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Greener and expeditious microwave assisted synthesis, spectral and antimicrobial evaluation of hydrazones and their transition metal complexes

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ABSTRACT

Two new series of Co (II) Ni (II) and Cu (II) metal complexes of the type [M ($C_{17}H_{16}N_4O_2$).$2H_2O$] Ac_2 and [M ($C_{17}H_{14}N_4O_4$).$2H_2O$], where M= Co (II)/ Ni (II)/ Cu (II) and Ac=CH_3COO^-, have been synthesized under microwave irradiation technique. All the synthesized compounds were characterized by running their TLC for single spot, elemental analysis, IR, ^{1}H-NMR, ^{13}C-NMR, magnetic susceptibility measurements and electronic spectral studies. Representative compounds have been screened for their antimicrobial activity. The zone of inhibition values of the compounds were determined by disc diffusion method against two bacteria Staphylococcus aureus and Escherichia coli and two fungi Aspergillus niger and Aspergillus flavus. The antimicrobial activity results indicated that metal complexes show increased activity in comparison of corresponding ligands.

Keywords: Microwave assisted synthesis, IR, ^{1}H-NMR, ^{13}C- NMR, Electronic spectral, Antimicrobial activity

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INTRODUCTION

In recent years sustainable chemistry or green chemistry has emerged as an important area of research. The field of green chemistry confront minimum hazard as the performance criteria while designing new chemical processes. One of the onset areas for achieving this target is to explore alternative reaction conditions and reaction media to accomplish the desired chemical transformations with minimized by products or waste as well as eliminating the use of conventional organic solvents, wherever possible [1].

Due to eco-friendly nature [2-5] microwave assisted syntheses are considered as a branch of green chemistry. Microwave irradiated reactions reduced pollution, offer high yields and low cost together with simplicity in processing and handling [6-8]. Time required for the synthesis of metal complexes by microwave methods have been reported comparatively less [9] than conventional methods.

Hydrazones are eminent compounds having important chemical properties with diverse biological, physical or medicinal applications [10]. Hydrazones have been demonstrated to possess anti-inflammatory, antimalarial [11,12], analgesic [13], antimicrobial [14-16], anticonvulsant [17], antidepressants [18], anti-tumoral [19], antimycobacterial [20], anticancer [21,22] and anti-HIV [23] activities. They are also used as intermediates in the syntheses of nitrogen containing heterocyclic compounds [24]. Transition metals complexes of hydrazones were used in the treatment of tuberculosis [25]. In continuation [26,27] of our research work, in this paper we have reported synthesis of two hydrazones bis-(benzylidene) malonyl dihydrazone (BBMDH) and bis-(salicylidene) malonyl dihydrzone (BSMDH) and their Co(II), Ni(II) and Cu(II) metal complexes by adopting greener approach and their antimicrobial activity.

EXPERIMENTAL SECTION

All the chemicals used were of AR grade and solvents were purified by suitable methods before use. The syntheses were carried out in a domestic microwave oven LG model MS-1927C fitted with water jacket.

Synthesis of malonyl dihydrazide (MDH)

20 ml ethanolic solution of diethyl malonate (7.62 ml, 0.05M) was mixed with hydrazine hydrate (4.82 ml, 0.1M), dissolved in 15 ml ethyl alcohol, in a round bottom flask and subjected to microwave irradiation at 360 W for 4 min. On cooling the solution over a freezing mixture a white solid product was obtained. It was filtered, washed with alcohol followed by ether. Finally, it was dried in a vacuum desiccator over anhydrous $CaCl_2$.

Synthesis of bis-(benzylidene) malonyl dihydrazone (BBMDH)

1.32g (0.01) malonyl dihydrazide was dissolved in 15 ml (30%) acetic acid and 2.06 ml benzaldehyde (0.02M) was mixed to it in a round bottom. The solution was placed in a microwave oven and irradiated at 180 W for 3 min. The contents were cooled over a freezing mixture, a white product was obtained. It was filtered, washed with alcohol followed by ether and then recrystallized from a mixture of 1:1 DMF and alcohol. Finally, it was dried in a vacuum desiccator over anhydrous $CaCl_2$. Similarly, bis-(salicylidine) malonyl dihydrazone was synthesized by irradiating the equimolar mixture of 1.32g (0.01M) malonyl dihydrazide and 2.08 ml (0.02 M) salicylaldehyde in 20 ml (30%) acetic acid in a microwave oven at 260 W for 4 min.

