ISSN : 0974 - 746X Volume 8 Issue 2

Inorganic CHEMISTRY

An Indian Journal

Full Paper

ICAIJ, 8(2), 2013 [41-49]

Synthesis, characterization, redox and biological screening studies of amino acids ternary complexes of nickel(II) with isonitrosoacetophenone

N.Tidjani-Rahmouni, S.Djebbar, O.Benali-Baitich*

Laboratory, Faculty of Chemistry, University of Science and Technology Houari Boumediene, BP 32, El Alia, Bab Ezzouar, Algiers, (ALGERIA)

E-mail : benali.baitich@gmail.com

ABSTRACT

Mixed ligand complexes having molecular formulae Ni(INAP)L $(H_2O)_2$ where INAP= isonitrosoacetophenone and L= amino acid such as L-Histidine, L-Phenylalanine and L-Tryptophan have been synthesized. Characterization of these complexes was carried out by elemental analyses, UV-Vis, IR and ^1H NMR spectroscopy. Molar conductance of the complexes in DMSO solution at 10^{-3} M concentration indicate their non-electrolyte nature. The IR spectra support the binding of the ligands with two N and two O donor sites to the metal (II) ion giving an arrangement of N_2O_2 donor groups. The magnetic and spectral data indicate an octahedral geometry for all the complexes. Electrochemical studies of the complexes have been investigated by cyclic voltammetry which shows that the chelated structure and electron donating effects of the ligands substituents are among the factors influencing the redox potentials of the complexes. The antioxidant activity which is related to redox properties was evaluated for Nickel complexes by the means DPPH assay. The antimicrobial activity was investigated against Gram-positive: *streptococcus pyogenes, staphylococcus aureus* and *bacillus subtilis* and Gram-negative: *Proteus mirabilis, Escherichia coli, Pseudomonas aeruginosa* and one yeast: *Candida albicans*. The Nickel complexes were found to be more active against Gram-positive than Gram-negative bacteria.

KEYWORDS

Ternary complexes;
Isonitrosoacetophenone;
Amino acids;
Cyclic voltammetry;
Biological study.

INTRODUCTION

Nickel is usually found in biological compounds as Nickel(II), since many enzymes are complexes of Nickel(II)[1-5]. The role of Nickel in bioinorganic chemistry has been developed only since 1975, when the urease was shown to be a nickel-containing enzyme[6]. The study of ternary complexes involving an oxime as the primary ligand, various amino acids as the 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 biochemical reactions[7].

While the binary complexes of HINAP (Figure 1) with transition metal ions are known and their use in the catalysts has been reported, its uses in the formation of ternary transition metal complexes has not been reported so far.

L-Tryptophan is an important and frequently used material in the chemicals synthesis of a range of phar-

Full Paper

maceuticals. He is a precursor of the vital neurotransmitter, serotonin, tryptophan levels in the body regulate moods and sleep[8-9].

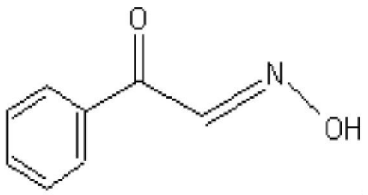


Figure 1 : Structure of isonitrosoacetophenone (HINAP).

L-Phenylalanine is essential to many functions and is one of the few amino acids that can directly affect brain chemistry by crossing the blood-brain barrier[10].

L-Histidine is an essential amino acid and has a positively charged imidazole functional group. It is a precursor for Histamine and carnosine biosynthesis[11,12].

The L-amino acids are known to bind to metal ions, via dissociation of the acidic proton, as bidentate N,O-donor. Isonitrosoacetophenone is expected to behave as potential ambidentate ligands. It forms stable chelates with transition ions showing a variety of structural features. The isonitroso moiety (>C=NOH), can coordinate either through nitrogen or oxygen atom producing chelate linkage isomers. The present paper describes the synthesis and the characterization of the mixed ligand Ni(II) complexes of isonitrosoacetophenone and these three amino acids. Ni(II), among other transition metal ions, are active centres of many enzymes.

Redox potentials in metal complexes and metalloproteins are often used as a useful physical measure to obtain information about the environment of the central metal ion. For this electrochemical study was carried out for these complexes.

The aim of this work is to study the chelating behavior of the oxime and the amino acids ligands towards Nickel ion. 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[13,14].

Antioxidant compounds play an important role as a health-protecting factor. Scientific evidence suggests that antioxidants reduce the risk for chronic diseases including cancer and heart disease.

