark yellow	82	>300	48.79	4.32	14.26	8.13	8.42	D	8.8
					(48.76)	(4.35)	(14.22)	(8.14)	(8.30)		
^a Melting points $({}^{\circ}C)$ are uncorrected: D – diamagnetic											

4-acetamidobenzenesulfonylhydrazide to afford intermediate in good yield, which upon acid hydrolysis gave AHQMBSH in moderate yield.

The synthesized novel 4-amino-N'-[(8-hydroxyquinoline-5yl)methyl]benzene sulfonohydrazide (AHQMBSH) appears as dark green crystals. It has partial solubility in acetone, methanol, ethanol and acetonitrile, while being soluble in polar aprotic solvents like dimethylformamide (DMF), dimethylsulfoxide (DMSO), organic acids and pyridine. All the metal(II) oxinates, M(II)(AHQMBSH)₂ had characteristic color, are stable in air and practically insoluble in water, ethanol, methanol, chloroform and hexane, while low solubility was observed in DMF as well as in DMSO.

Characterizations

The formation of the AHQMBSH was apparent from the dark blue and yellow spots by visualizing in long- and short-wavelength UV light respectively on the TLC. The mass spectrum (ESI-MS) of AHQMBSH was recorded in acetonitrile and the molecular ion peak observed at *m/z* 344.02 confirmed the proposed formula.

The results of elemental analyses (C, H, N, S) of ligand AHQMBSH and its metal(II) oxinates are given in Table 1 and were in good agreement with their predicted molecular formula, showing that the oxinates have 1:2 metal–ligand ratio.

FT-IR Spectra

The FT-IR spectrum of AHQMBSH and all of its oxinates shows all the important stretching and bending vibrations in the appropriate region.^[29] In the spectrum of AHQMBSH, the band appeared at 3379 cm⁻¹ due to O-H stretching vibration and a strong band at 1400 cm⁻¹ was due to O-H bending vibration and C-O stretching vibration.^[29] The -CH₂-shows C-H stretching vibration at 2964 cm⁻¹. The IR spectrum of AHQMBSH also shows the important bands at 1598 cm⁻¹ of C=N, 1500 cm⁻¹ of C=C and 1475 cm⁻¹ of C-C, assigned to the aromatic skeletal stretching vibrations of the parent heterocyclic ring.^[29] Further, two strong bands of S=O appeared at 1318 and 1144 cm⁻¹ due to asymmetric and symmetric stretching vibrations, suggesting

the presence of $-SO_2$ -group.^[30] The N-H stretching vibrations appeared near about 3200 cm⁻¹, while N-H and C-N bending vibrations appeared at 1659 and 1260 cm⁻¹, respectively, showing the presence of an amino group. The band observed at 1036 cm⁻¹ shows the presence of the -HN-NH-group.

However, comparisons of FT-IR spectra of ligand (AHQMBSH) and its metal(II)-coordinated oxinates showed some important characteristic differences.^[31] One of the significant differences to be expected was the presence of a more broadened band in the region of 2700-3400 cm⁻¹ for the chelates, as the oxygen of the -OH group of the ligand forms a coordination bond with the metal ions. It also explains the presence of coordinated water molecules.^[32] Another noticeable difference is that the band due to the C=N stretching vibration of 8HQ at around 1600 cm⁻¹ in the IR spectrum of AHQMBSH was shifted to lower frequency, whereas the band at 1400 cm⁻¹ in the IR spectrum of AHQMBSH assigned to in-plane - OH deformation was shifted towards higher frequency in the spectra of the chelates due to the formation of the M-O bond.^[33] This was further confirmed by a weak band at 1100 cm⁻¹ corresponding to C-O-M stretching, while bands around ${\sim}730$ and ${\sim}545\,\text{cm}^{-1}$ correspond to the $M \rightarrow N$ vibration.^[34] The bands due to the -HN-NH-group appear to be the same as in the spectrum of AHQMBSH. These characteristic features of the IR studies suggest the formation of AHQMBSH and its metal(II) oxinates.