Synthesis of metal complexes

20 ml ethanolic solution of bis-(benzylidene) malonyl dihydrazone (0.30 g, 0.001M) was mixed with 10 ml aqueous solution of cobalt acetate tetrahydrate (0.24 g, 0.001M)/ 0.24 g nickel acetate tetrahydrate (0.001 M)/ (0.20 g, 0.001M) of copper acetate monohydrate. The mixtures were irradiated in the microwave oven in the range 450-500 W for 5-7 min. and allowed to cool at room temperature. Colored precipitates were obtained. The precipitates, thus obtained, were filtered, washed with water and ethanol then with diethyl ether and recrystallized from mixture of acetone and acetonitrile. Finally, products were dried in vacuum desiccator over anhydrous $CaCl_2$. Similarly, metal complexes of bis-(salicylidine) malonyl dihydrazone were synthesized by irradiating 10 ml ethanolic solution of bis-(salicylidine) malonyl dihydrazone (0.34g, 0.001M) with 15 ml aqueous solution of cobalt acetate tetrahydrate (0.24 g, 0.001M) /0.24 g nickel acetate tetrahydrate (0.001M)/ (0.20 g, 0.001M) of copper acetate monohydrate in a microwave oven at 400-520W for 4-8 min. respectively.

RESULTS AND DISCUSSION

Physical and analytical data measurements

Melting points were taken in open capillaries and are uncorrected. The purity and formation of ligands and metal complexes were ascertained by running their TLC for single spot. C, H, N analyses Table.1. were carried out on Carlo Earba 1108 elemental analyzer. Infrared spectra were recorded on 'Bruker' Spectrophotometer using KBr pellets in the range 4,000–400 cm^{-1}. ^{1}H-NMR spectra were recorded in DMSO solvent on NMR Spectrophotometer Bruker DRX 300. Chemical shifts (δ) were expressed in ppm downfield from internal standard TMS. ^{13}C-NMR spectra were recorded on Mercury Plus 300MHz NMR Spectrometer by employing TMS as internal standard in DMSO-d_6 solvent. The electronic spectra of complexes were recorded in dry DMF/ DMSO at room temperature at UV-VIS-NIR Spectrophotometer Cary 5E. The magnetic susceptibilities were measured ats room temperature on a Gouy balance using $CuSO_4.5H_2O$ as calibrant.

Table 1: Physical properties and elemental analyses data of MDH, BBMDH, BSMDH & their metal complexes

S. No.	Name of Compounds	Molecular Formula	Colour	Elemental Analysis%			M.P. /D.T. (±2˚C)
				Carbon C/(F)	Hydrogen C/(F)	Nitrogen C/(F)	
1.	MDH	$C_3H_8N_4O_2$	White	27.27 (28.40)	6.06 (5.38)	42.42 (41.54)	120°C
2.	BBMDH	$C_{17}H_{16}N_4O_2$	White	66.23 (67.20)	5.19 (4.60)	18.18 (19.67)	185°C
3.	BSMDH	$C_{17}H_{16}N_4O_4$	Light yellow	60.00 (61.15)	4.70 (5.50)	16.47 (17.55)	220°C
4.	[Co(BBMDH).$2H_2O$]Ac_2	[Co($C_{17}H_{16}N_4O_2$).$2H_2O$]Ac_2	Dark brown	48.37 (49.39)	4.99 (5.80)	10.75 (9.55)	260˚C
5.	[Ni(BBMDH).$2H_2O$]Ac_2	[Ni($C_{17}H_{16}N_4O_2$).$2H_2O$]Ac_2	Dark brown	48.39 (49.47)	4.99 (3.64)	10.75 (11.67)	200^{0}C
6.	[Cu(BBMDH).$2H_2O$]Ac_2	[Cu($C_{17}H_{16}N_4O_2$).$2H_2O$]Ac_2	Black	47.95 (48.79)	4.94 (5.55)	10.65 (11.98)	180^{0}C
7.	[Co(BSMDH).$2H_2O$]	[Co($C_{17}H_{14}N_4O_4$).$2H_2O$]	Dark brown	47.12 (48.76)	4.15 (5.58)	12.93 (11.65)	201°C
8.	[Ni(BSMDH).$2H_2O$]	[Ni($C_{17}H_{14}N_4O_4$).$2H_2O$]	Dark green	47.19 (48.28)	4.16 (3.88)	12.94 (11.78)	270°C
9.	[Cu(BSMDH).$2H_2O$]	[Cu($C_{17}H_{14}N_4O_4$).$2H_2O$]	Dark green	46.62 (47.25)	4.11 (4.69)	12.79 (13.47)	230°C

Abbreviation: F = Found, C = Calculated, M.P. = Melting Point, D.T. = Decomposition Temperature

Malonyl dihydrazide (MDH)
IR (KBr, ν_{max} in cm^{-1}): 3398.79 ($-NH_2$), 3398.79 (N-H), 2930.10 (C-H of CH_2 moiety), 1718.57 (C=O), 1424.77 (C-H bending), 1216.44 (C–N), 1017.80 (N–N). **^{1}H NMR (300 MHz, DMSO, δ ppm):** 2.509 ($–NH_2$), 8.398 (1H, s, –CONH), 4.234 (1H, s, CH_2 proton).**^{13}C- NMR (300 MHz, DMSO-d_6): δ** 41.1(CH_2), 169.4(C=O).

