Artigo

THE INTERACTION BETWEEN MERCURY(II) AND SULFATHIAZOLE

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The interaction of mercury(II) with sulfathiazole has been analyzed. IR and NMR spectral studies suggest a coordination of Hg(II) with the $N_{thiazolic}$ atom, unlike related Hg-sulfadrugs compounds. The complex was screened for its activity against *Escherichia coli*, showing an appreciable antimicrobial activity compared with the ligand.

Keywords: mercury complexes; sulfonamides; sulfonamide metal complexes.

INTRODUCTION

The synthesis of metal sulfanilamide compounds has received much attention due to the fact that sulfanilamides were the first effective chemotherapeutic agents to be employed for the prevention and cure of bacterial infections in humans[1,2]. Furthermore, sulfadrugs and their metal complexes, possess many applications as diuretic, antiglaucoma or antiepileptic drugs, among others[3-8]. The sulfanilamides exert their antibacterial action by the competitive inhibition of the enzyme dihydropterase synthetase towards the substrate *p*-aminobenzoate[9]. Several authors have reported the antimicrobial activity of sulfanilamides and their metal complexes[10,11]. Studies on their metal chelates could have much physiological and pharmacological relevance because the metal chelates of sulfadrugs have been found to be more bacteriostatic than the drugs themselves[12]. Sulfathiazole, [4-amino-*N*-2-thiazolylbencenosulfonamide], (Figure 1), is clinically one of the most used[11]. Besides, Hg(II) has been used in medicine for many years[13,14] . Although the synthesis of metal complexes of sulfathiazole has been reported, the structural determination is often incomplete and conflicting[10]. Casanova *et al.*[10] reported the first crystal structure of a Zn-sulfathiazole complex, where the drug acts as a bridging ligand through both the N_{amino} and $N_{thiazole}$ atoms. On the other hand, coordination behavior of metal ions as Zn(II) and Cd(II) with sulfadrugs showed different from Hg(II) ones[9]. Considering the different behavior of sulfathiazole as ligand and Hg(II) as metal ion from another d^{10} metal ions, a comparative study of the interaction between sulfathiazole and Hg(II) must be of interest. As part of a research program devoted to the investigation of the structural and physicochemical properties of metal complexes of chemoterapeutic agents, in the present paper we report synthesis, spectral and microbiological studies of the mercury-sulfathiazole complex (Hg-ST). In order to compare, we also report the studies we have done with the mercury-sulfanilamide complex (Hg-SA) at the same time.
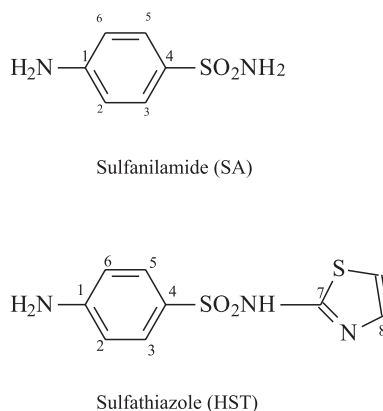

Figure 1. Notation used for sulfathiazole, sulfanilamide and their derivatives in this paper

EXPERIMENTAL PART

Caution: Hg(II) compounds are toxic[13]. Appropriate precautions should be taken to avoid skin and digestive contacts[15].

Synthesis of complexes: general procedure

Aqueous solution of mercuric chloride (1 mmol/10 mL) was added dropwise to a stirred aqueous solution of the corresponding sulfonamide: sulfathiazole as sodium salt; and sulfanilamide in alkaline medium, given by the minimum amount of sodium hydroxide 0.1 M necessary to dissolve the drug (2 mmol/20 mL)[16]. Immediately, the resulting mixture became white, because a white precipitate was formed. Then, the reaction mixture was left to stand at RT, protected from the light. After two days the precipitate was centrifuged, washed with water several times and dried under vacuum, protected from the light.

When the molar ratio [ligand]/[metal] was major than 2/1, only the same compounds were obtained.