The aims of our study is to examine in vitro, the capacity of the ternary complexes of oxime and amino acids to scavenge the form of RS such as 1,1-diphenyl-2-picrylhydrazyl (DPPH•).

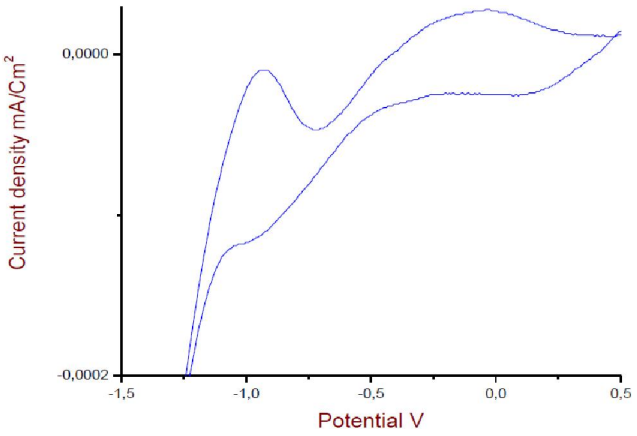


Figure 2 : Cyclic voltammogram of the Ni-INAP-Phen complex in DMSO (0.1 MTBAP); scan rate = 10mV.

EXPERIMENTAL

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 laboratoire de chimie, CNRS, Toulouse (France).

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

Conductivity measurements were carried out using 10-3 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,1100-200cm-1.

Magnetic measurements were performed at room temperature (300K) on a SQUID magnetometer after correction of diamagnetisme of the nacelle. The effective magnetic moment is calculated after correction of diamagnetic contribution of the complexes using Pascal's

constants.

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. The ionic strength is 1.

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) spectrophotometer (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[15]. 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[16]. The results were read by measuring the diameters of the inhibition zones in millimeters.

Antioxidant studies

Antioxidant properties of ternary complexes of Nickel(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 10-5mol/ 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[17]. All the tests were replicated thrice.

Synthesis of the complexes

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

To a green-colored ethanolic (50 mL) solution of Nickel(II) chloride hexahydrated (1.18g, 5mmol) was added an ethanolic (50mL) solution of HINAP (0.745 g,5mmol).

Full Paper

The mixture was stirred and kept in a water bath at 50°C for thirty minutes, during which time the mixture turned green dark. To this was added 1: 1 aqueous ethanolic (50ml) solution of the amino acid (5mmol) 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 Nickel(II) complexes by the reaction of Ni(II) and amino acids (L-isomer) in 1 : 1 : 1 molar proportion can be represented as follows :

Ni(II) + HINAP+ L-Amino acid ⟶ [Ni(INAP)(Aa)]

Where INAP and Aa represent deprotonated isonitrosoacetopenone and amino acids, respectively.

All the complexes are orange to green dark in color 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 data of the complexes 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 Nickel complexes were obtained as powders and attempts to obtain single crystal suitable for X-ray determination were unsuccessful.

TABLE 1 : Characterization and analytical data of nickel complexes

Compound	Colour	Yield (%)	Mp (°C)	Elemental analysis Found (Calc.)(%)				Molar conductance $\Omega^{-1}cm^2mol^{-1}$
				Ni	C	H	N	
[Ni(INAP)(Hist)(H_2O)$_2$]	Orange	65	235	15.09 (14.78)	42.45 (42.31)	3.68 (4.50)	14.74 (14.1)	1.08
[Ni(INAP)(Phen)(H_2O)$_2$]	Orange	55	270	14.25 (14.43)	50.88 (50.16)	3.92 (3.93)	7.55 (6.88)	0.92
[Ni(INAP)(Tryp)(H_2O)$_2$]	Green	50	230	14.15 (13.20)	52.02 (51.15)	4.44 (4.71)	9.81 (9.42)	3.08

Infrared spectra

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. The IR spectra of amino acids exhibited significant features in ν (NH^{3+}) ν (COO^-) regions. The broad band in the range 3015-3067 cm^{-1} is assigned to stretching vibration ν (NH^{3+}). The band in the range 1622-1666 cm^{-1} is due to the δ (NH^{3+}).

The ν (NH^{3+}) stretching vibration is shifted towards higher frequencies in the spectra of the complexes. The δ (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.

The bands at the wave number 1560-1591 cm^{-1} and 1409-1414 cm^{-1} regions, in the free amino acid (Phen, Tryp and Hist), are assigned to the asymmetric and symmetric stretching vibrations of the carboxylate group, respectively. The shift of these two bands to higher or lower frequencies suggest the participation of –COOH group in complex formation after deprotonation[18].

