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New nickel(II), palladium(II), platinum(II) complexes with aromatic methanesulfonylhydrazone based ligands. Synthesis, spectroscopic characterization and in vitro antibacterial evaluation

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ABSTRACT

Methanesulfonicacid hydrazide (a sulfonamide compound, *msh*: $CH_3SO_2NHNH_2$) derivatives: salicylalde hydemethanesulfonylhydrazone (*salmsh*), 2-hydroxyacetophenonemethanesulfonyl hydrazone (*afmsh*), 2-hydroxy-3-metoxybenzaldehydemethanesulfonylhydrazone (*o-vanmsh*) and their Ni(II), Pd(II) and Pt (II) complexes have been synthesized. The structure of these compounds has been investigated by using elemental analyses; FT-IR, ^{1}H NMR, LC–MS, UV–Visible spectrometric methods; magnetic susceptibility; conductivity measurements; thermal studies. The antibacterial activities of synthesized compounds have been determined in vitro against gram positive bacteria; *Staphylococcus aureus* ATCC 25923, *Bacillus cereus* RSKK 709, and gram negative bacteria; *Pseudomonos aeruginosa* ATCC 27853, *Escherichia coli* ATCC 35268 by paper disc diffusion and microdilution broth methods. The biological activity screening showed that metal complexes have more activity than their ligands against the tested bacteria.

1. Introduction

Sulfonyl hydrazones, derivatives of sulfonamide, exhibit several medicinal applications. For example, 4-substituted benzenesulfonylhydrazone has been studied for antibacterial activities [1], benzaldehyde arylsulfonylhydrazones possess antineoplastic activity against human stomach cancer SGC 7901 [2], N-arylsulfonyl hydrazones have been identified as novel inhibitors of IMP-1 a metallo-β-lactamase enzyme [3], imidazol[1,2-a] pyridines with arylsulfonylhydrazone substituents have been reported as novel PI3 kinase p110a inhibitors [4].

N-arylsulfonyl-3-acylindole derivatives have displayed potent anti-human immunodeficiency virus type 1 (HIV-1) activity [5]. In addition, numerous sulfonamide derivatives have been reported as carbonic anhydrase inhibitors [6], anticancerous [7] and anti-inflammatory agents [8]. Transition metal complexes of hydrazides and sulfonamides also find application in chemotherapy as well as their hydrazone derivatives [9]. Especially, the search for platinum (II) complexes with anti-tumor properties has been going on through the efforts of chemists from the medicinal chemistry field since the discovery of the anti-proliferation activity of cisplatin in the 1960s [10]. However, since the 1990s many trans platinum complexes have been discovered with significant anti-tumor activity against different tumor cells including these resistant to cisplatin [11–13]. Owing to the similar co-ordination modes of the cation Pd(II) and Pt(II) (d^8-electron configuration) there has also been renewed interest in attempts to obtain activity for cis and trans palladium(II) complexes [14–16]. Furthermore, some mixed ligand palladium(II) complexes have been shown to act as potential anticancer agents [17–19].

In our previous studies, we reported the antibacterial and cytotoxic effect of methanesulfonic acid hydrazide and its sulfonylhydrazone derivatives [20–22], as well as its metal carbonyl complexes [23,24]. Methane, ethane and prophanesulfonylhydrazone derivatives and their transition metal complexes were synthesized and screened for antimicrobial activity [25–27]. Furthermore, ethanesulfonylhydrazone derivatives and their transition metal complexes were investigated inhibitory effects on carbonic anhydrase II (CA II) enzyme [26].

As part of our ongoing studies, methanesulfonicacid hydrazide (sulfonamide compound) and its derivatives: salicylaldehydemeth anesulfonylhydrazone (*salmsh*), 2-hydroxyacetophenone methanesulfonylhydrazone (*afmsh*) and 2-hydroxy-3-metoxy benzalde hydemethanesulfonyl hydrazone (*o-vanmsh*) were synthesized. The structure of *salmsh* and *afmsh* ligands were reported in our previous work [20,28]. Ni(II) Pd(II) and Pt(II) complexes of aromatic methanesulfonylhydrazone derivatives and *ovanmsh* ligand were synthesized for the first time and characterized by using elemental

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analysis, FT-IR, LC–MS, UV–Visible spectrometric methods, magnetic susceptibility, conductivity measurements and thermal studies. The antibacterial activities of synthesized compounds have been determined in vitro against gram positive bacteria; *Staphylococcus aureus* ATCC 25923, *Bacillus cereus* RSKK 709, and gram negative bacteria; *Pseudomonas aeruginosa* ATCC 27853, *Escherichia coli* ATCC 35268 by paper disc diffusion and microdilution broth methods.