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Analysis and physical measurements

The content of Hg was determined by atomic absorption spectroscopy with a Perkin Elmer spectrometer, model 3110 with a flux injection system Fias 100 Perkin Elmer, in the laboratory of Analytical Services, UNL.

Elemental chemical analyses were performed in a microanalyser C.E. Instruments, model Eager 1108, at the Barcelona University (UB).

Infrared spectra in the solid state were carried out in the 4000-500 cm^{-1} range on a Nicolet 520-FTIR spectrophotometer (UB) , and on a Perkin Elmer-337 spectrophotometer (UNR), using both the KBr pellets technique.

Electronic spectra were recorded between 200 and 800 nm in a Jasco model 530 double beam spectrophotometer, using quartz cells of 1 cm path length, at RT and in the following solvents: water, hydrochloric acid 1 M, sodium hydroxide 1 M, ethanol 96%. DMSO was not employed for recording these spectra because the window of this solvent is not useful for wavelength below 250 nm.

The ^{1}H NMR spectra in DMSO-d_6 were performed on a Bruker Unity-300 spectrometer (UB) and on a Bruker AC-200 E (UNR) at 25 °C. ^{13}C {^{1}H} NMR spectra in deuteraded dimethyl sulfoxide, $(CD_3)_2SO$, (DMSO-d_6) were obtained on a Bruker Unity-300 spectrometer, using high-power proton decoupling, pulse sequence: s2pul. Proton and carbon chemical shifts in DMSO-d_6 were referenced to DMSO-d_6 (^{1}H NMR, $\delta_{(DMSO)}$ = 2.49 ppm; ^{13}C NMR, $\delta_{(DMSO)}$ = 39.5 ppm).

The conductivity of saturated aqueous solutions were measured at room temperature on a Horiba B-173 Conductivity Meter. These measurements suggested a nonelectrolytic nature for Hg-ST.

Spectrofluorometry analyses were recorded in a Aminco Bowman, for SA and Hg-SA in HCl 0.1M, at 25 °C; excitation wavelength: 262 nm; emission range: 280-420 nm. There were no changes neither in shape nor position of the peak of SA (341 nm) respect to Hg-SA, which indicates that the coordination of Hg(II) with SA does not affect directly the benzene ring[17]. HST and Hg-ST were not active in the same conditions.

Antimicrobial tests: Minimum inhibitory concentration (MIC) determination

MIC of the compounds against bacterial strains obtained from the American Type Culture Collection (ATCC) and from a Centennial Hospital's patient at the University of Rosario, were performed at the Laboratory of Microbiology -at the Biochemical Faculty, University of Rosario-, by the microdilution method following the National Committee for Clinical Laboratory Standard (NCCLS) specifications[18]. Briefly: 1mL of bacterial suspension in the last phase of growth was inoculated in 1 mL of Mueller Hinton Broth (Difco) containing the compounds at a final concentration ranging from 64 to 0.12 µg/mL derived from serial 2-fold dilutions. The final inoculum was approximately 1 x 10^5 viable bacteria/mL and the final volume, 2 mL. Inoculated tubes were incubated at 35 °C for 18 - 21 hs. Readings were made visually (by observed turbidity). The MIC was defined as the lowest concentration of antimicrobial agent showing complete inhibition of growth. MIC of the reference drugs (sulfathiazole -sodium salt- and sulfanilamide, both obtained from Sigma) were compared with those of the test compounds. Drug- and bacterial-free controls were included.

The complexes (0.0128 g of each one) were dissolved using the minimum amount of HCl 1 M for a final volume of 10 mL of aqueous solution [pH = 5 (Hg-SA, SA) and 3 (Hg-ST, NaST)]. The same treatment was employed for the corresponding ligand (sulfathiazole

or sulfanilamide). The solvent was used for further dilutions and tested as blank experiments.

