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Synthesis, spectroscopic and electrochemichal characterization of mixed cobalt complexes with aminoacids and isonitrosoacetophenone. Biological activities

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Abstract: Complexes formed from isonitrosoacetophenone and aminoacids such as L-Phenylalanine, L-Tryptophan and L-Histidine having the formula $[Co(INAP)L(H_2O)_2]$ have been synthesized.

The complexes have been characterized using elemental analyses, molar conductance, UV-Vis, IR and ^1H NMR spectroscopy. The value of molar conductance indicates them to be non-electrolytes.

The IR spectra support the binding of the ligands with two N and two O donor sites to the cobalt(II) ion giving an arrangement of N_2O_2 donor group.

Electrochemical behavior of the complexes have been investigated by cyclic voltammetry which shows that the chelate structure and electron donating effects of the ligand substituent are among the factors influencing the redox potentials of the complexes.

The antimicrobial activities of the complexes were evaluated against several pathogenic microorganisms to assess their antimicrobial potentials. The cobalt complexes were found to be more active against Gram-positive than Gram-negative bacteria.

Furthermore, the antioxidant efficiencies of the metal complexes were determined by 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavening activity. The antioxidant activity of the complexes indicates their high scavenging activity against the radical DPPH.

Keyword: Cobalt; aminoacids; isonitrosoacetophenone; cyclic voltammetry; biological study.

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Introduction

Transition metal complexes of aminoacids constitute model systems for the study of metalloproteins. Cobalt is an essential trace element in humans, exhibiting many useful biological functions[1]. As it is well known, the cobalt(II) ion performs several biological functions in all life forms, especially in the higher organism. To date, many cobalt complexes

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have been used successfully in the treatment of several diseases. Octahedral cobalt complexes are known to assume *cis* structure.

Cobalt complexes have been widely used to mimic cobalamine (B_{12}) coenzymes.
Oximes are versatile ligands [2] to form with cobalt complexes with interesting structures.

The study of ternary complexes involving an oxime as the primary ligand, a metal ion and an aromatic aminoacids as secondary one can serve as useful models for gaining a better understanding of enzyme-metal ion- substrate complexes, which play an important role in metalloenzyme- catalysed biochemicals reactions.

For the present study we have chosen α-aminoacids abbreviated in general as HL where H is the dissociable carboxylic proton. The α-aminoacids are known to bind to metal ion via dissociation of the acidic proton as bidentate N, O-donor forming five-membered chelate rings[3].

L-Histidine is an essential aminoacid and has a positively charged imidazole functional group. It is a precursor for Histamine and carnosine biosynthesis[4,5].

L-Phenylalnine is essential to many functions and is one of the few aminoacids that can directly affect brain chemistry by crossing the blood-brain barrier[6].

L-Tryptophan is an important and frequently used material in the chemicals synthesis of a range of pharmaceuticals. He is a precursor of the vital neurotransmitter, serotonin, tryptophan levels in the body regulate moods and sleep[7,8].

Isonitrosoacetophenone is expected to behave as potential ambidentate ligands. It forms stable chelates with transition metal ions showing a variety of structural features. It can coordinate either through nitrogen or oxygen atom.

The aim of this work is to study the chelating behavior of the oxime and the aminoacids ligands towards cobalt ion. Efficiency of these complexes has been evaluated by free radical scavenging properties with the 2,2'-diphenyl-1-picrylhydrazyl radical (DPPH•) and antibacterial activities.

As the biological activity of the complex strongly depends on the nature of the ligands and on the metal coordination pattern, we have been interested by the study of the ternary metal complexes which provides information about how biological systems achieve their specificity and stability. Thus, we report the antibacterial and antifungal activities of the complexes against certain human pathogenic organisms.

Formation of free radicals and reactive oxygen species (ROS) is an integral part of human metabolism[9-10]. Oxygen-centred free radicals and other reactive oxygen species, that are continuously produced in cell result death and tissue damage. So, antioxidant compounds defend the organisms against free radical damage and then help the human body to reduce oxidative damage[11]. Antioxidant compounds play an important role as a health-protecting factor. Moreover, we also conducted an investigation to explore whether the Co(II) complex has the antioxidant property.

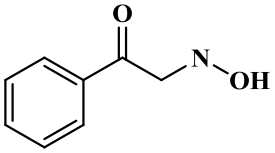

Figure 1: Structure of isonitrosoacetophenone (HINAP).