2. Experimental

2.1. Physical measurements

The solvents used were purified and distilled according to routine procedures. Methane sulfonyl chloride, hydrazine hydrate, salicylaldehyde, 2-hydroxyacetophenone, 2-hydroxy-3-metoxybenzaldehyde and anhydrous nickel , palladium and platinum chloride were commercial products (purum). The elemental analyses (C, H, N and S) were performed on a LECO–CHSNO – 9320 type elemental analyzer. 1H NMR spectra of dimethylsulfoxide-d_6 (DMSO-d_6) solutions of the compounds were recorded on a Bruker WM-400 spectrometer (400 MHz) using tetra methyl silane as internal standard. D_2O-exchange was applied to confirm the assignment of the NH- and OH-signals .The infrared spectra of the compounds as KBr-disks were recorded in the range of 4000–400 cm^{-1} with a Mattson 1000 FT spectrometer. UV–Vis spectra were recorded on UNİCAM-UV 2-100 spectrophotometer. Melting points of aromatic methanesulfonylhydrazone derivatives were determined with a Gallenkamp melting point apparatus. The molar magnetic susceptibilities were measured on powdered samples using Gouy method. The molar conductance measurements were carried out using a Siemens WPA CM 35 conductometer. A Du Pont Instrument 951 thermal analyzer was used to record simultaneously TG and DTA curves. The experiments were carried out in dynamic nitrogen atmosphere (20 ml min^{-1}) with a heating rate of 10 °C min^{-1} in the temperature range 30–400 °C using platinum crucibles. The microdilution broth and disc diffusion method were used to determine the antibacterial activity of compounds against the bacteria; *S. aureus* ATCC 25923, *B. cereus* RSKK 709, *P. aeruginosa* ATCC 27853, *E. coli* ATCC.

2.2. Synthesis of ligands

The procedure of preparation of aromatic methanesulfonylhydrazone derivatives are similar to that applied by us [27]. Thus, solution of 1.10 g (10 mmol) methanesulfonicacid hydrazide in 5 ml of ethanol was mixed with hot solution of 12 mmol of the corresponding carbonyl compound (salicylaldehyde, 2-hydroxyacetophenone,2-hydroxy-3-metoxybenzaldehyde respectively) in 10 ml of ethanol and stirred for 1 h. Upon cooling, the obtained crystalline precipitates were filtered, washed with ethanol–ether, recrystallized from water and dried in vacuo over P_2O_5. They are light yellow crystalline solids, stable at normal conditions and soluble in methanol, ethanol, acetonitrile, dimethylformamide, DMSO; poorly soluble in benzene and water.

2.3. Synthesis of Ni(II), Pd(II), Pt(II) complexes

All complexes are prepared by the following general method. A sample of anhydrous MCl_2 (M = Ni, Pd, Pt) (0.53 mmol) was dissolved in a mixture of methanol and acetonitrile (25 mL), and solution of methanesulfonylhydrazone derivatives (1.60 mmol) in a mixture of acetonitrile (25 mL) and NaOH solution in methanol (1.60 mmol) was added. The reaction mixture was heated under reflux for 1 h, at 40 °C and left in ice bath for 3 h. The solid complexes formed was collected by filtration, washed with a small volume of methanol and ether, and then, were left in glass oven at 170 °C for a 2 h in vacuo to prevent the hydration dried in a desiccators over $CaCl_2$.

2.4. Procedure for antibacterial activity

The in vitro antibacterial activity of the free ligands and their complexes were tested against the gram positive bacteria; *S. aureus* ATCC 25923, *B. cereus* RSKK 709, and gram negative bacteria, *P. aeruginosa*, ATCC 27853, *E. coli* ATCC 35268 by paper disc diffusion and micro dilution broth methods.

Bacteria cultures were obtained from Gazi University, Biology Department. Bacterial strains were cultured overnight at 310 K in Nutrient Broth. During the survey, these stock cultures were stored in the dark at 277 K. The inocula of microorganisms were prepared from 12 h broth cultures and suspensions were adjusted to 0.5 McFarland standard turbidity.

2.4.1. Disc diffusion method

The synthesize compounds and complexes were dissolved in dimethylsulfoxide (20% DMSO) to a final concentration of 5.0 mg mL^{-1} and sterilized by filtration by 0.45 μm Millipore filters. Antimicrobial tests were then carried out by the disc diffusion method using 100 μL of suspension containing 10^8 CFU mL^{-1} bacteria spread on a nutrient agar (NA) medium. The discs (6 mm in diameter) were impregnated with 20 μL of each compound (100 μg/disc) at the concentration of 5.0 mg mL^{-1} and placed on the inoculated agar. DMSO impregnated discs were used as negative control. Sulfamethoxazole (300 μg/disk) and sulfisoxazole (300 μg/disk) were used as positive reference standards to determine the sensitivity of one strain/isolate in each microbial species tested. The inoculated plates were incubated at 37 °C for 24 h for bacterial strains isolates. Antimicrobial activity in the disc diffusion assay was evaluated by measuring the zone of inhibition against the test organisms. Each assay in this experiment was repeated twice [29]. The values obtained are average of the two results. Percentage of inhibition by comparing distance of the compounds to the positive control using (sulfamethoxazole) the equation below [30]:

$$\%\text{Inhibition} = \left[\frac{\text{diameter of the sample}}{\text{diameter of the positive control}}\right] * 100.$$