Diffuse Electronic Spectral and Magnetic Properties Data

The diffuse electronic spectra of $[Cu(AHQMBSH)_2(H_2O)]$ exhibited two bands at 26235 cm⁻¹ due to charge transfer and a broad band having maxima at 15576 cm⁻¹ due to the ${}^{2}E_{g} \rightarrow {}^{2}T_{2g}$ transition. The broadening of the signal might be due to Jahn–Teller distortion. The absorption bands of the diffuse electronic spectra and the value of their magnetic moment favor a tetragonally distorted octahedral geometry around Cu(II) ion.^[35,36] [Ni(AHQMBSH)_2(H_2O)_2] showed three weak absorption bands at 9981, 16 025 and 24 470 cm⁻¹ corresponding to the characteristic transitions ${}^{3}A_{2g} \rightarrow {}^{3}T_{2g}$, ${}^{3}A_{2g} \rightarrow {}^{3}T_{1g}(F)$, ${}^{3}A_{2g} \rightarrow {}^{3}T_{1g}(P)$. [Co(AHQMBSH)₂(H₂O)₂] exhibited three absorption bands at



Figure 1. Thermogravimetric curve of AHQMBSH and its oxinates.

9830, 15490 and 22115 cm⁻¹, respectively, due to ${}^{4}T_{1g}(F) \rightarrow$ ${}^{4}T_{2g}(F)$, ${}^{4}T_{1g}(F) \rightarrow {}^{4}A_{2g}(F)$ and ${}^{4}T_{1g}(F) \rightarrow {}^{4}T_{1g}(P)$ transitions. The absorption bands of the diffuse electronic spectra and values of their magnetic moments show an octahedral geometry around Ni(II) and Co(II) ions.^[37,38] The spectra of [Mn(AHQMBSH)₂(H₂O)₂] showed weak bands at 16798, 18435 and 23816 cm⁻¹ assigned to the ${}^{6}A_{1g} \rightarrow {}^{4}T_{1g}, {}^{6}A_{1g} \rightarrow {}^{4}T_{2g}, {}^{6}A_{1g} \rightarrow {}^{4}A_{1g}, {}^{4}E_{g}$ transitions and their magnetic moment values suggest an octahedral geometry for the Mn(II) ion. The spectrum for [Fe(AHQMBSH)₂(H₂O)₂] shows bands at 18 985 and 36 738 cm⁻¹ assigned to the ${}^{5}T_{2q} \rightarrow {}^{3}E_{q}$ and ${}^{5}T_{2q} \rightarrow {}^{3}T_{1q}$ transitions, respectively, suggesting its octahedral structure in support of the magnetic moment value around the Fe(II) ion. As the spectrum of [Zn(AHQMBSH)₂(H₂O)₂] was not well resolved, it was not well interpreted, but its magnetic moment value shows that it is diamagnetic in nature, as expected.^[28] The results of the magnetic moment value (Table 1) were shown to have octahedral geometry for all the M(II) oxinates. Hence, the observed values of magnetic moments and the electronic spectra of M(II) oxinates supported octahedral geometry for all the structures.^[39]

Thermogravimetric Analysis

Thermogravimetric analysis (TGA) for the AHQMBSH and its oxinates was carried out within the temperature range of 40-900 °C in air at the heating rate of 10 °C min⁻¹ to establish their compositional differences and to ascertain the nature of associated water molecules. The thermogravimetric curves of all the compounds are presented in Fig. 1. The determined temperature ranges and corresponding percentage mass losses accompanying the changes on heating revealed the following findings.

Securitization of this data envisages that AHQMBSH follows single-step thermal decomposition. The initial weight loss of 1% might be due to loosely held solvent in AHQMBSH. The weight loss commences in the range of 150–550 °C up to 74% and further slower degradation takes place up to 900 °C.