Bis-(benzylidene) malonyl dihydrazone(BBMDH)
IR (KBr, ν_{max} in cm^{-1}): 3215.62 (N-H), 3078.90 (C-H of aromatic ring), 2923.90 (C-H of CH_2 moiety), 1715.14 (C=O), 1599.21 (C=N), 1559.16 (C=C), 1428.90 (C-H bending), 1240.98 (C–N), 1007.14 (N–N), 976.61 (C-H out of plane). **^{1}H-NMR (300 MHz, DMSO, δ ppm):** 8.723 (1H, s, –CONH), 3.620(1H, s, CH_2 proton), 8.233 ((1H, s, -N=CH), 7.285-7.361 (5H, m, aromatic ring).**^{13}C- NMR (300 MHz, DMSO-d_6): δ** 42.3(CH_2), 172.7(C=O), 153.7(C=N), 130.2, 128.6, 127.5, 130.1(C_6H_5).

Bis-(salicylidene) malonyl dihydrazone(BSMDH)
IR (KBr, ν_{max} in cm^{-1}): 3572.53 (Phenolic –OH), 3277.49 (N-H), 3062.47 (C-H), 2937.28 (C-H of CH_2 moiety), 1700.87 (C=O), 1592.82 (C=N), 1584.91 (C=C), 1487.20 (C-H bending), 1266.53 (C–N), 1035.05 (N–N), 959.22 (C-H out of plane). **^{1}H-NMR (300 MHz, DMSO, δ ppm):** 5.924 (1H, s, phenolic proton), 8.434 (1H, s, –CONH), 6.856-7.005 (4H, m, phenolic ring), 3.626(1H, s, CH_2 proton), 8.297 ((1H, s, -N=CH). **^{13}C-NMR(300 MHz, DMSO-d_6): δ** 41.8(CH_2), 172.0(C=O), 154.1(C=N), 117.9, 129.9, 121.4, 133.2,114.3,157.2(C_6H_4).

IR spectral data of metal complexes
Co (II), Ni (II), Cu (II) complexes of bis-(benzylidene) malonyl dihydrazone
(KBr, ν_{max} in cm^{-1}): 3434.88–3424.93 (coordinated H_2O), 3217.44-3215.24 (N-H), 3079.77–3078.38 (C–H of aromatic ring), 2930.18-2924.01(C-H of CH_2 moiety),1692.07–1680.29 (C=O), 1575.68–1565.82 (C=N), 1559.26–1491.87 (C=C), 1420.58- 1404.53 (C-H bending), 1270.34–1240.93 (C–N), 1067.63–1025.46 (N–N), 957.09-955.70 (C-H out of plane), 853.33–847.50 (OH deformation of coordinated water), 510.64–507.66 (M–N), 445.02–434.22 (M–O).

Co (II), Ni (II), Cu (II) complexes of bis-(salicylidene) malonyl dihydrazone
(KBr, ν_{max} in cm^{-1}): 3439.97–3406.67 (coordinated H_2O), 3296.83-3272.47 (N-H), 3058.96–3053.37 (C–H of aromatic ring), 2931.39-2923.00(C-H of CH_2 moiety), 1716.04–1703.87 (C=O), 1575.54–1565.97 (C=N), 1562.13–1547.82 (C=C), 1467.41-1448.62 (C-H bending), 1273.67–1253.48 (C–N), 1047.24–1033.28 (N–N), 968.82-942.16 (C-H out of plane), 877.58–867.11 (OH deformation of coordinated water), 552.71–548.06 (M–N), 450.22–431.64 (M–O).

Electronic spectral Studies
The electronic spectra of Co (II) complexes displayed three bands in the region 12970-12738, 15455-14044, 18416-18181cm^{-1} corresponding to transitions $^4T_{1g}\rightarrow{}^4T_{2g}$ [F], $^4T_{1g}\rightarrow{}^4A_{2g}$ [F], and $^4T_{1g}\rightarrow{}^4T_{1g}$ [P]. Hence, it suggested that the synthesized Co (II) complexes have octahedral geometry [28]. The magnetic moment values of the cobalt (II) complexes were found 4.60- 4.30 B.M. which are also supportive of octahedral geometry.