2.4.2. Micro dilution assays

The inocula of microorganisms were prepared from 12 h broth cultures and suspensions were adjusted to 0.5 McFarland standard turbidity. The test compounds dissolved in 20% dimethylsulfoxide (DMSO) were first diluted to the highest concentration (8.0 mg mL^{-1}) to be tested, and then serial, twofold dilutions were made in a concentration range from 15.625 to 4000 μg mL^{-1} in 10 mL sterile test tubes containing nutrient broth. The MIC values of each compound against bacterial strains were determined based on a micro-well dilution method.

The 96-well plates were prepared by dispensing 95 μL of nutrient broth and 5 μL of the inoculums into each well. One hundred microliters from each of the test compounds initially prepared at the concentration of 4000 μg mL^{-1} was added into the first wells. Then, 100 μL from each of their serial dilutions was transferred into nine consecutive wells. The last well containing 195 μL of nutrient broth without compound, and 5 μL of the inoculum on each strip, was used as negative control. The final volume in each well was 200 μL. The contents of the wells were mixed and the micro plates were incubated at 37 °C for 24 h. All compounds tested in this study were screened twice against each microorganism and the average was taken. The MIC was defined as the lowest

Table 1
Analytical and physical data for aromatic methanesulfonylhydrazone derivatives and their complexes.

Compound	Empirical formula (formula weight)	Color	M.p. (°C)	Yield (%)	Found (calculated)			
					%C	%H	%N	%S
salmsh	$C_8H_{10}N_2SO_3$ 214.11	White	149–150	50	44.38 (44.87)	4.49 (4.67)	12.92 (13.07)	14.41 (14.97)
afmsh	$C_9H_{12}N_2SO_3$ 228.12	White	161–162	55	49.1 (49.5)	5.3 (5.8)	11.5 (11.6)	13.0 (13.2)
o-vanmsh	$C_9H_{12}N_2SO_4$ 244.11	Light yellow	120–121	40	44.02 (44.27)	4.65 (4.91)	10.92 (11.47)	12.50 (13.13)
Ni(salmsh)$_2$	$C_{16}H_{18}N_4S_2O_6Ni$ 484.93	Green	275>	40	40.63 (39.62)	3.99 (3.71)	11.76 (11.54)	11.33 (13.22)
Pd(salmsh)$_2$	$C_{16}H_{18}N_4S_2O_6Pd$ 532.62	Orange	248>	50	35.85 (36.07)	3.25 (3.37)	9.88 (10.51)	11.75 (12.03)
Pt(salmsh)$_2$	$C_{16}H_{18}N_4S_2O_6Pt$ 621.31	Light brown	258>	35	29.98 (30.92)	2.59 (2.89)	8.81 (9.01)	10.03 (10.32)
Ni(afmsh)$_2$	$C_{18}H_{22}N_4S_2O_6Ni$ 512.95	Green	242>	45	41.80 (42.14)	4.00 (4.28)	9.90 (10.91)	11.55 (12.05)
Pd(afmsh)$_2$	$C_{18}H_{22}N_4S_2O_6Pd$ 560.64	Orange	260>	40	39.2 (39.3)	4.3 (4.7)	9.9 (10.2)	11.2 (11.7)
Pt(afmsh)$_2$	$C_{18}H_{22}N_4S_2O_6Pt$ 649.33	Brown	220>	40	39.9 (40.4)	5.1 (5.4)	9.0 (9.4)	10.6 (10.8)
Ni(ovanmsh)$_2$	$C_{18}H_{22}N_4S_2O_8Ni$ 544.93	Green	234>	35	39.06 (39.67)	3.85 (4.03)	9.50 (10.27)	10.98 (11.76)
Pd(ovanmsh)$_2$	$C_{18}H_{22}N_4S_2O_8Pd$ 592.93	Orange	260>	40	34.95 (36.45)	3.01 (3.71)	8.84 (9.44)	9.85 (10.81)
Pt(ovanmsh)$_2$	$C_{18}H_{22}N_4S_2O_8Pt$ 681.31	Brown	230>	30	30.85 (31.73)	3.14 (3.22)	8.76 (8.22)	9.65 (9.41)

concentration of the compounds to inhibit the growth of microorganisms [31].

