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Synthesis and characterization of a symmetrically substituted cyclodiphosph(V)azane ligand ($H4L^1$) and its transition metal complexes for antimicrobial and antitumor investigation.

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A NEW ligand of geminal cyclodiphosph(V)azane derivatives, 1,3-di-[N/-2,6-dimethoxy-4-pyrimidnylsulfanilamide]2,4-di-[N/-2-quinoxalinylsulfanilamide]-2,4dichlorocyclodiphosph(V)azane ($H4L^1$) was prepared. The ligand and its related complexes were characterized by different physicochemical techniques, namely; IR, UV–vis, mass, ^{1}H NMR, molar conductance, magnetic, solid reflectance, and thermal analysis. The spectral data revealed that the ligand behaves as ionic in nature and coordinated to the metal ions via enolic-OH of sulphonamide group and pyrimidine–N. The molar conductance data reveal that the complexes were electrolytes, while UV–vis, solid reflectance and magnetic moment data have been shown that the complexes have octahedral geometry. The thermal behavior of the complexes was also studied. The ligand and its metal complexes showed a high to moderate antimicrobial activities against deferent strains of bacteria and fungi, also showed anticancer activity against colon carcinoma HCT116.

Keywords: Physicochemical techniques, cyclodiphosph(V)azane ligand, metal complexes, antimicrobial, anticancer activities.

Introduction

No congeners in the periodic table of the elements form compounds of a greater structural variety than nitrogen and phosphorus [1]. These nonmetals have the ability to form single, double, and triple bonds. It was, also due to the strength of P–N bonds, which render most phosphorus–nitrogen compounds exceptionally thermally stable [2,3]. Much of earlier investigation is on the substitution reactions involving the P–Cl bond and on the relative geometry of the substituents on phosphorus [1, 2]. Several groups of workers, in later years, explain the potential of these compounds as highly versatile ligands as well as macrocyclic precursors [4, 5]. The interest of these compounds resulted from recognition of the value of such compounds for a variety of industrial and chemical synthesized as flame retardant [6].

Sulfonamide is a generic name for derivatives of para-aminobenzene sulfonamide which possess enormous efficient bioactivities such as antiangiogenic [7,8], antitumor [9], anti-inflammatory and anti-analgestic [10]. Sulphonamides belong to the group of antibacterial drugs, which are used for human and animal therapy, to cure infectious diseases of digestive and respiratory systems, affections

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of the skin (in the form of ointments) and for prevention or therapy of coccidiosis of small domestic animals [11,12]. Quality control of sulphonamide formulations and their quick systematic monitoring in body fluids are important analytical tasks. A number of articles have been published concerning the determination of sulphonamides by different analytical methods. Sulfamerazine is one of the well-known and widely used sulfonamide antibacterial drugs to treat bacterial disease in human and animals like cattle, sheep, pigs and poultry [11,12].

Among the many different families of organic inorganic chemicals being currently investigated because of their applications, sulfonamides and their N-derivatives are one of the outstanding groups. Sulfonamides were the first effective chemotherapeutic agents employed systematically for the prevention and cure of bacterial infections in humans.

The sulfonamide derivatives are also known to exhibit a wide variety of pharmacological activities [13-15] through exchanges of different functional groups without the modification of the structural $–S(O)_2N(H)–$ feature.

The pharmacological activities of sulfonamides derivates are well known for many years [16] and it has been demonstrated that their efficiency is linked to the inhibition of the bacterial enzyme DHPS (dihydropteroate synthetase) by imitation of the paraamino- benzoic acid which is required by bacteria for the synthesis of folic acid [17]. Even if the introduction of new molecules such as penicillin or its derivates and other modern antibiotics have reduced the importance of sulfonamides, the latter remain excellent ligands in order to elaborate new complexes based on 3d or 4f metals [18]. One goal here is to increase the bioligand activity by introducing a metal and/or to combine the ligand properties to the metal's one. Indeed, the ion metal plainly takes part of the molecular structure and thus, can greatly improve the biological effect of the organic entity [19].

The cyclodiphosphazanes of sulfonamides had been prepared and their ability to form more biologically active complexes have been studied [20-23]. Metal complexes are well known with accelerating drug action and the efficiency of a therapeutic agent can often be enhanced upon coordination with a metal ion i.e., the complexation represented an effective strategy for the improvement of the biological activities of the ligands [23].