Ni (II) complexes exhibited three bands in the region 12953-12610, 19083-14285, 26809-21321cm^{-1}corresponding to transitions $^3A_{2g}\rightarrow{}^2T_{2g}$, $^3A_{2g}\rightarrow{}^3T_{1g}$ [F], and $^3A_{2g}\rightarrow{}^3T_{1g}$ [P] respectively which suggested [28] that these complexes have octahedral geometry. The magnetic moment values 3.42-3.29 B.M for Ni (II) complexes also supports the suggested geometry.

The electronic spectra of Cu (II) complexes exhibited three bands in the region 12903-12626, 15723-15455, 23980-23094 cm^{-1} corresponding to transitions $^2B_{1g}\rightarrow{}^2A_{1g}$, $^2B_{1g}\rightarrow{}^2B_{2g}$, and $^2B_{1g}\rightarrow{}^2E_{1g}$ respectively. These bands indicating distorted octahedral geometry [29] for these complexes. The distorted octahedral geometry was further confirmed from their magnetic moment values 1.45-1.40 B.M.

On the basis of IR, electronic spectral data and magnetic susceptibility values it seems reasonable to assume that the M (II) complexes have the following structures. (Fig. 1 & 2)

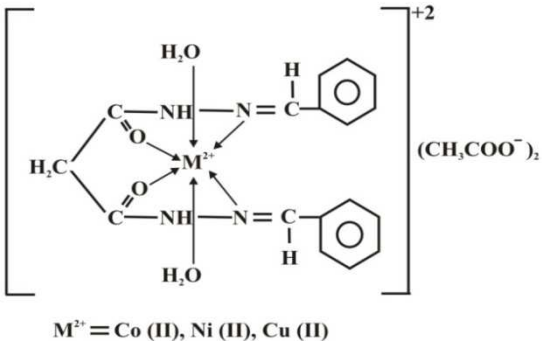

Fig. 1: Metal complexes of bis-(benzylidene) malonyl dihydrazone

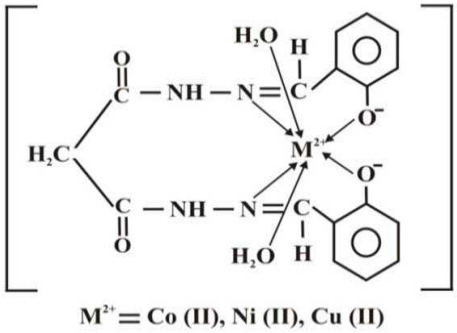

Fig. 2: Metal complexes of bis-(salicylidene) malonyl dihydrazone

Antimicrobial activity

Disc diffusion method [30] was used to screen the antimicrobial activity of all the synthesized compounds against two bacteria *Staphylococcus aureus* (gram +ve) and *Escherichia coli* (gram -ve) and fungi *Aspergillus niger* and *Aspergillus flavus*. In this method, discs of 6 mm were loaded with different concentrations 100, 50, 25, 12.5, 6.25 µg/ml of compounds. The compounds were dissolved in 10 % DMSO which was found to be biologically inactive. The bacteria were subcultured in Muller–Hinton Agar medium and the fungi were subcultured in Saboured's dextrose agar medium. These discs were placed on the solidified culture plates of different microorganisms against which the sensitivity has to be measured. These plates were incubated at 37^{o}C for 24 h in the case of bacteria and 28^{o}C for 96 h in the case of fungi. The zones of inhibition were measured in mm. Ciprofloxacin compound was screened in triplicate and the mean of maximum zone of inhibition values in diameter (in mm) with standard deviation have been reported in Table. 2, 3, 4, 5, 6, 7, 8.

Table 2: The maximum zone of inhibition values (in mm) with standard deviation for MDH, BBMDH and its metal complexes against the bacteria *Staphylococcus aureus*

Conc. (µg/ml)	MDH	BBMDH	Co(II) BBMDH	Ni(II) BBMDH	Cu(II) BBMDH	Ciprofloxacin
100 µg/ml	12.9±0.50	14.1±0.41	15.5±0.20	16.3±0.45	17.9±0.30	20.4±0.52
50 µg/ml	11.7±0.25	12.9±0.10	13.5±0.15	14.7±0.20	16.0±0.30	17.7±0.25
25 µg/ml	10.5±0.25	11.5±0.20	12.2±0.32	13.0±0.50	14.2±0.25	16.4±0.30
12.5 µg/ml	9.0±0.10	10.0±0.40	11.2±0.25	12.1±0.65	13.0±0.37	15.3±0.30
6.25 µg/ml	8.0±0.15	9.0±0.40	10.0±0.25	11.1±0.10	12.0±0.40	13.9±0.40