3. Results and discussion

Analytical data and some physical properties of aromatic methanesulfonylhydrazone and their complexes are listed in Table 1. The elemental analysis results show 1:2 (metal:ligand) stoichiometry for all the complexes. The analytical results are in good agreement with those required by the general formula (ML_2).The molar conductivity (Λ_m) of 10^{-3} M solutions of the complexes in MeOH at 25 °C were measured and all the complexes were found non-electrolytic nature in the range of 3.3–5.9 $^{-1}$ cm^2 mol^{-1}.

3.1. The characterization of compounds

3.1.1. IR spectra

The important diagnostic i.r. bands of aromatic methanesulfonylhydrazone and their complexes are summarized in Table 2. Bands in the region of 3210, 3203 and 3217 cm^{-1} may be due to ν(NH) stretching vibration for *salmsh*, *afmsh* and *ovanmsh*. The strong bands at 1624, 1622 and 1618 cm^{-1} are assigned to ν(C=N) stretching mode of the imine group for ligands. These bands are shifted to lower wave number in all complexes. These shifts support the participation of the imine group of these ligands in binding to the metal ions [25–27]. Ligands also display bands at 1268, 1232 and 1247 cm^{-1} which are assigned to ν(C–O) stretching vibrations for *salmsh*, *afmsh*, *ovanmsh* respectively. These bands are strongly affected by chelation through the phenolic-C*O* groups of the aromatic methanesulfonylhydrazone and the shift to higher wave numbers indicates the coordination of phenolic-O donor atoms [32].

Table 3
^{1}H NMR spectroscopic data for aromatic methanesulfonylhydrazone derivatives in DMSO-d$_6$ (ppm).

Assign.	*salmsh*[a]	*afmsh*[a]	*ovanmsh*
CH_3C=N	–	2.31 (s, 3H)	–
SO_2CH_3	3.06 (s, 3H)	3.08 (s, 3H)	2.95 (s, 3H)
OCH_3	–	–	3.86 (s, 3H)
CH=N	8.27 (s, 1H)	–	8.17 (s, 1H)
NH	10.21 (s, br)	10.45 (s, 1H)	10.20 (s, 1H)
Ar	6.88–7.60 (mH)	6.89–7.55 (mH)	6.80–7.10 (mH)
OH	11.00 (s, br)	11.68 (s, 1H)	11.06 (s, 1H)

[a] Taken from [20].

Table 2
Major i.r. absorption bands (cm^{-1}) of aromatic methanesulfonyl hydrazone derivatives and their complexes.

Assign	Comp.						
	ν(NH)	ν(C=N)	$\nu_{as}(SO_2)$	ν(CO)	$\nu_s(SO_2)$	δ(NH)	$\delta(SO_2)$
salmsh	3210s	1624s	1320s	1268s	1152s	670w	524m
afmsh	3203s	1622s	1322s	1232s	1153s	626m	515m
o-vanmsh	3217s	1618s	1320s	1247m	1159s	651m	520m
Ni(salmsh)$_2$	3127s	1608s	1320s	1277m	1154s	652m	522m
Pd(salmsh)$_2$	3180s	1602s	1321s	1290m	1157s	660m	527m
Pt(salmsh)$_2$	3203s	1602s	1319s	1295m	1154s	678m	539m
Ni(afmsh)$_2$	3210s	1606s	1324s	1259m	1155s	625m	519m
Pd(afmsh)$_2$	3196s	1578s	1340s	1273m	1157s	623m	515m
Pt(afmsh)$_2$	3210s	1600s	1324s	1254m	1159s	628m	520m
Ni(ovanmsh)$_2$	3198s	1604s	1320s	1257m	1159s	647m	514m
Pd(ovanmsh)$_2$	3210s	1600s	1317s	1265m	1143s	650m	520m
Pt(ovanmsh)$_2$	3208s	1600s	1317s	1265m	1143s	650m	542m

Table 4
The mass spectral data of aromatic methanesulfonyl hydrazone complexes.

Compounds	MW	Relative intensities of the major ions (*m/z*, %) and assignment
Ni(salmsh)$_2$	484.93	$[M-2H]^+$ (482.0, 30%), $[L+H]^+$ (215.06, 100%)
Pd(salmsh)$_2$	532.62	$[M]^+$ (532.97, 79%), $[M-H]^+$(531.0, 45%), $[M+Na]^+$ (554.96, 9%), $[L+H]^+$ (215.04, 100%)
Pt(salmsh)$_2$	621.31	$[M+Na]^+$ (644.20, 10%), $[L+CH3]^+$ (229.90, 100%)
Ni(afmsh)$_2$	512.95	$[M-2H]^+$ (510.03, 20%), $[M]^+$ (511.0, 3%), $[L+H]^+$ (229.05, 100%)
Pd(afmsh)$_2$	560.64	$[M]^+$ (561.01, 28%), $[M+Na]^+$ (582.9, 62%), $[L+H]^+$ (229.03, 100%)
Pt(afmsh)$_2$	649.33	$[M-CH_3]^+$ (634.1, 30%), $[L+H]^+$ (229.07, 100%)
Ni(o-vanmsh)$_2$	544.93	$[M-2H]^+$ (542.0, 40.1%), $[L+H]^+$ (245.04, 100%)
Pd(o-vanmsh)$_2$	592.93	$[M]^+$ (592.9, 5.1%), $[L-OCH_3]^+$ (211.9, 5%)
Pt(o-vanmsh)$_2$	681.31	$[M-CH_3]^+$ (666.1, 20%), $[L+H]^+$ (245.05, 100%)