In continuation to our interest to prepare hexachlorocyclodiphosph- (V)azane of sulfa drugs, the present paper aims chiefly to prepare substituted hexachlorocyclodiphosph(V)azane of sulfadimethoxine H2L. The behavior of these ligands towards transition metal ions was studied. The characterization of the prepared compounds was performed using different physicochemical methods. Also, the biological and anticancer activity of the prepared ligands and their complexes were studied.

Materials and Methods

Materials

All chemicals reagents were purchased from Aldrich Sigma and used without purification. Solvents were purified according to standard procedures [24]. All chemicals used were of analytical reagent grade. They included $FeCl_3 \cdot ٦H_2O$, $CoCl2 \cdot 6H_2O$, $NiCl_2 \cdot ٦H_2O$, $CuCl_2 \cdot ٢H٢O$, $ZnCl_2$, and $UO_2(NO_3)_2 \cdot ٢H_2O$, sulfamethoxazole, and phosphorus pentachloride supplied from BDH. The solvents used were ethanol, benzene, dimethyformamide (DMF), and deutrated dimethyl sulfoxide (DMSO).

Methods

Synthesis of cyclodiphosph(V)azane ligand

1,3-di-[N\-2,6-dimethoxy-4-primidnylsulfanil-amide] -2,2,2,4,4,4-hexachloroc yclodipho - sph(V) azane (H4L1) was prepared as mentioned in the lecture work [25] using the methods of Chapman et al. [26] and Zhumurova and Kirzanov [27].

Synthesis of the metal complexes

A solution of metal salts (10 mmol) in 50 ml dry well-stirred ethanol was added drop wise to the solution of $H4L^1$ (5 mmol) in 100 ml dry ethanol at room temperature. The reaction mixture was heated under reflux for 2 h. The product was separated and washed several times with ethanol and diethyl ether and dried in vacuo.

Instrumentation techniques

The IR spectra were recorded on a Perkin–Elmer 437 IR spectrophotometer (400 – 4000cm^{-1}) (KBr technique). ^1H NMR spectra were measured at Pruker FT-400MHZ spectrophotometer using an internal standard solvent (DMSO-d6). The electronic spectra were measured using a Shimadzu PC 3101 spectrophotometer. The magnetic susceptibilities of the complexes in the solid state were recorded on a Sherwood Scientific Magnetic Susceptibility Balance using Faraday method. Thermogravimetric analysis was performed under a nitrogen atmosphere using a Shimadzu TGA-

50H with a flow rate of 20°C min^{-1}. The UV–vis spectra were recorded on a Perkin-Elmer Lambda 3B UV–vis spectrophotometer. The Antimicrobial activity was performed using DMF as solvent at Fermentation Biotechnology and Applied Microbiology (FERM-BAM) Center. The test was done using diffusion agar technique [28,29]. Potential cytotoxicity of the compounds was tested on HCT116 cell line, at Cairo University, National Cancer Institute, Cancer Biology Department, Pharmacology Unit.

Results and Discussion

Characterization of the ligand

In the present investigation, novel hexachlorocyclodiphosph(V)azane derivative of 1,3-di-[N/-2,6-dimethoxy-4-pyrimidnylsulfanilamide]2,4-di-[N/-2-quinoxalinylsulfanilamide]-2,-4-dichlorocyclodiphosph(V)azane (H_4L^1) was prepared. The suggest the structure of the prepared ligand (H_4L^1) is represented in Fig. 1. The ^{1}H NMR spectrum of the H4L1 free ligand shows a broad signal at δ = 4.80 – 6.40 ppm which assigned to $–SO_2NH$ protons of this ligand (–SO2NH of original ligand H2L and of the substituted sulfaquinoxaline). In addition to the appearance of signals which attributed to aromatic protons in their expected regions multiples around 6.63 − 7.77 ppm for H4L1 [9]. The signal due to OCH_3 protons appears at 3.5 ppm for H4L1. Also, the heterocyclic protons appear at 8.64, 7.02 and 8.51 ppm [20] as shown in Fig.2. Also, the structure of the new substituted cyclodiphosph(V)azane sulfa drugs ($H4L^1$) free ligand confirmed by IR spectra. The IR spectra of the free ligand showed the characteristic stretching vibration bands at 1152 which characteristic for υ(P–N) for $H4L^1$ ligand [22]. The ligand exhibits two bands at 1340, 1088 cm^{-1} assigned to υasym. SO_2, υsym.SO_2 stretching vibrations for ligand. The presence of the band at 3436 which is characteristic for υ(NH) for $H4L^1$ ligand. Also, the spectra of $H4L^1$ showed new bands at 1639, 1585 cm^{-1} which are due to υ(C=N) vibrational bands of quinoxaline and diazine rings [30,31]. In addition to the band at 572 cm^{-1} due to υ(P–Cl) [22] for the original ligand, H2L were shifted to 595 and 555 cm-1 upon the replacement of one Cl atom by one molecule of each sulfa drug in both sites of the dimeric structure of the ligand $H4L^1$ as shown in Fig. 3.