Similarly, securitizations of the TGA data of oxinates of corresponding Mn(II), Fe(II), Co(II), Ni(II), Cu(II) and Zn(II) have shown two-step decomposition. The initial weight loss occurring might be due to the solvent molecules or loosely held moisture trapped inside the oxinates, whereas the weight loss observed

in the range of 125–180 °C might be attributed to the metalcoordinated two water molecules.^[40] This also satisfies the six coordination sites of the metal ions of metal(II) oxinates. For metal(II) oxinates maximum weight loss (74.64, 75.30, 75.55, 74.40, 73.32 and 73.40%) was observed in the temperature range of 210–900 °C, and the remaining weights of 18.85 (878 °C), 18.80 (779 °C), 18.35 (697 °C), 19.40 (664 °C), 21.00 (631 °C) and 19.70 (784 °C) correspond to a mixture of metal oxide and some ashes as the ultimate pyrolysis products.

There was a remarkable difference in the mode of thermal degradation for AHQMBSH and its oxinates. Oxinates have shown fast decomposition patterns as compared with AHQMBSH. These results of thermal behavior can be explained by the fact that the decomposition of chelates was catalytically induced by the metal ions.^[41]

The energy of activation (E_a) for thermal decomposition of AHQMBSH and its oxinates was estimated by the reported method using following equation:^[42]

$$\ln[\ln(1/y)] = (E_a/RT + 1) \ln T + \text{constant}$$

The energy of activation (E_a) was computed from the slope $(-E_a/R)$ of the plot of $\ln[\ln(1/y)]$ vs ($\ln T$), and is noted in Table 1. The energy of activation for AHQMBSH was found to be 12 kcal mol⁻¹, while the activation energy observed for oxinates was between 8.8 and 10.9 kcal mol⁻¹.

¹H NMR Spectra

The ¹H NMR spectrum of ligand exhibited a broad singlet at δ 9.99 ppm due to the –OH proton.^[43,44] Disappearance of this signal in the spectrum of Zn(II) complex suggested that this proton had been lost due to coordination of oxygen atom to the metal ion.^[45] The signal due to H² of Zn(II) complex appeared at very low magnetic field compared with that of ligand, suggesting the involvement of N¹ in the formation of complex. The protons of N⁽¹⁾ and N⁽²⁾ in AHQMBSH and its Zn(II) complex resonated as a singlet at δ 10.74, δ 12.48 and δ 10.71, δ 12.47 ppm respectively. This suggested that neither of the nitrogen atoms participated in the complex formation as the chemical shifts remained almost unchanged both in ligand as well as in complex. The N⁽³⁾H₂ protons appeared as singlet at δ 6.19. All the quinoline protons shifted slightly downfield, except H⁷, which shifted slightly upfield.^[45,46]

Table 2. Antimicrobial activity of all the compounds											
		Zone of inhibition (mm) ^a									
Sample no.	Compounds	S. aureus	B. subtilis	E. coli	P. aeruginosa	A. niger	A. flavus				
1	Sulfanilamide	18	14	20	19	24	22				
2	Sulfahydrazone	16	15	17	21	22	20				
3	8HQ	24	22	26	22	21	19				
4	AHQMBSH	34	35	31	28	37	32				
5	[Mn(AHQMBSH) ₂ (H ₂ O) ₂]	16	13	13	14	12	11				
6	[Fe(AHQMBSH) ₂ (H ₂ O) ₂]	22	19.5	21	19	23	21				
7	[Co(AHQMBSH) ₂ (H ₂ O) ₂]	17	15	16	17	13.5	18				
8	[Ni(AHQMBSH) ₂ (H ₂ O) ₂]	18	16	14	19	17	15				
9	[Cu(AHQMBSH) ₂ (H ₂ O)]	19.5	22	21	20	20	19.5				
10	$[Zn(AHQMBSH)_2(H_2O)_2]$	13	15	11	12	12	15				
^a Zone of inhibition (mm) obtained upon subtraction of control (DMSO) $pprox$ 11.											