RESULTS AND DISCUSSION

General physicochemical characteristics of the complexes

It was not possible to obtain crystals in order to analyze the metallic complexes structure by single-crystal XRD technique. The main difficulty to obtain suitable crystals is their poor solubility in water and in the most of the organic solvents. Thus, the spectroscopic techniques are an alternative to infer about the molecular structure. Conclusions about the structure of the complexes under study were obtained from NMR, IR and electronic spectra.

In water, the solubility at RT was 0.69 mg/100 mL for Hg-ST and 1.05 mg/100 mL for Hg-SA. The solubility was enhanced by HCl 1 M for both complexes: 0.450 g/100 mL for Hg-ST, and 1.84 g/100 mL for Hg-SA. NaOH dissolved the Hg-ST compound, but not the Hg-SA one.

Presence of Hg(II) in both complexes was tested by reaction with KI[19]. Absence of Cl$^-$ and Na$^+$ in both complexes was tested by the Vohlard method[20] and using a flame spectrophotometer Metrolab-305, respectively. Elemental analyses gave satisfactory results for Hg(sulfanilamidato)$_2$ in the case of Hg-SA complex and for Hg[(sulfathiazolato)$_2$ (OH)$_2$] in the case of the Hg-ST one.

Hg(sulfanilamidato)$_2$: white solid (61.8 % yield). Found (calculated for $C_{12}H_{14}N_4S_2O_4Hg$): C, 27.5 (26.6) ; H, 3.2 (2.6); N, 10.4 (10.3); S, 11.2 (11.8); Hg, 37.4 (36.9).

Hg[(sulfathiazolato)$_2$(OH)$_2$]: white solid (99.4 % yield). Found (calculated for $C_{18}H_{20}N_6S_4O_6Hg$): C, 30.3 (29.0); H, 2.5 (2.7); N, 11.5 (11.3); S, 17.3 (17.2); Hg: 26.3 (26.9).

The anhydrous character of both compounds was confirmed by thermal analyses between 100 and 120 °C at the Barcelona University.

NMR spectra

^{1}H and ^{13}C of the complexes sulfa-Hg and the respective ligands are presented in Tables 1-3. In order to make an accurate assignment of the signals to the corresponding resonances[21], we have also recorded the ^{1}H and ^{13}C NMR DMSO-d_6 solutions of SA, HST and its sodium salt (NaST).

Hg-SA complex

The proton spectrum of DMSO-d_6 solution of the Hg-SA complex showed signals at 7.37, 6.52, 6.86 and 5.52 ppm (Table 1). All signals of the complex shifted to low frequencies compared with those of the ligand, and the most affected one was the peak of the protons of the -SO2NH$_2$ (amide group), integrated for only one ^{1}H. This fact could be a consequence of the coordination with the Hg(II).

Table 1. ^{1}H NMR shift assignments of sulfanilamide (SA) and its Hg(II) complex (Hg-SA) in DMSO-d_6 [a] (δ, ppm)

Assignment	SA	Hg-SA	$\Delta \delta$ (ppm)[b]
C(3)-H/ C(5)-H	7.28	7.37	+0.09
C(2)-H/ C(6)-H	6.41	6.52	+0.11
SO$_2$-NH$_2$	6.64	6.86	**+0.22**
-NH$_2$	5.39	5.52	+0.13

[a] Relative to TMS with DMSO-d_6 peak as reference (^{1}H, 2.49 ppm)
[b] $\Delta\delta$ = δ (sulfonamide complex) - δ (sulfonamide)

Hg-ST complex

^{1}H and ^{13}C NMR of the complex Hg-ST are presented in Tables 2 and 3.

García-Raso et al founded that Hg(sulfamidato)$_2$ complexes (sulfamidato corresponds to one of the following ligands: sulfadimethoxine, sulfamethoxypyridazine, sulfadiazine, sulfamerazine, sulfadimidine and sulfamethoxazole) presented a similar NMR pattern, with two equivalent sulfonamide groups[9] . In these compounds, upon complexation, a downfield shift (+1.0 to +4.0 ppm) was observed for the carbon directly bonded to the sulfonamidic nitrogen. No proton resonance was observed for the amidic group in the H[1] NMR of these complexes in any case[9].