Characterization of the metal complexes

The results of the elemental analyses of the isolated complexes (1−7) are in good agreement with those required by the proposed formula of complexes according to the following general equations:

$$2MX_z + (H_4L^1 \text{ or } H_4L^2) + n\,H_2O \longrightarrow \left[(M)_2(H_4L^1 \text{ or } H_4L^2)Cl_y(H_2O)_n\right] X_z$$

Where, M = (1) Fe(III) , (2) Mn(II), (3) Co(II), (4) Cu(II), (5) Zn(II), (6) Cd(II), and (7) UO2(II).

Molar conductance

The conductivity Λ_m value of the complexes (**1**−**7**) were calculated by using the relation Λ_m = K/C, where C is the molar concentration of the metal complex solutions and K is the specific conductance. The complexes were dissolved in (10^{-3}M) DMF and the molar conductivities of their solutions at 25±2°C were measured. Tables 1 shows the molar conductance values of the H_4L^1 and its metal complexes (**1**−**7**). It is concluded from the results that, the complex compounds (**1**−**6**) were found to have molar conductance values lie in the range 193.70 –2 15.20 ohm^{-1} cm^2mol^{-1} for H_4L^1 metal complexes. It was indicated that these complexes are ionic in nature and they are of the type 2:1 electrolyte [32]. The exception was found for UO_2(II) complex (**7**) of H_4L^1 ligand which has molar conductance values of 416.00 ohm^{-1} cm^2mol^{-1} respectively. On the base of these data, it was clear that these chelates were considered as 4:1 electrolyte, indicating the ionic nature of the bonding of the nitrate group to the cationic complex [33].

^{1}H NMR spectra

The proton magnetic resonance of the free ligands H_4L^1 and its metal complexes were performed in DMSO-*d6*. From the chemical shifts data, it was shown that the very broad bands observed at δ = 4.80 – 6.40 ppm attributed to the secondary amine protons of $–SO_2$-NH groups for H_4L^1 free ligand, which exchangeable with D_2O. In Cd(II) complex (**6**), a new signals appear at δ = 3.45 , 6.03 ppm which show definitely the enolization of $–SO_2$-NH groups to the S(O)OH=N and the participate in the chelation with Cd(II) ion[22]. Also, a new signal observed at δ = 3.90 ppm corresponding to coordinated water molecules [22,34]. Unfortunately, the insolubility of all diamagnetic complexes (**5** and **7**) in deuterated organic solvents make it difficult to carry out ^{1}H NMR spectra of these complexes to further clarify the way of binding of the free ligands to the metal ions as shown in Fig 2 [34].