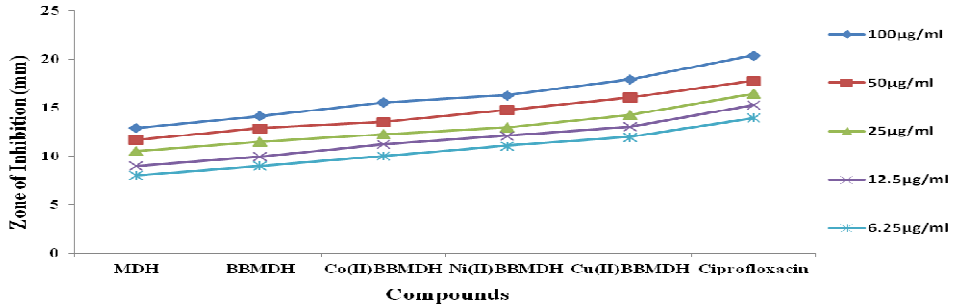

Fig. 3: Antibacterial activity trends of MDH, BBMDH and its metal complexes

Table 3: The maximum zone of inhibition values (in mm) with standard deviation for MDH, BBMDH and its metal complexes against the bacteria *Escherichia coli*

Conc. (µg/ml)	MDH	BBMDH	Co(II) BBMDH	Ni(II) BBMDH	Cu(II) BBMDH	Ciprofloxacin
100 µg/ml	13.5±0.35	14.4±0.41	17.0±0.43	16.1±0.26	18.0±0.25	23.0±0.2
50 µg/ml	12.1±0.1	13.0±0.15	14.0±0.20	15.0±0.2	16.0±0.25	20.2±0.2
25 µg/ml	11.1±0.36	12.0±0.25	13.0±0.1	14.0±0.15	15.0±0.20	18.5±0.41
12.5 µg/ml	9.9±0.20	10.8±0.2	12.6±0.52	11.7±0.20	14.4±0.40	17.0±0.2
6.25 µg/ml	8.6±0.41	9.7±0.30	11.6±0.25	10.6±0.43	12.9±0.3	15.8±0.30

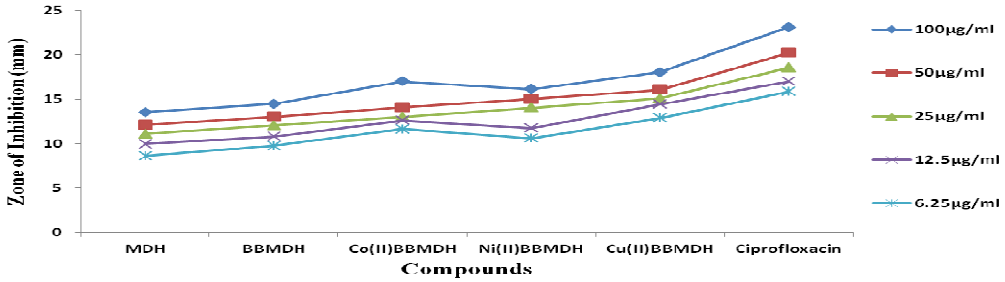

Fig. 4: Antibacterial activity trends of MDH, BBMDH and its metal complexes

Table 4: The maximum zone of inhibition values (in mm) with standard deviation for MDH, BBMDH and its metal complexes against the fungi *Aspergillus niger*

Conc. (µg/ml)	MDH	BBMDH	Co(II) BBMDH	Ni(II) BBMDH	Cu(II) BBMDH	Fluconazole
100 µg/ml	13.6±0.40	14.6±0.10	16.0±0.2	17.0±0.2	18.2±0.30	20.9±0.85
50 µg/ml	12.0±0.20	13.0±0.40	14.8±0.15	15.3±0.35	16.1±0.15	18.4±0.66
25 µg/ml	10.7±0.64	11.9±0.10	13.0±0.15	12.6±0.15	14.3±0.40	16.7±0.3
12.5 µg/ml	9.0±0.10	10.0±0.20	12.1±0.1	11.0±0.20	13.1±0.26	15.3±0.35
6.25 µg/ml	8.0±0.10	9.2±0.26	11.0±0.25	10.0±0.62	12.3±0.45	14.3±0.36