Experimental Section

Analytical and physical measurements

All the chemical reagents and solvents used in the preparations were Fluka p.a. products and used without further purification.

The elemental microanalysis was carried out by the Faculté de Pharmacie, Angers (France).

Melting points were measured using a Büchi 512 digital melting point apparatus.

Conductivity measurements were carried out using 10^{-3} M solution in ethanol on a SELECTA CD 2005 apparatus employing a calibrated dip-type cell at 25°C.

The IR spectra were recorded on Perkin Elmer FT-IR spectrometer Spectrum-One Model, in the range 4000-400 cm^{-1}, using KBr disks.

The electronic absorption spectra in ethanol solution were recorded on a UV-Visible JASCO V 560 spectrophotometer using quartz cells, in the UV and visible range,1100-200 nm.

Cyclic Voltammograms were obtained using PG210 VOLTA Lab. The working, counter and reference electrodes were, respectively, a platinum wire, a platinum foil and SCE (saturated calomel electrode). The SCE was separated from the test solution by a bridge filled with the solvent and supporting electrolyte which was tetrabutylammonium perchlorate (TBAP).The inert gas used was nitrogen.

Coulometric measurements were made using a double circular platinum net as working electrode. The auxiliary and reference electrodes, the blank electrolyte solution and the inert gas were the same as in voltammetric measurements.

^{1}H NMR spectra were obtained with a Jeol GSX 270 MSB (270 MHz) spectrometer (Université d'Angers, France) in DMSO-d_6 solution of the complexes and the HINAP and in D_2O solutions of the amino acids ligands using TMS as internal reference.

Biological studies

Microorganisms and culture conditions

The growth inhibitory activity of the chemical matter was tested against six bacteria[*Escherichia coli(ATCC 4157) , Staphylococcus aureus(ATCC 6538) , Streptococcus pyogenes(ATCC 12358), Proteus mirabilis(ATCC 49565), Pseudomonas aeruginosa(ATCC 9027) , Bacillus subtilis(ATCC 9372)*] and one yeast *Candida albicans(ATCC 24433).* The antimicrobial and antifungal activities of the ligands and their metal complexes were determined using the agar-disc diffusion method as will be described below.

Mueller-Hinton agar (MHA) and Sabouraud dextrose agar (SDA) were used to test the sensitivity of the bacteria and the yeast. The MHA and SDA, sterilized and cooled to 45-50° C, were distributed into sterile Petri dishes[12].The bacteria were first incubated at 37°C for 24 h in nutrient agar, MHA and when melted poured into plastic Petri dishes. The yeast was incubated in Sabouraud dextrose agar at 25°C for 48h. The cultures of the bacteria and yeast

were injected into the Petri dishes (9cm) in the amount of 0.1 mL.The compounds were dissolved at a concentration of 10mg/mL in DMSO.

Controls were performed for each bacteria strain and the yeast, where 0.1mL of the pure solvent was inoculated into the well. The mean value obtained for three individual replicates was used to calculate the zone of growth inhibition of each sample.

Sulfamethoxazole (SMX) and Ampicillin were used as a standard reference in the case of bacteria while ketoconazole, Amphotericine B were used as a standard antifungal reference [13]. The results were read by measuring the diameters of the inhibition zones in millimeters.

Antioxidant study

Antioxidant properties of ternary complexes of cobalt(II) were determined spectrophotometrically in one test.

Radical scavenging DPPH has a violet coloring, the intensity of which decreases in the presence of antioxidant proportionally to the ability to "sweep of "free radicals by the tested compound.

DPPH is characterized as a stable free radical due to the delocalization of the spare electron over the molecule. The delocalization gives rise to a deep violet color characterized by an absorption band at 517 nm.

The sample of complexes (0.1mL) were mixed with 3.9mL of methanolic solution containing DPPH radicals (6.34 10^{-5}mol/ L).The mixture was shaken vigorously and left in the dark until stable absorption value was obtained. The reduction of the DPPH radical was measured by monitoring continuously the decrease of absorption at 517nm. DPPH scavenging effect was calculated as percentage of DPPH discoloration using the equation:

$$\% \text{ scavenging effect} = [(A_{DPPH} - A_S)]/ A_{DPPH}] \times 100$$

Where A_S is the absorbance of the solution when the sample has been added and ADPPH is the absorbance of the DPPH solution [14]. All the tests were replicated thrice.