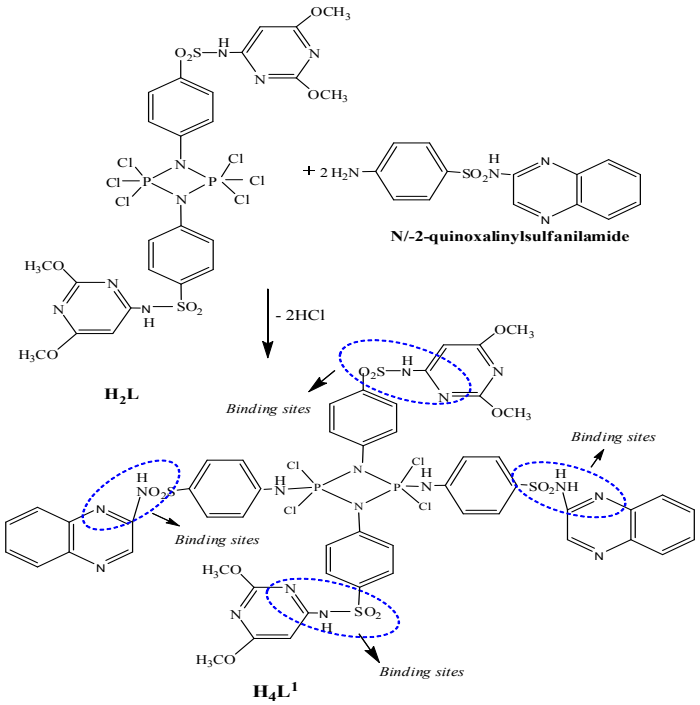


Fig.1. Schematic route for preparation of 1,3-di-[N/-3,4-dimethyl-5-isoxa- zolylsulfanilamide]-2,4-di-[N/-2-quinoxalinylsulfanilamide]-2,4dichlorocyclodi- phosph(V)azane (H4L^1) free ligand.

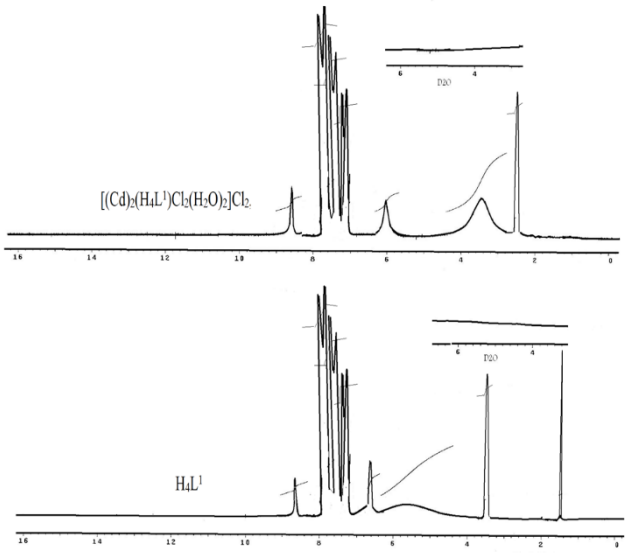
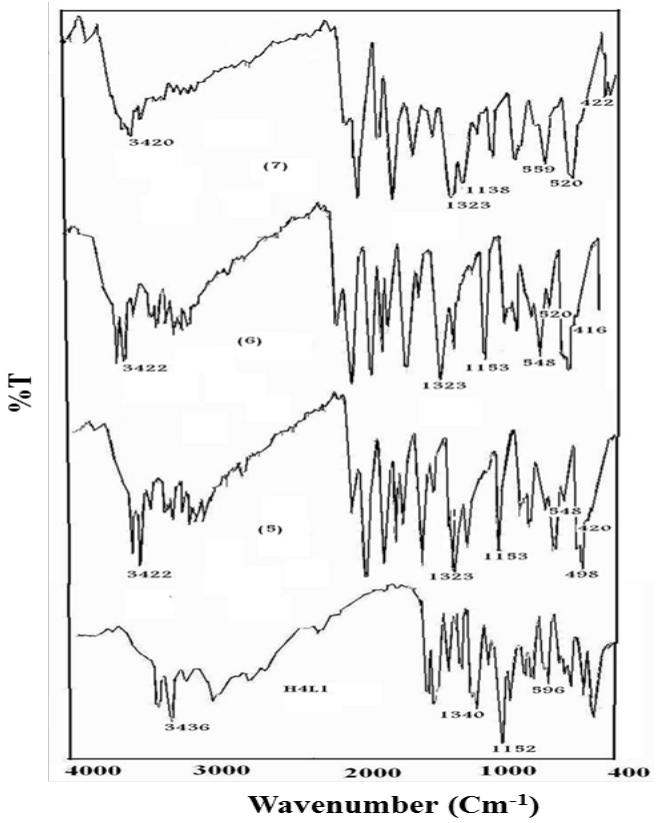


Fig.2. ^{1}HNMR spectrum of: H_4L^1 and $[(Cd)_2(H_4L^1)Cl_2(H_2O)_2]Cl_2$.