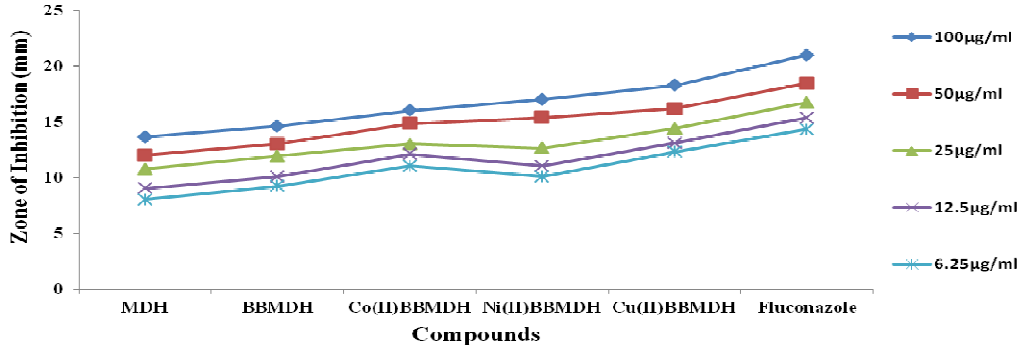

Fig. 5: Antifungal activity trends of MDH, BBMDH and its metal complexes

Table 5: The maximum zone of inhibition values (in mm) with standard deviation for MDH, BBMDH and its metal complexes against the fungi *Aspergillus flavus*

Conc. (µg/ml)	MDH	BBMDH	Co(II) BBMDH	Ni(II) BBMDH	Cu(II) BBMDH	Fluconazole
100 µg/ml	13.2±0.25	14.4±0.45	17.0±0.25	15.9±0.58	17.7±0.25	20.6±0.87
50 µg/ml	12.7±0.20	13.1±0.20	15.4±0.35	14.4±0.33	16.4±0.36	18.4±0.50
25 µg/ml	11.0±0.37	12.1±0.15	13.0±0.20	13.9±0.10	15.5±0.47	16.9±0.10
12.5 µg/ml	9.6±0.32	10.3±0.15	11.8±0.65	12.9±0.10	14.0±0.43	15.5±0.61
6.25 µg/ml	8.7±0.20	9.1±0.20	11.0±0.35	10.7±0.70	12.0±0.15	14.5±0.51

Antimicrobial activity of the synthesized hydrazide, hydrazones and their metal complexes was carried out in *vitro* against two bacteria *Staphylococcus aureus* and *Escherichia coli* and two fungi *Aspergillus niger* and *A.niger*. All tested compounds showed good antimicrobial activity against both bacteria and fungi. The metal complexes showed more activity as compared to hydrazide (MDH) and hydrazones (BBMDH & BSMDH).

Among the metal complexes of BBMDH the maximum zone of inhibition was found 12.0 mm against *Staphylococcus aureus* and 12.9 mm against *Escherichia* coli for copper complex at the lowest sconcentration 6.25µg/ml. For metal complexes of BSMDH maximum zone of inhibition against *Staphylococcus aureus* and *Escherichia coli* was found 12.4 mm and 14.5 mm respectively for copper complex at the lowest concentration of

6.25 µg/ml. However, at this concentration the standard drug ciprofloxacin exhibited maximum zone of inhibition 13.9 mm against *Staphylococcus aureus* and 15.8 mm against *Escherichia coli.*

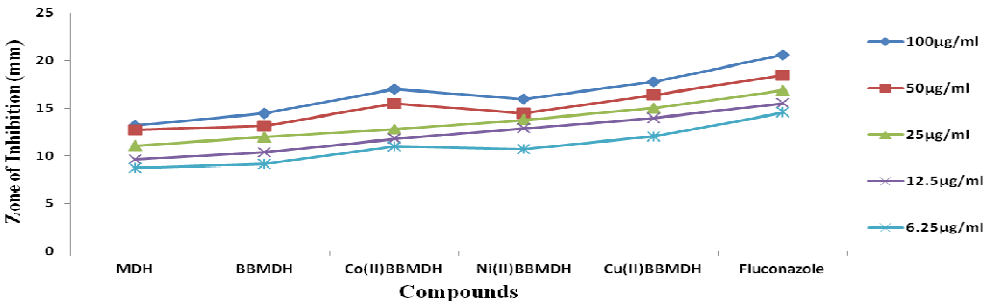

Fig. 6: Antifungal activity trends of MDH, BBMDH and its metal complexes

Table 6: The maximum zone of inhibition values (in mm) with standard deviation for MDH, BSMDH and its metal complexes against the bacteria *Staphylococcus aureus*