In our case, on the contrary, one of the most significative difference between the ^{1}H NMR spectra of DMSO-d_6 solutions of NaST (the ligand) and Hg-ST was a new signal that could be assigned to the amidic proton (7.04 ppm in the Hg-ST spectrum). This signal was absent in the ^{1}H NMR spectrum of the employed ligand (NaST) in the same conditions.

The ^{13}C NMR of DMSO-d_6 solutions of Hg-ST showed resonances at 151.97 [C(7)], 151.84 [C(1)], 128.24 [C(8)], 127.77 [C(4)], 127.68 [C(3) / C(5)], 112.34 [C(2) / C(6)], 107.35 [C(9)] ppm (Table 3). The most affected signals, compared with the HST ones, were those of C(7) and C(8), both belonging to the thiazole ring.

There are at least two very important differences between the ^{13}C NMR spectrum of the Hg(II)-sulfadrugs compounds coordinated by the sulfonamidic nitrogen[9] and the Hg-ST compound reported in the present work: first: the large shielding observed for C(7) and the large deshielding observed for C(8); second: only a very little shift for the carbon directly bonded to the sulfonamidic group, both in the ^{13}C NMR spectrum of Hg-ST. These results suggest that the coordination of HST with Hg(II) would not be by the sulfonamidic nitrogen, but probably by the N$_{thiazolic}$. Anyway, it is not possible to discard at all the participation of the amidic nitrogen in the mercury coordination with sulfathiazole.

IR spectra

The analyses of the IR spectra of the sulfadrugs and its metal complexes have been one of the most used techniques applied to the knowledge of the interaction between the metal ions and the donor atoms of these molecules[10].

IR selected spectral data of the sulfa-Hg complexes and the respective ligands are presented in Tables 4 and 5.

Participation of the amino group

The bands that appeared near 3500 and 3400 cm^{-1} due to $\upsilon_{asym}(NH_2)$ and $\upsilon_{sym}(NH_2)$ vibrations of the NH$_2$ group were modified with respect to those of the free respective ligands. For the Hg-SA and Hg-ST compounds, these vibration modes appeared at higher (Hg-ST) and lower (Hg-SA) wavenumbers, compared with those of the free ligand. It has been proposed that the difference between the $\upsilon^*(NH_2)$ of silver-sulfadrugs compounds and those of the parent ligands, being $\upsilon^*(NH_2) = \upsilon_s + \upsilon_{as} / 2$, gives information about the involvement of the NH$_2$ group in the silver complexation[10]. According to this, if the value of $\upsilon^*_{free\ ligand} - \upsilon^*_{coordinated\ ligand}$ is ≥ 70, the amino moiety is involved in the coordination. Casanova et al[10] founded that the IR spectrum of Zn(ST)$_2$.H$_2$O showed υ (N-H) stretching vibrations at 3480 and 3390 cm^{-1} , shifted to higher frequencies with respect to the equivalent ones in the uncoordinated ligand (3320 and 3280 cm^{-1}). This fact was interpreted, with regard to the crystal structure of the Zn(II) complex, as indicative of the coordination of the NH$_2$ group. However, this parameter as a measure of the coordination of the amino group must be taken into account carefully[11], because when the amino N atom does not interact directly with the metal ion, it is possible that these modifications would be consequently due to the hydrogen bonds involving the amino group[9, 22].