Table 5
Inhibition zone of aromatic methanesulfonylhydrazone derivatives and their complexes by disc diffusion method (mm).

Compounds (μg/mL)	Diameter inhibition zone* (mm, 100 μg/disk)			
	Gram-positive		Gram-negative	
	S. aureus ATCC 25923	*B. cereus* RSKK 709	*P. aeruginosa* ATCC 27853	*E. coli* ATCC 35268
salmsh	13	12	10	10
afmsh	12	10	7	8
o-vanmsh	14	13	14	11
Ni(salmsh)$_2$	15	-	12	11
Pd(salmsh)$_2$	16	16	14	13
Pt(salmsh)$_2$	15	13	11	12
Ni(afmsh)$_2$	10	–	11	–
Pd(afmsh)$_2$	15	12	12	11
Pt(afmsh)$_2$	13	8	14	12
Ni(o-vanmsh)$_2$	12	10	14	14
Pd(o-vanmsh)$_2$	18	16	15	16
Pt(o-vanmsh)$_2$	16	14	11	13
SD1	15	28	17	17
SD2	25	17	8	20

SD1: Sulfamethoxazole (300 μg/disk), SD2: sulfisoxazole (300 μg/disk). <10: weak; >10 moderate; >16: significant.
* Average values.

3.1.2. NMR spectra

^{1}H NMR data of DMSO-d_6 solutions of the aromatic methanesulfonylhydrazone are collected in Table 3. *salmsh* and *ovanmsh* show signals at 8.27–8.17 ppm which are attributed to the imines protons (–N=CH –). *afmsh* (ketone derivative) show signals at 2.31 ppm which is attributed to the –CH_3C=N– protons [26].

The signals of the HC=N and CH_3C=N protons show no splitting, and the positions of the signals of the ring protons are typical. In general, the multiplates observed at 6.88–7.60 ppm, 6.89–7.55 ppm and 6.80–7.10 ppm are assigned to *salmsh*, *afmsh* and *ovanmsh* ring protons; respectively. Signals at 10.21 ppm and 11.00 ppm; 10.45 ppm and 11.68 ppm; 10.20 ppm and 11.06 ppm are assigned to the NH and OH protons, respectively for *salmsh*, *afmsh* and *ovanmsh*. The high field shift of NH protons may be due to the involvement of this group with a hydrogen bond in DMSO-d_6, which is well known for its interaction with an amide proton [33].

3.1.3. Mass spectra

LC–MS data of aromatic methanesulfonyl hydrazone complexes are summarized in Table 4. LC–MS spectra shows that [*Ni(salmsh)*$_2$], [*Ni(afmsh)*$_2$], and [*Ni(ovanmsh)*$_2$], give the molecular

Table 6
The MIC's (μg/mL) values of aromatic methanesulfonyl hydrazone derivatives and their complexes.

Compounds	MIC* (μg/mL)			
	Gram-positive		Gram-negative	
	S. aureus ATCC 25923	*B. cereus* RSKK 709	*P. aeruginosa* ATCC 27853	*E. coli* ATCC 35268
salmsh	250	125	1000	1000
afmsh	500	500	1000	1000
o-vanmsh	31.25	62.5	500	500
Ni(salmsh)$_2$	500	500	1000	1000
Pd(salmsh)$_2$	62.50	250	500	500
Pt(salmsh)$_2$	250	500	1000	1000
Ni(afmsh)$_2$	500	500	2000	2000
Pd(afmsh)$_2$	125	250	250	1000
Pt(afmsh)$_2$	125	500	1000	500
Ni(o-vanmsh)$_2$	500	500	500	1000
Pd(o-vanmsh)$_2$	31.25	31.25	500	500
Pt(o-vanmsh)$_2$	31.25	62.5	2000	1000
SD1	32	16	64	64
SD2	93.75	375	375	23.5

SD1: Sulfamethoxazole, SD2: sulfisoxazole.
* Average values.