¹³C NMR (APT) Spectra

The ¹³C NMR (APT) spectra of the AHQMBSH and Zn(II)(AHQMBSH)₂ were in acceptable patterns.^[44,45] In the ¹³C NMR spectrum of AHQMBSH all the aromatic carbon peaks were observed in between δ 110.04–153.99 ppm and a peak of C¹¹ appeared at δ 58.27. C², C⁵ signals at δ 148.13, 116.40 ppm, respectively, in AHQMBSH significantly shifted upfield at δ 144.68, 112.32 ppm, respectively, in the complex. The C⁸, C¹⁰ signal (δ 153.99, 138.53 ppm respectively) underwent a downfield shift (δ 161.86, 143.69 ppm respectively) in Zn(II)(AHQMBSH)₂, indicating coordination of Zn with N¹ and oxygen attached to C⁸ of quinoline ring.

Antimicrobial Activity

The synthesized novel ligand AHQMBSH and its oxinates, M(II)(AHQMBSH)₂, were subjected to invitro antimicrobial activity against the Gram-positive bacteria Staphylococcus aureus and Bacillus subtillis and the Gram-negative bacteria Pseudomonas aerugionsa and Escherichia coli, using agar nutrient as medium, and fungi Aspergillus niger and Aspergillus flavous, using potato dextrose agar as medium. A stock solution of 25 ppm was prepared by dissolving compounds in 20% DMSO solution. The antimicrobial and antifungal activity was performed at a concentration $25 \,\mu g \, m l^{-1}$, using the agar-cup method,^[47] and using DMSO as a control for comparisons of antibacterial and antifungal activity with parent 8HQ, sulfanilamide and 4-aminobenzenesulfonylhydrazide. The results of the measured zone of inhibition (in millimetres) of comparative biological study for AHQMBSH and its oxinates against each of species are shown in Table 2. This suggested that AHQMBSH ligand exhibited higher activity than parent moieties sulfanilamide, 4-aminobenzenesulfonylhydrazide and 8HQ, while oxinates showed less bioactivity as compared with AHQMBSH.

AHQBMSH was found to be more active. The enhancement in the activity of AHQMBSH might be due to the synergistic^[13] effect of sulfonamide and 8HQ moieties within a single molecular framework. AHQMBSH is similar to sulfonamides that, having the heterocyclic tail of that 8HQs, involve chelation with metal ions to form lipophilic chelates, which rapidly transfer the metal across the intact plasma membrane of endothelial cells of Grampositive bacteria and increase their sensitivity to oxidants. The outer membrane of the Gram-negative bacteria might serve as a selective barrier that hinders the passage in the cell in comparison to the AHQMBSH and oxinates attributed less activity. Thus, it was suggested that AHQMBSH exerts its biological activities similarly to 8HQ as a membrane-active agent through metal-ion chelation.^[48]

The biological activity of the above compounds also depends on the nature of the ligand, concentration, lipophilicity, nature of metal ion, coordinating sites and geometry of the complex. All the M(II) oxinates have also shown moderate or less activity as compared with AHQMBSH, as the mechanisms of inhibition are different. The activity of oxinates against bacteria and fungi was explained by assuming that these complexes first penetrate the cell-wall due to lipid solubility and at the site of action undergo dissociation to 1:1, 8HQ: complex which then becomes a toxic entity by combining with the metal binding sites of enzymes as well as by blocking the same.^[22]

Conclusion

In the present investigation novel AHQMBSH and its octahedral metal(II) oxinates (1:2 metal-ligand ratio) were synthesized and characterized, and showed good antibacterial and antifungal activities compared with the parent moieties 8-hydroxyquinoline and sulfonamides. Among the oxinates, Fe(II) and Cu(II) chelates showed better activity, but were found to be less active than AHQMBSH.

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Supporting information

Supporting information may be found in the online version of this article.

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