Hg-SA complex

The bands due to $\upsilon_{asym}(NH_2)$ and $\upsilon_{sym}(NH_2)$ vibrations of the NH$_2$

Table 2. ^{1}H NMR shift assignments of sulfathiazole (HST), its sodium salt (NaST) and its Hg(II) complex (Hg-ST) in DMSO-d_6[a] (δ, ppm)

Assignment	HST	NaST	$\Delta \delta$ (ppm)[b]	Hg-ST	$\Delta \delta$ (ppm)[c]
SO$_2$-NH-	12.34	—	—	7.04	**- 5.30**
C(3)-H/ C(5)-H	7.45	7.42	- 0.03	7.45	0.00
C(9)-H	7.18	6.91	- 0.27	7.19	+ 0.01
C(8)-H	6.74	6.41	- 0.33	6.68	**- 0.06**
C(2)-H/ C(6)-H	6.58	6.48	- 0.10	6.54	- 0.04
-NH$_2$	5.79	5.47	- 0.32	5.76	- 0.03

[a] Relative to TMS with DMSO-d_6 peak as reference (^{1}H, 2.49 ppm); [b] $\Delta \delta = \delta$ (NaST) - δ (HST); [c] $\Delta \delta = \delta$ (Hg-ST) - δ (HST)

Table 3. ^{13}C NMR shift assignments of sulfathiazole (HST), its sodium salt (NaST) and its Hg(II) complex (Hg-ST) in DMSO-d_6[a] (δ, ppm)

Assignment	HST	NaST	$\Delta \delta$ (ppm)[b]	ST-Hg	$\Delta \delta$ (ppm)[c]
C(7)	167.90	170.30	+ 2.40	151.97	**- 15.93**
C(1)	152.18	150.47	- 1.71	151.84	- 0.34
C(4)	127.86	132.13	+ 4.27	127.77	- 0.09
C(3) / C(5)	127.69	127.84	+ 0.15	127.68	- 0.01
C(8)	124.24	137.18	+ 12.94	128.24	**+ 4.00**
C(2) / C(6)	112.42	112.26	- 0.16	112.34	- 0.08
C(9)	107.42	106.81	- 0.61	107.35	- 0.07

[a] Relative to TMS with DMSO-d_6 peak as reference (^{13}C, 39.5 ppm); [b] $\Delta \delta = \delta$ (NaST) - δ (HST); [c] $\Delta \delta = \delta$ (Hg-ST) - δ (HST)

group appeared at lower frequencies than in the free ligand. The sharp and intense bands at 1319 and 1153 cm^{-1}, which were assigned to the asymmetric and symmetric υ (SO$_2$) modes, respectively[23], shifted both to lower frequencies. The band at 697 cm^{-1} in the SA infrared spectrum (attributed to the υ (S-N)[24]), was shifted to 670 cm^{-1} in the IR spectrum of the Hg-SA complex.

Table 4. Assignment of the vibrational spectra (frequency: υ, cm^{-1}) of sulfanilamide (SA) and its Hg(II) complex (Hg-SA)

Assignment	SA	Hg-SA	$\Delta \upsilon$ (cm^{-1})*
-NH$_2$ (sym)	3380	3335	-55
-NH$_2$ (asym)	3482	3420	-62
-SO2- (asym)	1319	1223	-96
-SO2- (sym)	1153	1115	-38
RSO$_2$**S-N**	697	670	-27

* $\Delta \upsilon$ = υ (sulfonamide complex) - υ (sulfonamide)

Hg-ST complex

The bands due to υ_{asym}(NH$_2$) and υ_{sym}(NH$_2$) vibrations of the NH$_2$ group appeared at higher frequencies than in the free ligand. The frequency υ(N-H) of the sulfonamido group[24], which in the IR spectrum of HST was founded at 3210 cm^{-1}, in the Hg-ST one appeared at 3233 cm^{-1}.

The sharp and intense bands at 1330 and 1140 cm^{-1} were assigned to the asymmetric and symmetric υ (SO$_2$) modes, respectively[23]. These energies were not shifted with respect to those of the ligand, suggesting no interaction of the -SO$_2$ -group with the metal ion.