IR spectra and mode of bonding

The IR spectra of the free ligands H_4L^1 and its metal complexes (**1**−**7**) were carried out in the range of 4000−400 cm^{-1}. The IR spectra of the complexes were compared with those of the free ligand in order to determine the possible coordination sites that may involve in chelation. There were some guide peaks, in the spectra of the free ligands, which were of good help for achieving this goal. The intensities of these peaks were expected to be changed upon chelation. From a careful comparison of the free ligands H_4L^1, and its metal complexes, it was found that the stretching vibration band; υ(NH), of the sulfonamide group, which found at 3436 cm^{-1} for the free ligand H_4L^1 was hidden under the broad bands at 3420 – 3422 of the isolated complexes (**1**–**7**) for the free ligand H_4L^1 as shown in Fig.3.



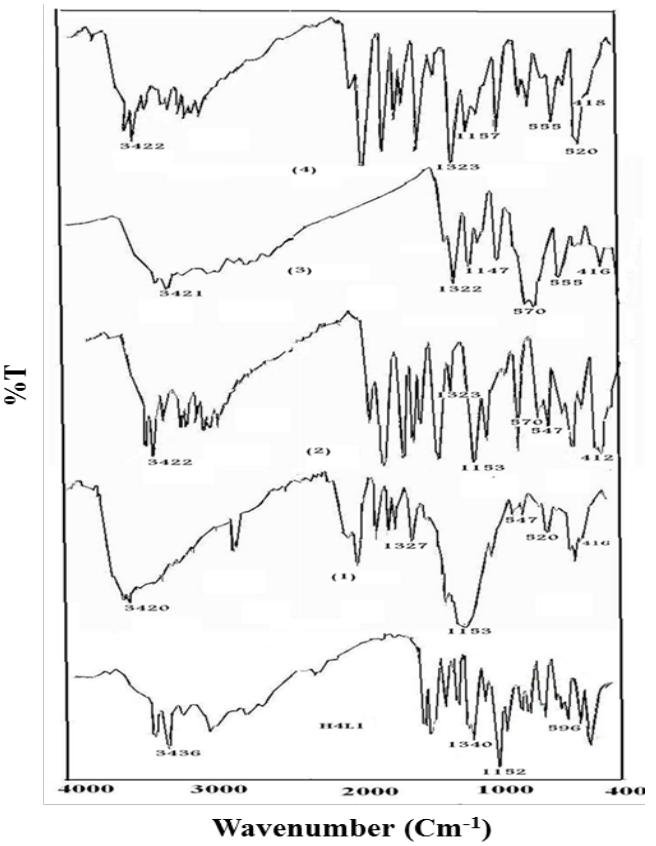


Fig.3. IR spectra of H_4L^1 free ligand and its metal complexes .

Electronic spectra and magnetic properties

Electronic and magnetic spectra of the ligand and its metal complexes were displayed in DMF (10^{-3}M) at room temperature at a wavelength range from 200 – 800 nm. As shown in Tables (1 and 2) the electronic spectra of the ligand showed a sharp and intense band at 266 nm, corresponding to phosphazo four–membered ring of the ligands H_4L^1 [26,30]. On complexation, these bands suffer considerable shifts to blue or red regions in the spectra of the complexes depend on the type of metal ions coordinated to the ligand [34,35]. While the band observed at 300 nm in the spectra of the free ligand corresponding to the π-π* transition. This band shifts to blue or red regions upon complexation are shown in (Figs.7) [35]. Also, the spectra of the complexes further display a band in the range 350 – 460 for H_4L^1, which assigned to n-π* transition [36]. However, a band observed at 560 – 750 nm for H_4L^1 metal complexes; assigned to the *d–d* transition within the metal complexes [37].

Thermal analysis

In order to give more insight into the structure of the complexes, the thermal studies of the complexes were carried out using thermogravimetry (TG) technique in the temperature range of 25−900°C. The estimated mass losses were computed based on TG results and the calculated mass losses were computed using the results of microanalyses as shown in Table S1 (supporting information).

TABLE 1. Electronic spectral data of H_4L^1 ligand and its metal complexes (1−7).