Conc. (µg/ml)	MDH	BSMDH	Co(II) BSMDH	Ni(II) BSMDH	Cu(II) BSMDH	Ciprofloxacin
100 µg/ml	12.9±0.50	15.0±0.30	16.1±0.55	17.0±0.15	18.2±0.30	20.4±0.52
50 µg/ml	11.7±0.25	13.6±0.30	14.7±0.20	15.6±0.26	16.6±0.36	17.7±0.25
25 µg/ml	10.5±0.25	12.3±0.55	13.2±0.30	14.1±0.56	15.6±0.15	16.4±0.30
12.5 µg/ml	9.0±0.10	10.9±0.15	12.8±0.25	11.8±0.15	14.1±0.36	15.3±0.30
6.25 µg/ml	8.0±0.15	10.0±0.87	12.0±0.20	11.0±0.15	12.4±0.45	13.9±0.40

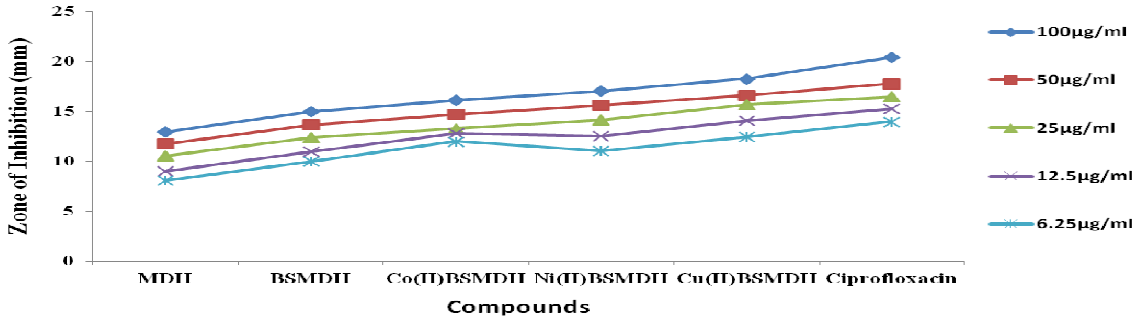

Fig. 7: Antibacterial activity trends of MDH, BSMDH and its metal complexes

Table 7: The maximum zone of inhibition values (in mm) with standard deviation for MDH, BSMDH and its metal complexes against the bacteria *Escherichia coli*

Conc. (µg/ml)	MDH	BSMDH	Co(II) BSMDH	Ni(II) BSMDH	Cu(II) BSMDH	Ciprofloxacin
100 µg/ml	13.5±0.35	16.2±0.45	17.2±0.3	18.0±0.20	19.0±0.40	23.0±0.20
50 µg/ml	12.1±0.1	15.3±0.30	16.2±0.2	17.3±0.1	18.1±0.25	20.2±0.20
25 µg/ml	11.1±0.36	14.3±0.47	15.2±0.15	16.2±0.25	17.2±0.25	18.5±0.41
12.5 µg/ml	9.9±0.20	13.4±0.25	14.1±0.10	15.2±0.30	15.9±0.35	17.0±0.20
6.25 µg/ml	8.6±0.41	12.2±0.02	13.0±0.15	13.7±0.26	14.5±0.45	15.8±0.30

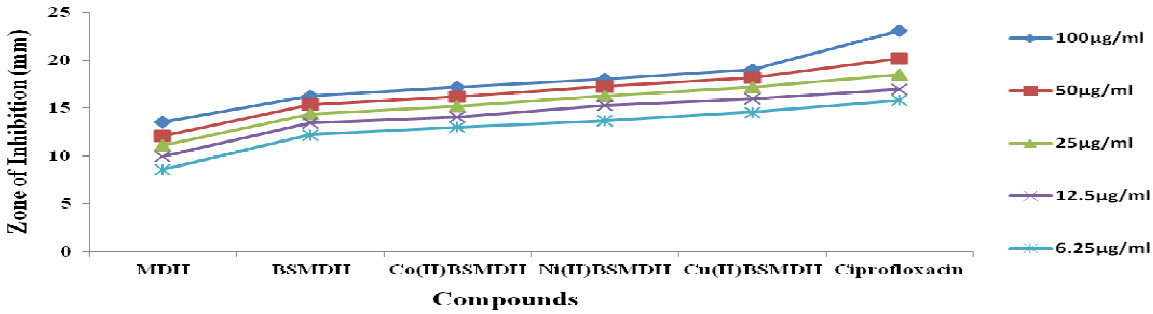

Fig. 8: Antibacterial activity trends of MDH, BSMDH and its metal complexes

In the case of antifungal study, the maximum zone of inhibition equal to12.3 mm was found against the fungi *Aspergillus niger* and 12.0 mm for *Aspergillus flavus* which was exhibited by copper complex of BBMDH at the lowest concentration 6.25 µg/ml whereas for metal complexes of BSMDH against *Aspergillus niger* and *Aspergillus*

flavus, the maximum zone was shown by copper complex which was found to be 12.2 mm and 11.7 mm at the lowest concentration 6.25 µg/ml. However, the standard drug Fluconazole exhibited maximum zone of inhibition 14.3 mm and 14.5 mm at this concentration against *Aspergillus niger* and *Aspergillus flavus* respectively.