The strong band at 1540 cm^{-1}, attributed in the sulfadrug to the stretching C=N thiazole ring vibration, was shifted to lower frequencies, appearing at 1485 cm^{-1} in the IR of the complex. This fact is in agreement with the interaction through the N$_{thiazole}$ atom[25]. The band at 660 cm^{-1} in the IR spectrum of Hg-ST can be attributed to the υ (C-S) vibrations (thiazole ring mode)[25], shifted to higher frequency (in the IR spectrum of HST, appeared at 635 cm^{-1}).

Table 5. Assignment of the vibrational spectra (frequency: υ, cm^{-1}) of sulfathiazole (HST) and its Hg(II) complex (Hg-ST)

Assignment	HST	Hg-ST	$\Delta \upsilon$ (cm^{-1})*
-SO$_2$**N-H** amide	3210	3233	+23
-NH$_2$ (sym)	3260	3378	+118
-NH$_2$ (asym)	3320	3461	+141
-SO2- (asym)	1330	1326	–4
-SO2- (sym)	1140	1139	–1
RSO$_2$**S-N**	690	697	+7
Thiazole ring modes			
C=N	1540	1485	-55
C-S	635	660	+25

* $\Delta \upsilon$ = υ (sulfonamide complex) - υ (sulfonamide)

Electronic spectra

Hg-SA complex

The electronic spectrum of SA in water showed one band with the absorption maximum at 259 nm, which was shifted in HCl 1 M to 217 nm. The same absorbance maximum was observed for aqueous

solution of Hg-SA (259 nm), which was shifted to 224 nm in HCl 1 M. The band observed in the electronic spectrum of SA could be assimilated to the allowed E band ($\pi \longrightarrow \pi^*$) in the aniline, at 230 nm, which shifts to lower wavelength in acidic media (203 nm for the protonated aniline)[26]. Similar shift was observed in the UV-Vis spectrum of the Hg-SA complex, suggesting a similar behavior than the SA one. This fact could imply no metal coordination with the amino group, which would be free to accept a proton.

Hg-ST complex

In water, the electronic spectrum of HST (as sodium salt) showed two bands, with absorbance maxima at 259 and at 283 nm. In HCl 1 M these absorption maxima shifted to 217 and 280 nm respectively.

Aqueous solution of the Hg-ST complex showed two bands too, with absorbance maxima at practically the same wavelength (260 and 283 nm). These maxima were shifted to lower wavelength in HCl 1 M (222 and 279 nm respectively), similarly as it could be observed with Hg-SA.

These facts were in agreement with the observations of NMR and IR spectra, and with the facts that both complexes were dissolved by HCl, suggesting that the amino group would be free in both compounds.

The coordination chemistry of mercury(II)

A diversity of coordination numbers for mercury complexes can be found. In monoorganomercury(II) compounds, the primary bonds leave the Hg atom with enough residual acidity for it to be able to reach a coordination number of seven when the donor atoms forming the secondary bonds are small. Besides, the tendency of Hg to be involved in inter- or intramolecular secondary interactions results in there being only a small number of Hg complexes with coordination number two[27]. On the other hand, Hg(II), which has an extremely high affinity for thiol-containing compounds, forms 1:2 metal:ligand linear complexes with them[28].

Tetrahedral geometry were postulated in mercury(II) complexes of the type HgX$_2$L$_2$ (L = 1,3-imidazole-2-thione, 1-methyl-1,3-imidazole-2-thione; X = Cl$^-$, Br$^-$) on the basis of IR and NMR data[29]. In the complex of Hg(II) with 2-(α-hydroxybenzyl)thiamine the metal coordination unit consists of two distorted tetrahedra sharing two vertexes, and the high basicity of the N of the pyrimidine ring allows the coordination with the metal[30]. An example of octahedral local geometry is the complex of Hg(II) with the bidentate ligand lactobionic acid (L): [HgL$_2$].2H$_2$O[31].

With respect to Hg(II)-sulfadrugs complexes, both local geometries (linear arrangement[9] and tetrahedral[13]) were founded by X-ray crystal structure.