Complex	Geometry	μ_{eff} (B.M.)	Band assignments	Absorption bands (cm^{-1})
(1)$[(Fe)_2(H_4L^1)Cl_4]Cl_2$	Octahedral	5.63	$^6A_{1g}\rightarrow{}^4T_{2g}(G)$ $^6A_{1g}\rightarrow{}^4T_{1g}$ LMCT(L→M)	23.697 14.005, 17.241 23.697
(2)$[(Mn)_2(H_4L^1)Cl_2(H_2O)_2]Cl_2$	Octahedral	5.55	$^6A_{1g}\rightarrow{}^4T_{1g}$ $^6A_{1g}\rightarrow{}^4T_{2g}(G)$ $^6A_{1g}\rightarrow{}^4T_{1g}(G)$	15.625 22.222 26.455
(3)$[(Co)_2(H_4L^1)Cl_2(H_2O)_2]Cl_2$	Octahedral	4.61	$^4T_{1g}(F)\rightarrow{}^4A_{2g}(F)$ $^4T_{1g}(F)\rightarrow{}^4T_{2g}(P)$	17.212 20.040
(4)$[(Cu)_2(H_4L^1)Cl_2(H_2O)_2]Cl_2$	Octahedral	1.87	$^2T_{2g}\rightarrow{}^2E_g(x^2–y^2)$ L→M CT	17.545 24.449
(5)$[(Zn)_2(H_4L^1)Cl_2(H_2O)_2]Cl_2$	Octahedral	d^{10}		
(6)$[(Cd)_2(H_4L^1)Cl_2(H_2O)_2]Cl_2$	Octahedral	d^{10}		
(7)$[(UO_2)_2(H_4L^1)](NO_3)_4$	Octahedral	d^{10}		

TABLE 2. Magnetic moment and electronic spectral data of the H_4L^1 metal complexes (1−7).

Compd. No.	Absorption bands (nm)			
	Phosphazo ring	π-π*	n-π*	*d-d* transition
H_4L^1	266	300	–	–
(1)	249	320	350, 420, 445, 460	560, 640 ,714
(2)	249	325	352, 420,	582, 640, 750
(3)	249	320	355, 420, 440	581, 649, 720
(4)	263	325	355, 420	580, 628
(5)	269	330	351,422	–
(6)	265	315, 329	430	–
(7)	250	320	359,440	–

TABLE S1. Thermogravimetric results (TG) of Fe(III), Co(II) and Zn(II) complexes (**1, 3, 5**).

Complex	Temp. range(°C)	n*	Loss in weight Estim./ (calcd.)%		Loss in weight Estim. / (calcd.)%	Metallic residue
			Mass loss	Total mass loss		
(1)$[(Fe)_2(H_4L^1)Cl_4]Cl_2$	220-320 320-450 450-610 610-670	4	26.21(26.09) 15.48(15.44) 31.92(30.58) 7.38(7.62)	80.99(79.73)	-Loss of 4HCl and $C_{10}H_{11}N_3O_3S_2$ -Loss of $C_{13}H_9N_3O_3$ -Loss of $C_{17}H_{18}N_5Cl_6$ -Loss of C_5H_4NOS leaving $C_5H_4N_2P_2S$	Fe_2O_3
(3)$[(Co)_2(H_4L^1)Cl_2(H_2O)_2]Cl_2$	80-120 166-409 409-600	3	5.94(4.46) 33.85(33.86) 45.96(45.94)	85.75(84.26)	-Loss of $2H_2O$ Coord. and HCl -Loss 3HCl and $C_{20}H_{23}N_7O_5$ -Loss of $C_{30}H_{17}N_7O_5P_2S_4$	$2CoCl_2$
(5)$[(Zn)_2(H_4L^1)Cl_2(H_2O)_2]Cl_2$	50-320 320-550 550-650	3	23.49(23.46) 46.88(46.27) 13.64(13.64)	84.01(83.37)	-Loss of $2H_2O$ Coord., 4HCl and $C_{16}H_{11}$ -Loss of $C_{34}H_{29}N_{14}O_4P_2$ -Loss of $3SO_2$ and 1/2 S_2	$2ZnCl_2$

n* = number of decomposition steps.