Synthesis of the Complexes

The mixed-ligand cobalt(II) complexes were prepared from cobalt(II) chloride, HINAP and various chiral amino acids such as Histidine, Phenylalanine and Tryptophan as described below.

To a blue-colored ethanolic (50 mL) solution of cobalt(II) chloride hexahydrated (23.7mg, 5mmol) was added an ethanolic (50 mL) solution of HINAP (745 mg, 5 mmol).

The mixture was stirred and kept in a water bath at 50°C for thirty minutes, during which time the mixture turned green. To this was added 1: 1 aqueous ethanolic (50ml) solution of the amino acid (5 mmol) the mixture (1: 1: 1 molar proportion) was refluxed for four hours, when an orange colored solid precipitated.

The mixture was cooled and the solid was filtered, washed with ice-cold water followed by ice-cold ethanol. The complexes thus prepared were dried under vacuum.

Results and Discussion

Characterization of Metal Complexes

Analytical data

The synthesis of the mixed ligand Cobalt(II) complexes by the reaction of Co(II) and amino acids (L-isomer) in 1 : 1 : 1 molar proportion can be represented as follows :

$$Co(II) + HINAP + L\text{-Amino acid} \dashrightarrow [Co(INAP)(Aa)]$$

Where INAP and Aa represent deprotonated isonitrosoacetopenone and amino acids, respectively. All the complexes are orange to green dark in colour and are in general, non-hygroscopic solids, insoluble in water but soluble in common organic solvents such as ethanol, methanol, DMSO, and DMF. The conductivity measurements of the complexes at 25°C in 10^{-3}M ethanol solution indicate that they are non-electrolytes. The physical properties and analytical data of the complexes are summarized in Table 1. The Cobalt complexes were obtained as powders and attempts to obtain single crystal suitable for X-ray determination were unsuccessful.

Table 1. Characteristic and analytical data of cobalt complexes

Compound	Colour	Yield (%)	Mp (°C)	Elemental analysis Found (Calc.)(%) Co	C	H	N	Conductance in ethanol $\Omega^{-1}cm^2mol^{-1}$
$[Co(INAP)(Hist)(H_2O)_2]$	Orange	62	180	15.19 (14.84)	42.45 (42.32)	3.68 (4.53)	14.84 (14.1)	7.86
$[Co(INAP)(Phen)(H_2O)_2]$	Orange	65	173	14.25 (14.47)	50.78 (50.13)	4.52 (4.91)	7.55 (6.88)	1.09
$[Co(INAP)(Tryp)(H_2O)_2]$	Orange	60	210	13.85 (13.20)	51.42 (51.13)	4.44 (4.70)	9.89 (9.42)	2.87

Infrared Spectra

The most important assignments IR bands are shown in Table 2. The ligands coordination sites which are involved in bonding with the metal ions have been determined by careful comparison of the infrared absorption spectra of the complexes with those of the parent ligands.

Compound	ν(O-H)	$\nu(NH_3^+)_{as}$	V(C=O) INAP	$\nu(COO^-)_{as}$	$\nu(COO^-)_s$	ν(C=N)	ν(N-O)	ν(M-N)	ν(M-0)
HINAP	3291s	--	1667s	--	--	1593m	1238s	--	--
Histidine	3439m	3015m	--	1587s	1414m	--	--	--	--
Phenylalanine	3465s	3067m	--	1560s	1409m	--	--	--	--
Tryptophan	3404s	3039m	--	1591s	1414m	--	--	--	--
$Co(INAP)(Hist)(H_2O)_2$	3422s	2924s	1619s	1600m	1450w	1502m	1227s	551	467
$Co(INAO)(Phen)(H_2O)_2$	3465s	2926s	1635s	1597m	1452w	1502s	1225s	565w	472
$Co(INAO)(Tryp)(H_2O)_2$	3413s	2918s	1638s	1619s	1456w	1502m	1224s	580w	483