Sulfathiazole conformation

It is known that sulfathiazole posseses at least five crystalline or polymorphic forms: I, II, III, IV and V[32]. The main difference between them being in the types of hydrogen bonds present. Although both amido and imido forms are possible for the sulfathiazole molecule, the sulfathiazole exists in the solid state in the imido form. In the Zn-sulfathiazole complex, as a result of the deprotonation and coordination with the metal via the N$_{thiazole}$, the sulfadrug in the complex adopts an intermediate form between the imido and the amido[10].

In our case, we propose that the local geometry around the Hg atom would be linear for Hg-SA (Hg bounded to two N$_{amido}$ atoms) and tetrahedral for Hg-ST (Hg bonded to two N$_{thiazole}$ atoms and to two O$_{hydroxyl}$ atoms).

Anyway, on the basis of all these measurements, no definite molecular formulation for the Hg-St and Hg-SA compounds can be inferred. Other studies might be made (e.g. EXAFS, extended X-ray absorption fine structure) in order to confirm the molecular structures.

Antibacterial studies

Some metal complexes of sulfadrugs promote rapid healing of skin disorders (e.g. the Ag(I)-sulfadiazine complex is used for human burnt treatment, and the Zn(II)-sulfadiazine, in preventing bacterial infection in burnt animals[13]. Cobalt(II), Nickel(II) and Copper(II) complexes of sulfacetamide were screened for their activity against E. coli and S. aureus, showing an appreciable antimicrobial activity compared with the ligands[3]. Copper(II), zinc(II) and cadmium(II) complexes of trimethoprim (which is not a sulfadrug but it is used within sulfametoxazole, a sulfadrug) were screened for their activity against several bacteria (*E. coli* ATCC 25922; *E. aerogenes* ATCC 134048; *E. cloacae* ATCC 13047; *K. pneumoniae* ATCC 13883; *S. marcescens* ATCC 8100; *C. freundii* ATCC8090; *S. flexneri* ATCC 12022; *P. bulgaris* ATCC 13315; *P. morganii* NCTC 235; *P. aeruginosa* ATCC 9721; *P. aeruginosa* ATCC 27853; *A. calcoaceticus* ATCC 19606; *S. aerus* ATCC25923) showing activity similar to that of trimethoprim[22].

Sulfadrugs are among the drugs of first election (together with ampicilin, gentamicin and trimethoprim-sulfametoxasol) as chemotherapeutic agents in bacterial infections by *E. coli* in humans[33]. In the present work, the antibacterial activity of the Hg(II)-sulfadrugs complexes obtained and the corresponding ligand was evaluated against both *Escherichia coli* ATCC 25922 and an *Escherichia coli* obtained from a Centennial Hospital's patient at Rosario University (Table 6).

Table 6. Minimal inhibitory concentration (MIC, µg/ml) of the drugs for *E. coli* ATCC 25922 and *Escherichia coli* obtained from a patient of the Centennial Hospital from Rosario University

sulfadrug	MIC, µg/ml, for *E. coli* ATCC 25922	MIC, µg/ml, for *E. coli* from Centennial Hospital
sulfanilamide	> 128	> 128
Hg-SA	64	8
sulfathiazole (sodium salt)	>128	> 128
Hg-ST	16	8

Hg-SA and Hg-ST presented similar antibacterial activity against the assayed *E. coli*, and their MIC values were lower than the corresponding ligands in the same conditions. The activity of both complexes was better against the *E. coli* from the Hospital's patient than against the ATCC 25922 one.

CONCLUSION

The results obtained allow us to suggest that the amidic nitrogen would be the responsible for the coordination of Hg(II) with sulfanilamide, while the coordination of Hg(II) with sulfathiazole would be different from the common pattern observed in related compounds[9], that is, the coordination between Hg(II) and sulfathiazole would be through the $N_{thiazolic}$, with two hydroxyl groups bonding to the Hg atom, in a local tetrahedral geometry.

The microbiological results imply that the metal complexes Hg-SA and Hg-ST presented better antibacterial activity against *Escherichia coli* than the corresponding ligands.

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