Antimicrobial activity

The inhibition of the causal microbe without any side effects on the patients is the main aim of the production and synthesis of any antimicrobial compound. To increase the chance of detecting the antibiotic potential of the tested materials, we used more than one test organism in the antimicrobial screening of the newly synthesized compound H_4L^1 free ligand with its metal complexes (**1-7**). By using the assay plates, the sensitivity of a microorganism to antibiotics and other antimicrobial agents was determined (Fig.5) [28], which were incubated at 28°C for 2 days (for Fungi) and at 37 °C for 1 day (for bacteria). The parent free ligands and their metal complexes (100µg/l in DMF as a solvent) were screened against bacterial species namely, Staphylococcus aureus, Micrococcus sp and Staphylococcus epidemidis as a Gram–positive bacteria, Escherichia coli, Pseudomonas aeruginosa, Acinetobacter species, Proteus mirabilis, and Klebsiella pneumoniae as a Gram–negative bacteria. Also, the antifungal activity against Candida species was carried. The Chloramphenicol antibiotic was used as standard antibacterial control and Cefotaxime was used as standard antifungal control using agar nutrient as a medium. A solvent control using DMF were done for the set of assays. From the data obtained as shown in Table S2 (Supporting information), it was found that H_4L^1 free ligand showed no antimicrobial activity towards all the tested strains (Gram-positive, Gram-negative bacteria and fungi). This might be reasonably accounted to that the replacement of two chlorine atoms in H_2L free ligand by two molecules of sulfaquinoxaline to give the H_4L^1 free ligand retarded the high activity of H_2L free ligand. But, when the metal ions combined with this H_4L^1 free ligand to form complexes (**1-7**), the antimicrobial activities of the ligand become present. So, all complexes showed a remarkable activity against all bacterial and fungal strains except $[(Cd)_2(H_4L^1)Cl_2(H_2O)2]Cl_2$ complex compound (6) and $[(UO_2)_2(H_4L^1)](NO_3)_4$(7) which then have no antimicrobial activity towards Pseudomonas aeruginosa as well as the free ligand itself. Among the prepared complexes (1-7), both $(Fe)_2(H_4L^1)Cl_4]Cl_2$ complex compound (1) and $[(Cd)_2(H4L1)Cl_2(H_2O)_2]Cl_2$(6) showed a very high activity towards Gram-positive bacteria (Staphylococcus aureus) and Gram-negative bacteria (Klebsiella pneumoniae). Also $[(Cu)_2(H_4L^1)Cl_2(H_2O)_2]Cl_2$, and $[(UO_2)_2(H_4L^1)](NO_3)_4$ complexes showed a very high activity against Gram-positive bacteria (Staphylococcus epidemidis).

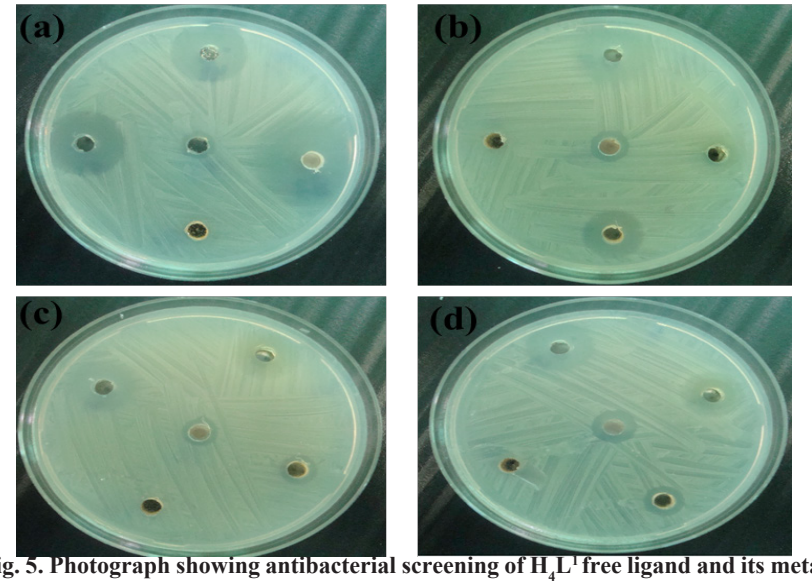


Fig. 5. Photograph showing antibacterial screening of H_4L^1 free ligand and its metal complexes against (a) Staphylococcusepidemidis, (b) Klebsiella pneumoniae, (c) Pseudomonas aeruginosa, and (d) Proteus mirabilis.