Table 2. Relevant IR data (cm^{-1}) of the ligands and complexes

S= strong m= medium w= weak

The IR spectra of aminoacids exhibited significant features in $\nu(NH_3^+)$ ν(COO-) regions. The broad band in the range 3015-3067 cm^{-1} is assigned to stretching vibration $\nu(NH_3^+)$. The band in the range 1622-1666 cm^{-1} is due to the $\delta(NH_3^+)$. The $\nu(NH_3^+)$ stretching vibration is shifted to higher wavenumbers in the spectra of the complexes. The $\delta(NH_3^+)$ band, which is a characteristic for the zwitter ion, disappeared in the spectra of the complexes. This fact indicates that the NH_2 group must be involved in coordination. A broad band in the IR spectra of the oxime observed at 3290 cm^{-1} is attributed to ν(OH) . This band is absent in the spectra of cobalt complexes, suggesting the deprotonation of the HINAP. A strong absorption band at 1677 cm^{-1} may be assigned to the coupled vibration of C=O stretching and aromatic C—C stretching [15]. This frequency appears in the region 1619-1638 cm^{-1} in the complexes of cobalt(II).

Such an appreciable red shift(39-58 cm^{-1}) indicates the formation of a bond between the metal ion and the C=O group [16]. The medium band around 1593 cm^{-1}in the oxime is a coupled vibration of C=N stretching mode. This band shift to lower frequency and appears at 1502 cm^{-1} for all complexes. This indicates that the oxime acts as a bidentate anion and that the coordination is both through the nitrogen donor atom of the azomethine group and the oxygen of the carbonyl group. Medium intensity bands are observed in the range 1227-1224 cm^{-1} attributed to the N→O stretching vibration[16,17]. The non-ligand absorption bands in the regions 483-467cm^{-1} -and 620-618cm^{-1} are tentatively assigned to ν(M—N) and ν(M—O) vibrations, respectively. It may be noted that these vibrational bands are absent in the infrared spectra of HINAP as well as the aminoacids.

The presence of a broad band at 3450 cm^{-1} and another one of weak intensity in the region 895-772 cm^{-1} are ascribed to the stretching and deformation vibration of OH. This confirms the presence of coordination water.

Electronic spectra and magnetic studies

The electronic spectra of the cobalt(II) complexes recorded in ethanol solution display three characteristic bands of high intensity absorption in the near UV region 25974-35715 cm^{-1} which are due to the intraligand transitions ($n\rightarrow \pi^*$ and $\pi\rightarrow \pi^*$)[18].

The intraligand band in the Cobalt chelate at 25974 cm^{-1} is unsymmetrical Gaussian analysis of the 25974 cm^{-1} bands indicates that it is constituted of two absorption bands involving the azomethine group C=N and the phenyl ring[19,20].

In the visible region, the electronic spectra of cobalt(II) mixed complexes display one shoulder in the range 18500-19230cm^{-1} which can be assigned along with appropriate electronic transition transition ($^2E_g\rightarrow{}^2T_{1g}$) by the use of Tanabe-Sugano diagrams[21] assuming octahedral stereochemistry for Co(II) low-spin complexes.

The magnetic moments of these complexes are of particular interest. Effective moments were calculated from room temperature magnetic susceptibilities and using diamagnetic corrections from the literature [22,23]. These values are within the range for low-spin cobalt(II) complexes in general 1.5-2.02BM, and within the ranges reported for octahedral substituted six-coordinate Co(II) with two dianionic ligands and two water molecules[23].

The low moments in these complexes may reveal an antiferromagnetism interaction in the complexes in the solid state. Indeed, the variation of the applied field, which increases readily and the decrease of magnetic moments, reveal an important antiferromagnetism. Both of the room temperature magnetic moments, the electronic spectral data and the assignments are given in Table 3.

Table 3. Magnetic and Electronic Spectral Data and Ligand Field Parameters of Cobalt(II) Complexes