Table 7
The MIC's values of aromatic methanesulfonylhydrazone derivatives and their complexes (mM of 20% DMSO).

Compounds	Gram-positive		Gram-negative	
	S. aureus ATCC 25923	*B. cereus* RSKK 709	*P. aeruginosa* ATCC 27853	*E. coli* ATCC 35268
salmsh	1.167	0.584	4.670	4.670
afmsh	2.192	2.192	4.383	4.383
o-vanmsh	0.128	0.256	2.048	2.048
$Ni(salmsh)_2$	1.031	1.031	2.06	2.06
$Pd(salmsh)_2$	0.058	0.469	0.938	0.938
$Pt(salmsh)_2$	0.050	0.805	1.609	3.219
$Ni(afmsh)_2$	0.974	0.974	3.900	3.900
$Pd(afmsh)_2$	0.223	0.446	0.446	1.784
$Pt(afmsh)_2$	0.1925	0.770	1.540	0.770
$Ni(o\text{-}vanmsh)_2$	0.917	0.917	0.917	1.835
$Pd(o\text{-}vanmsh)_2$	0.052	0.052	0.844	0.844
$Pt(o\text{-}vanmsh)_2$	0.046	0.092	2.935	1.468
SD1	0.126	0.063	0.253	0.253
SD2	0.351	1.403	1.403	0.088

SD1: Sulfamethoxazole, SD2: sulfisoxazole.

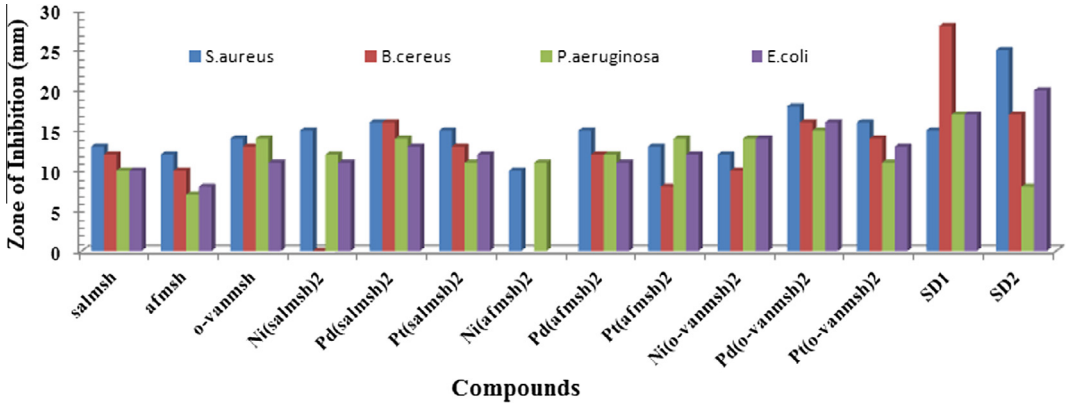


Fig. 1. Comparison of antibacterial activite of ligands, metal (II) complexes.and antibiotics.

ions, $[NiL_2+2H]^+$ with the expected *m/z* values (intensity %) = 482.0 (30.0), 510.03 (20.0) and 542.0 (40.1), $[L+H]^+$ fragments are observed at 215.0 (100.0) , 229.05 (100.0) and 245.0 (100.0) as main peak for *salmsh*, *afmsh* and *ovanmsh*; respectively. $[Pd(salmsh)_2]$, $[Pd(afmsh)_2]$, and $[Pd(ovanmsh)_2]$, give the molecular ion peaks, $[PdL_2]^+$ at the desired positions : *m/z* (intensity %) = 532.9 (79.0), 561.01 (28.0) and 592.0 (5.1). $[Pt(afmsh)_2]$, $[Pt(ovanmsh)_2]$, give the molecular ions, $[PtL_2-CH_3]^+$ at the desired positions. *m/z* (intensity %) = 634.1 (30), 666.1 (20) and $[Pt(salmsh)_2]$ gives molecular ion, $[PtL_2+Na]^+$ at 621.20 (10).

3.1.4. Electronic spectra and magnetic behavior

The significant electronic spectra of the complexes are recorded in methanol. The important bands of the ligands and the