TABLE S2. Antimicrobial activity of H_4L^1 free ligand and its metal complexes (1−7)*.

Compound No.	Gram-positive bacteria			Gram-negative bacteria					Fungi
	Staphylocos aureus	Micrococcus sp	Staphylocous epidemidis	Escherichia coli	Pseudomonas aeruginosa	Acinetobacter sp	Prous mirabilis	Klebsiella pneumoniae	Candida sp
H_4L^1	0	0	0	0	0	0	0	0	0
(1)$[(Fe)_2(H_4L^1)Cl_4]Cl_2$	10	13	11	11	11	12	12	16	10
(2)$[(Mn)_2(H_4L^1)Cl_2(H_2O)_2]Cl_2$	14	14	12	13	10	11	12	13	13
(3)$[(Co)_2(H_4L^1)Cl_2(H_2O)_2]Cl_2$	11	12	10	12	11	10	10	15	0
(4)$[(Cu)_2(H_4L^1)Cl_2(H_2O)_2]Cl_2$	12	15	16	12	13	10	10	14	16
(5)$[(Zn)_2(H_4L^1)Cl_2(H_2O)_2]Cl_2$	12	15	15	15	12	13	12	14	14
(6)$[(Cd)_2(H_4L^1)Cl_2(H_2O)_2]Cl_2$	16	14	12	11	0	12	11	14	14
(7)$[(UO_2)_2(H_4L^1)](NO_3)_4$	11	15	16	12	0	13	12	12	16
R.S. **	30	39	0	25	0	0	0	0	0

*The test done using the diffusion agar technique. Inhibition values 1-5 mm beyond control = (less active). Inhibition values 6-10 mm beyond control = (moderate active). Inhibition values 11-15 mm beyond control = (highly active). Inhibition values over 15 mm beyond control = (very highly active). Not active = 0.**The antibiotic Chloramphenicol was used as standard antibacterial control and Cefotaxime was used as standard antifungal control.

Potential cytotoxicity measurement

In vitro anticancer activity evaluation of the newly synthesized compounds was carried out against human cancer cell lines(HCT116) (also, called colorectal cancer or bowel cancer), which is the third most common form of cancer. Also, the relationship between drug concentrations and cell viability was plotted to calculate IC_{50} (µg) (the value which corresponds to the concentration required for 50% inhibition cell viability) and the data were presented in Table 5. In the anticancer screening test in case of H_4L^1 free ligand, it was found that, the $[(Zn)_2(H_4L^1)Cl_2(H_2O)_2]Cl_2$ complex, (**5**) was highly effective against colon carcinoma cell line (HCT116) compared with that of its free ligand (63%). The order of the effectiveness of all the tested complexes was recorded as: Zn(II)(**63%**) > H_4L^3 > Mn(II)(58%) > UO_2(II)(52%)> Cu(II)(51%) > [Fe(III) =Cd(II) (46%)] > Co(II)(44%).

TABLE 5. Antitumor activity of H_4L^1 and H_4L^2ligands and their metal complexes (1− 7) .

HCT116	
Sample	**Inhibition %**
H_4L^1	63
(1)$[(Fe)_2(H_4L^1)Cl_4]Cl_2$	46
(2)$[(Mn)_2(H_4L^1)Cl_2(H_2O)_2]Cl_2$	58
(3)$[(Co)_2(H_4L^1)Cl_2(H_2O)_2]Cl_2$	44
(4)$[(Cu)_2(H_4L^1)Cl_2(H_2O)_2]Cl_2$	51
(5)$[(Zn)_2(H_4L^1)Cl_2(H_2O)_2]Cl_2$	65
(6)$[(Cd)_2(H_4L^1)Cl_2(H_2O)_2]Cl_2$	46
(7)$[(UO_2)_2(H_4L^1)](NO_3)_4$	52

Conclusion

In this study novel symmetrically cyclodiphosphazane ligand ($H4L^1$) and some selected metal complexes have been synthesized and characterized using different physicochemical methods. The antimicrobial and antitumor activity of the ligands and the metal complexes were investigated. It was found that the ligands and their complexes show a high to moderate antimicrobial activities against deferent strains of bacteria and fungi and show anticancer activity against colon carcinoma HCT116.

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