Table 8: The maximum zone of inhibition values (in mm) with standard deviation for MDH, BSMDH and its metal complexes against the fungi *Aspergillus niger*

Conc. (µg/ml)	MDH	BSMDH	Co(II) BSMDH	Ni(II) BSMDH	Cu(II) BSMDH	Fluconazole
100 µg/ml	13.6±0.40	15.1±0.15	17.0±0.26	16.0±0.15	18.1±0.26	20.9±0.85
50 µg/ml	12.0±0.20	13.7±0.15	16.0± 0.15	15.1±0.41	17.0±0.88	18.4±0.66
25 µg/ml	10.7±0.64	12.8±0.30	13.5±0.35	14.2±0.20	15.2±0.45	16.7±0.3
12.5 µg/ml	9.0±0.10	10.2±0.65	11.4±0.45	12.7±0.20	13.5±0.40	15.3±0.35
6.25 µg/ml	8.0±0.10	9.2±0.43	10.5±0.2	11.2±0.26	12.2±0.30	14.3±0.36

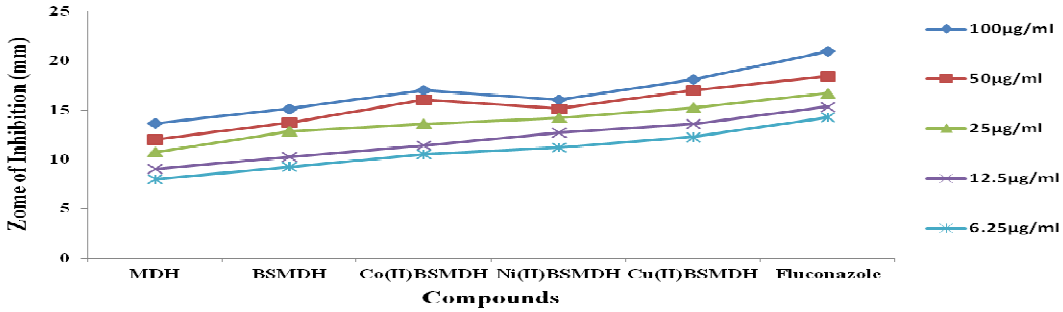

Fig. 9: Antifungal activity trends of MDH, BSMDH and its metal complexes

Table 9: The maximum zone of inhibition values (in mm) with standard deviation for MDH, BSMDH and its metal complexes against the fungi *Aspergillus flavus*

Conc. (µg/ml)	MDH	BSMDH	Co(II) BSMDH	Ni(II) BSMDH	Cu(II) BSMDH	Fluconazole
100 µg/ml	13.2±0.25	14.6±0.35	16.3±0.35	17.2±0.30	18.2±0.20	20.6±0.87
50 µg/ml	12.7±0.20	13.3±0.36	14.7±0.10	15.7±0.25	16.3±0.36	18.4±0.50
25 µg/ml	11.0±0.37	12.2±0.25	13.0±0.20	13.9±0.26	14.7±0.25	16.9±0.10
12.5 µg/ml	9.6±0.32	10.5±0.15	12.0±0.26	11.7±0.92	12.3±0.61	15.5±0.61
6.25 µg/ml	8.7±0.20	8.3±0.35	10.7±0.70	9.7±0.20	11.7±0.30	14.5±0.51

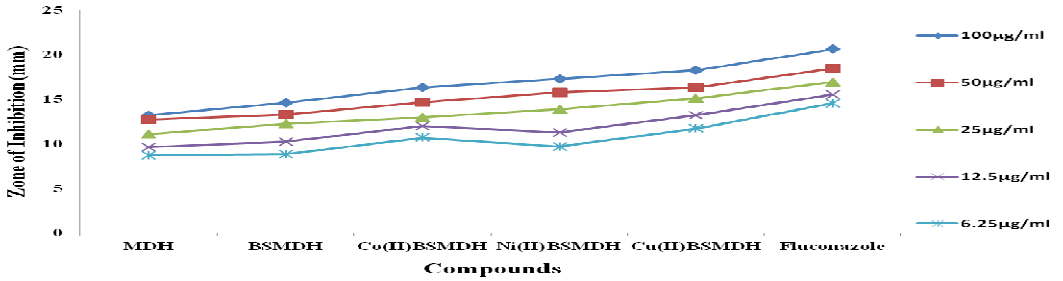

Fig. 10: Antifungal activity trends of MDH, BSMDH and its metal complexes

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