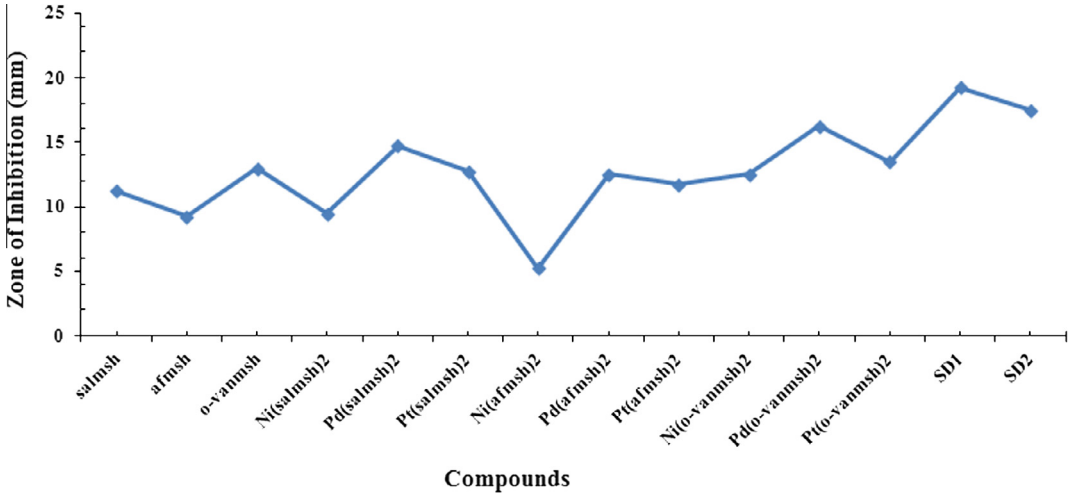


Fig. 2. Average antibacterial activity of ligands and metal (II) complexes.

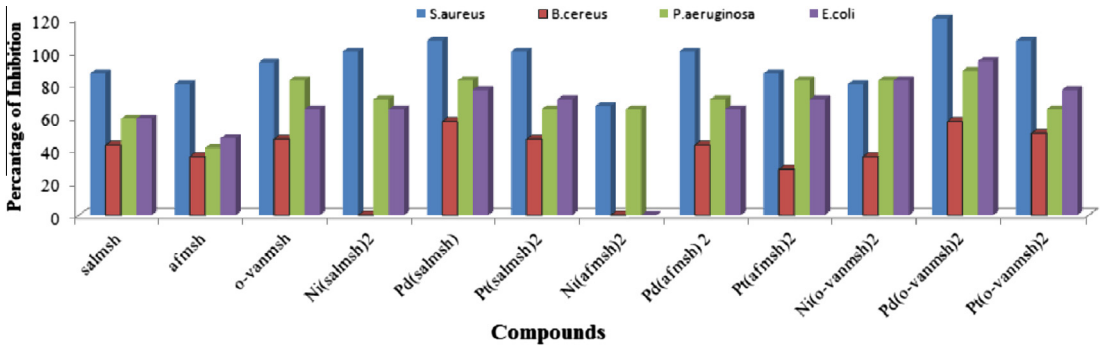


Fig. 3. Percentage of inhibition of ligands and metal (II) complexes.

complexes are observed in the region of 294–245 nm and 340–313 nm. These may be attributed, respectively, to $\pi \rightarrow \pi^*$ type and charge-transfer transitions. The spectra of the Ni^{2+}, Pd^{2+} and Pd^{2+} complexes show bands in the range of 460–498 nm. Hence, square-planar structures may be assigned to these complexes [34].

The magnetic moments of complexes (as B.M.) were measured at room temperature. The diamagnetic character of the nickel(II), platinum (II) and palladium (II) complexes shows square-planar geometry for these complexes.

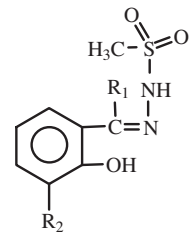
3.1.5. Thermal decomposition studies

The Ni(II), Pd(II) and Pt(II) complexes were left in glass oven at 170 °C for a 2 h in vacuo to prevent the hydration. The thermo grams of anhydrous of all complexes were observed in the range of 35–700 °C. As expected there was no mass loss up to 220 °C. All complexes have thermally decompose in the range of 220–700 °C which means all complexes does not contain any coordinated or crystal water molecules [27].

3.2. Antibacterial activity results

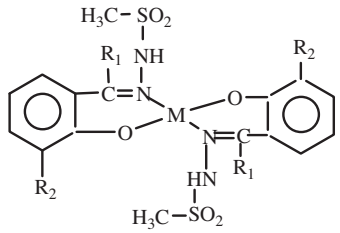
The test compounds were screened in vitro for their antibacterial activity against two Gram-positive species (*B. cereus* and *S. aureus)* and two Gram-negative species (*E. coli* and *P. aeruginosa)* of bacterial strains by the disc diffusion and micro dilution methods. The antibacterial results were given in Table 5 by disc diffusion and Tables 6 and 7 micro dilution methods. The results were compared with those of the standard drugs sulfamethoxazole and sulfisoxazole (Figs. 1 and 2).