Compound	μ_{eff}	Electronic transition [a] $(\varepsilon)^b$	
$[Co(INAP)(Hist)(H_2O)_{2]}]$	1.49	18500 (70)	$^2Eg \rightarrow {}^2T_1g$, ^2T_2g
$[Co(INAP)(Phen)(H_2O)_2]$	1.54	19047 (50)	$^2Eg \rightarrow {}^2T_1g$, ^2T_2g
$[Co(INAP)(Tryp)(H_2O)_2]$	2.02	19230 (160)	$^2Eg \rightarrow {}^2T_1g$, ^2T_2g

a: wave number in cm^{-1}

b: absorption molar coefficient in $l.cm^{-1}.mol^{-1}$

^{1}H NMR spectra

The ^{1}H NMR spectra of ligands and the corresponding cobalt(II) complexes were recorded in DMSO d_6 show broad signals due to their paramagnetic nature. The signal attributed to the proton of the =NOH group observed at 9 ppm, disappeared in the NMR spectra of ternary Cobalt(II) complexes. This is due to the participation of the –OH (oxime) with the displacement of a hydrogen atom. The spectra also do not reveal a proton signal due to –COOH group of the amino acids. The hydrogen peaks of the aromatic ring (8H) appeared in the range 7-8 ppm, and are not modified in the spectra of the complexes. These results indicate deprotonation of HINAP as well as replacement of the carboxylique acid proton of the amino acid by the metal ion during complexation.

Complexes structures

On the basis of these results, it appears that the ligands are coordinated in a deprotonated form, through oxygen and nitrogen atoms leading to neutral complexes. The Cobalt complexes are found to be octahedral with two coordinated water molecules probably in *cis* position. The proposed structure is illustrated by the Co-INAP-Hist complex given in Figure 2.

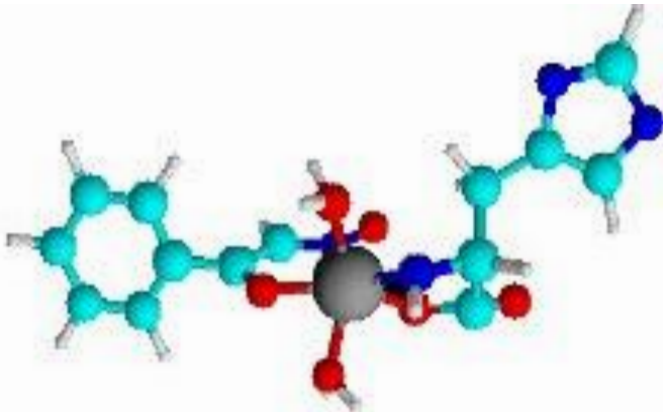

Figure 2. Structural scheme for ternary cobalt complex of Histidine

Cyclic Voltammetry

Voltammetry measurements were therefore carried out in order to obtain a correlation between the electrochemical properties and oxidation level of central metal ion with nitrogen and nitrogen/oxygen mixed donor complexes. Cobalt(II) N/O mixed complexes and the electron density of the metal ion in the complex which, in turn, directly influences their binding ability in DMSO. The electrochemical behavior of the cobalt(II) complexes is due to the Co(II)/Co(I) couple.

Cyclic voltammogram of $CoCl_2$ compound shows one irreversible reduction process at -1.5V. The cyclic voltammograms of the ligands are all characterized by the same anodic wave at 0.92V, which can be attributed to an irreversible oxidation process.(Figure 3)