As the disc diffusion assay results evidently show (Table 5, Figs. 1 and 2) that *o-vanmsh* has exhibited the strong inhibition effect against most of test bacteria whereas *salmsh* and *afmsh* have



R_1=H R_2=H; salmsh
R_1=CH_3 R_2=H; afmsh
R_1=H R_2=OCH_3;ovanmsh

(a)



R_1=H, R_2=H; M=Ni; **Nisalmsh**; M=Pd;**Pdsalmsh**; M=Pt;**Ptsalmsh**
R_1=CH_3,R_2=H; M=Ni; **Niafmsh**; M=Pd;**Pdafmsh**; M=Pt;**Ptafmsh**
R_1=H, R_2=OCH3; M=Ni; **Niovanmsh**;M=Pd;**Pdovanmsh**; M=Pt;**Ptovanmsh**

(b)

Fig. 4. Structures of ligands (a) and complexes (b).

weaker activity. The structure–activity relationships (SAR) suggest that both methoxy and azomethine (–NH–N=CH–) groups containing *o-vanmsh* have important effects on maximum antibacterial activity. Similar results were also reported by Govindasami et al. [35].

All ligands and their complexes show the highest activities against *S. aureus* which is the mostly effected by $Pd(o\text{-}vanmsh)_2$ having the diameter zone of 18 mm.

All compounds except *afmsh* have moderate activity against *P. aeruginosa* at in the diameter zone of 10–15 mm whereas sulfisoxazole, the drug used as standard, has been found less active (8 mm) against the bacteria mentioned above. The aromatic methanesulfonylhydrazone complexes show remarkable increase in antimicrobial activity than the parent ligands.

Percentage of inhibition for the compounds exhibited in Fig. 3 that was expressed as excellent activity (120–200% inhibition), good activity (90–100% inhibition), moderate activity (75–85% inhibition), significant activity (50–60% inhibition), negligible activity (20–30% inhibition) and no activity [36]. As seen in Fig. 3, $Pd(o\text{-}vanmsh)_2$ shows excellent activity while other metal complexes except $Ni(afmsh)_2$ have good activity or moderate activity against *S. aureus*. $Pt(afmsh)_2$, $Ni(o\text{-}vanmsh)_2$, $Pd(o\text{-}vanmsh)_2$ and $Pd(salmsh)_2$ exhibit moderate activity against *P. aeruginosa*, whereas rest of the complexes show negligible activity. $Pd(o\text{-}vanmsh)_2$, $Pd(salmsh)$ and $Pt(o\text{-}vanmsh)_2$ exhibit significant activity against *B. cereus*.

According to the MIC's results shown in Table 6, the compounds possess a broad spectrum of activity against the tested bacteria at the concentrations of 31.25–2000 μg/mL [37]. The *o-vanmsh*, $Pd(o\text{-}vanmsh)_2$ and $Pt(o\text{-}vanmsh)_2$ have shown activity against *S. aureus* ATCC 25923 and *B. cereus* RSKK 709 at a concentration of 31.25 μg/mL, 62.5 μg/mL whereas sulfisoxazole, the drug used as standard, has been found less active against the bacteria. Also, the antimicrobial activity is highly influenced by the nature of the sulfonylhydrazone derivatives and the order of the activity in mM for all test bacteria is as follows (Table 7):$Pd(o\text{-}vanmsh)_2$ > $Pd(salmsh)_2$ > $Pd(afmsh)_2$ > $Ni(o\text{-}vanmsh)_2$ > $Pt(o\text{-}vanmsh)_2$ > $Pt(afmsh)_2$ > *o-vanmsh* > $Pt(salmsh)_2$ > $Ni(salmsh)_2$ > $Ni(afmsh)_2$ > *salmsh* > *afmsh*

As seen in Table 7, metal complexes show significant activity against the microorganisms. It is supposed that the increased lipophilic character of bulky complexes may be responsible for their potent antimicrobial activity than ligands. The permeation of complexes through the lipid layer of the cell membranes deactivates diverse cellular enzymes, which play a vital role in various metabolic systems of these microorganisms [38,39]. As a results, Pd(II) and Pt(II) complexes are more active than Ni(II) complexes.

4. Conclusions

In this study we have reported the synthesis of aromatic methanesulfonyl hydrazone derivatives and their Ni(II), Pd(II) and Pt(II) complexes. The structural characterizations of the synthesized compounds were made by using the elemental analyses, spectroscopic methods, magnetic and conductance studies, and thermal analysis. From the spectroscopic characterization, it is concluded that aromatic methanesulfonylhydrazones act as a bidentate ligands, coordinating through >C=N and phenolic –OH via deprotonation. Based on physicochemical evidence, the proposed structure of sulfonamide derivatives and their complexes are exhibited in Fig. 4. N, O, S donors in sulfonylhydrazones are the most important factors affecting the bioactivity. The biological activity screening showed that complexes have more activity than ligands against the tested bacteria. Furthermore, our Pd(II) and Pt(II) complexes showed the most activity against all bacteria.

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