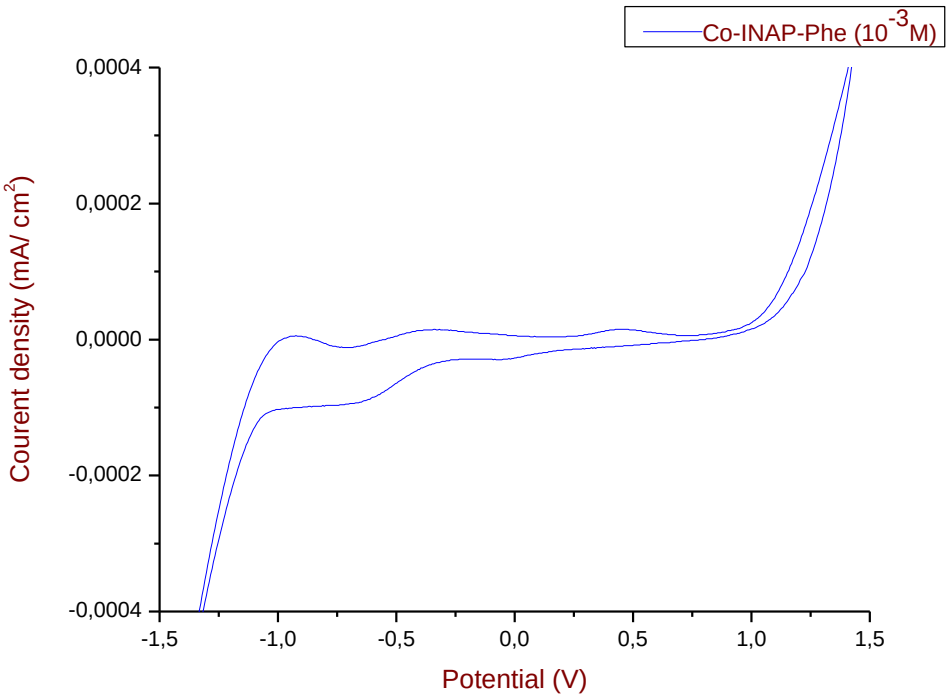

Figure 3 . Cyclic voltammogram of Co-INAP-Phen complex in DMSO (0.1 M TBAP); Scan rate= 10mV.

The cathodic region of histidine and phenylalanine and tryptophan shows one irreversible reduction at cathodic potential peaks values: Epc =- 0.466,- 0.542 ,0.549V respectively.
On the other hand, the isonitrosoacetophenone (HINAP) exhibit reduction signals at the cathodic potential peak Epc_1 = -0.524 V and Epc_2 = -0.756 V, ascribed to the insaturation of the ligand. (Table 4)

Table 4. Electrochemical Data for the reduction of the Ligands, $CoCl_2$ and the Co(II) complexes[a] in 0.1 M TBAP in DMSO

Compound	Epc(V)	Epa(V)	ΔE(mV)
HINAP	-0.524 -0.756	-- -0.554 - 0.554	-- 202
Histidine	-0.466	--	--
Phenylalanine	-0.542	--	--
Tryptophan	-0.549	--	--
$CoCl_2$	-1.500	-0.100	800
$[Co(INAP)(Hist)(H_2O)_2]$	-0.485	-0.251	270
$[Co(INAP)(Phen)(H_2O)_2]$	-0.634	-0.359	275
$[Co(INAP)(Tryp)(H_2O)_2]$	-0.981	-0.748	233

a: Solute concentration $=10^{-3}$ M, Scan rate = 10mV/s; Epc and Epa are the cathodic and the anodic peak potentials respectively; ΔE = Epa-Epc

The metal centered reduction for all the cobalt complexes is in agreement with an irreversible electron transfer[24]. Further, in the negative potential range and on the cathodic scan, the peaks observed for the complexes are of medium intensity.

It was noted in this study that the reduction potentials for the couple Co(II)/Co(I) are sensitive to electronic effect of the R group of the amino acid. These potentials shift towards more negative values on going from histidine to tryptophan. Thus, the electron density on the cobalt increases and this increases the difficulty of reducing the metal center and stabilize the high oxidation state for the metal ion[25,26]. This is probably due to the high stability of the ternary complexes of Cobalt (II), where the power of ligand field increases on going from histidine to phenylalanine to tryptophan.

Antibacterial activity

The ternary cobalt (II) complexes were screened in vitro for their microbial activity against pathogenic bacterial and fungal species using disc diffusion method. The results of the bacterial screening of the synthesized compounds are recorded in Table 5. As expected, no growth inhibition was observed for DMSO and Cobalt chloride salt.

The primary ligand , HINAP and the aminoacids have moderate activity with *Staphylococcus aureus, Proteus mirabilis* and *Echerichia coli* and are less active in comparison with *Streptococcus pyogenes*, *Pseudomonas aeruginosa.* They have no activity against *Bacillus subtilis* and *Candida albicans*.

The complexes of tryptophan and phenylalanine were found to exhibit considerable activity against Gram positive and Gram negative.

Table 5. Results of antibacterial activity screening of ligands and cobalt complexes[a]

Compound	Diameter of zone of inhibition (mm)						
	S. aureus	*Strep,py.*	*B.subtillis*	*E.coli*	*P.aeruginosa*	*P.mirabilis*	*C.albicans*
HINAP	14	13	11	12	---	13	---
Histidine	12	---	---	14	---	11	---
Phenylalanine	16	---	---	20	11	13	---
Tryptophan	19	---	---	18	12	14	---
Co-INAP-Hist	13	25	15	14	0	14	20
Co-INAP-Phen	14	22	20	16	11	14	24
Co-INAP-Tryp	15	30	19	18	0	18	28
Sulfamethoxazol	28	Nt	29	36	0	Nt	---
Ampicillin	11	12	Nt	08	Nt	0	---
Ketoconazol	---	---	---	---	---	---	38
Amphotericin B	---	---	---	---	---	---	29

a=Where INAP represent isonitrosoacetophenone and Hist, Phen and Tryp represent deprotonated histidine, phenylalanine and tryptophan, respectively.

Nt= Not tested

Therefore, of these Gram negative bacteria, *Pseudomonas aeruginosa* was the most resistant to the synthesized compounds. The cobalt mixed complexes did not produce any inhibitory zone against *Pseudomonas aeruginosa* .

In our biological experiments, we have observed high antimicrobial activity against Gram positive than Gram negative bacteria. The cobalt complexes are also very active against fungus *Candida albicans.*

The antibacterial screening data show that the complexes exhibit antimicrobial properties and we note that the metal chelates have more inhibitory effects than the free ligands.

This would suggest that chelation could facilitate the ability of the complex to cross a cell membrane and can be explained on the basis of Tweedy's chelation theory[27].

Chelation considerably reduces the polarity of the metal ion because of the positive charge of the metal partially shared with the donor atoms present in the ligand, and there may be π-electron delocalization over the whole chelating space[28,29].

This increases the lipohilic character of the metal chelates and favors its permeation through the lipoid layer of the bacterial membranes. We conclude that complexation increases the antimicrobial activity.

Antioxidant Activity

Oxidative stress is closely associated to free radicals. It is involved in many chronic diseases such as cancer, inflammation and neurodegenerative disorders diseases. Antioxidants may act as free radicals scavengers to protect cells from biological damages.

Free radical scavenging capacities of the complexes was determined according to the previous reported method using the stable 2,2-diphenyl-1-picrylhydrazyl radical (DPPH)[1].

The antioxidant activity of ternary cobalt complexes was measured in terms of their hydrogen donating or radical scavenging ability by UV–visible spectrophotometer using the stable DPPH.

When the reaction between antioxidant molecules and DPPH• radical, which results in the scavenging of the radical by hydrogen donation, the antioxidants cause to a decrease of the absorbance of DPPH• radical. This is visually noticeable as the color changes from purple to yellow.

DPPH• is a stable free radical and accepts an electron or hydrogen radical to become a stable diamagnetic molecule.

All the Co(II) complexes are more active than the free ligands against DPPH with complex of tryptophan being the most active one.

It can be explaining on the basis of the indole, the aromatic heterocycle that terminates the tryptophan side chain, which is both electron rich and posses an H-bond donor [30].

The effect of antioxidants on DPPH• radical scavenging was thought to be due to their hydrogen donating ability. DPPH• is a stable free radical and accepts an electron or hydrogen radical to become a stable diamagnetic molecule [31]. (Table 6)

Table 6. Results of antioxidant activity of cobalt(II), ligands and complexes

Compounds	Eq. Trolox	AA%
HINAP	129.62	16
Histidine	130.6	19
Phénylalanine	132.65	22.4
Tryptophane	136.7	23
$CoCl_2.6H_2O$	3	3.6
Co-INAP-His	222	30.68
Co-INAP-Phe	275	33
Co-INAP-Tryp	315	35.5
Chlorogenic acid	51	17

Conclusion

Three new mixed complexes of aminoacids and isonitrosoacetophenone of cobalt(II) have been synthesized. The spectroscopic studies we have described have demonstrated that the ligands are bonded to the metal ion in a bidentate manner through two N and two O donor sites. The complexes are proposed to be pseudo octahedral.

The ternary complexes isolated are monomeric and non-electrolytes. The electronic absorption spectra show that the ligand field is decreasing from Co-INAP-Tryp complex to the Co-INAP-Hist complex. This can be explained by the presence of the indole group which is both electron rich aromatic compound and possesses and H-bond donor. The electron donor effect of indole group is greater than that of imidazole one of histidine.

The potential redox shift towards more negative values on going from histidine to tryptophan. The biological studies reveal that the ternary cobalt complexes may be a good candidate for employment as antimicrobial and antioxidant agent, especially the Co-INAP-Tryp complex which is the most active one. Indeed, these complexes present a high antioxidant activity with the DPPH assay.

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