The broad band at 3290 cm^{-1} observed in the spectra of the oxime and attributed to ν (OH) disappeared completely on complex formation[19].

A strong absorption band at 1677 cm^{-1} may be assigned to the coupled vibration of C=O stretching and aromatic C—C stretching[18]. This frequency appears in the region 1630-1663 cm^{-1} in the complexes of Nickel(II).

Such an appreciable red shift (14-47 cm^{-1}) indicates the formation of and between the metal ion and the C=O group[19].

The medium band around 1593 cm^{-1} in the oxime is coupled vibration of C=N stretching mode. This band shifts to lower frequency and appears in the region 1546-1568 cm^{-1}, for Ni(II) 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 at 1197, 1177 and 1144 cm^{-1} in Ni-INAP-Hist, Ni-INAP-Tryp and Ni-INAP-phen respectively. They are attributed to the N'!O stretching vibration[20,21].

New bands of weak intensity observed in the region 618-609 cm^{-1} and 534-523 cm^{-1} are assigned to M—N and M—O vibrations, respectively.

The presence of a broad band at 3432 cm^{-1} and another one of weak intensity in the region 866-864 cm^{-1} are ascribed to the stretching and deformation vibration of OH. This confirms the presence of coordination water.

The most important infrared spectra bands and their assignments are reported in TABLE 2.

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

Compound	ν (O-H)	$\nu(NH_3^+)_{as}$	ν(C=O) INAP	$\nu(COO^-)_{as}$	$\nu(COO^-)_s$	ν(C=N)	ν(N-O)	ν(M-N)	ν(M-O)
HINAP	3291s	--	1677s	--	--	1593m	1238s	--	--
Histidine	3439m	3015m	--	1587s	1414m	--	--	--	--
Phenylalanine	3465s	3067m	--	1560s	1409m	--	--	--	--
Tryptophan	3404s	3039m	--	1591s	1414m	--	--	--	--
$[Ni(INAP)(Hist)(H_2O)_2]$	3427s	3002m	1630s	1547s	1420w	1546m	1197m	615w	534w
$[Ni(INAP)(Phen)(H_2O)_2]$	3447s	3059m	1634s	1594s	1395w	1563s	1144s	618w	584w
$[Ni(INAP)(Tryp)(H_2O)_2]$	3417s	3058s	1663s	1597m	1381w	1568m	1177m	609w	523w

s= strong; m= medium; w= weak

Electronic spectra and magnetic studies

The electronic spectra of the Nickel(II) complexes recorded in ethanol solution display three characteristic bands of high intensity absorption in the near UV region 29412-37735 cm^{-1} which are due to the intraligand transitions ($n \longrightarrow \pi^*$ and $\pi \longrightarrow \pi^*$)[22].

The intraligand band in the Nickel chelate at 29412 cm^{-1} is unsymmetrical Gaussian analysis of the 29412 cm^{-1} bands indicates that it is constituted of two absorption bands involving the azomethine group C=N and the phenyl ring[23,24].

In the visible region, the electronic spectra of the Nickel(II) mixed complexes, exhibit three bands in the range 12000-12200, 16490-16980 and 26906-28200 cm^{-1}which may be assigned to $^3A_{2g} \longrightarrow {}^3T_{2g}$ (F) (ν_1), $^3A_2 \longrightarrow {}^3T_{2g}$ (F)(ν_2) and $^3A_{2g} \longrightarrow {}_3T_{1g}$ (P) (ν_3), respectively. The position of these bands are similar to those reported for Ni(II) complexes with an octahedral geometry[25-26].

The room temperature magnetic moments of these complexes indicates the paramagnetic nature of the Ni(II) ion, the magnetic moments of these complexes have been found in the range 1.94-2.43BM. The sub normality in magnetic moments has been ascribed to an antiferromagnetism interaction.

The ligand field parameters (10Dq, B, β) are calculated for these complexes (TABLE 3). The complexes show a lower value of B than that of the free ion value[27]. The value of the Nephelauxitic parameter β is less than unity which suggests the strong covalent nature of metal-ligand bond[28]. This parameter was readily obtained by using the relation:

β = B (Complex) × B (free ion)

The value of the ν_2/ν_1 ratio is in the range expected for an octahedral geometry[29].

The results of TABLE 3 show that tryptophan causes a higher crystal field than phenylalanine and histidine. The order of crystal field is Hist<Phen<Tryp.

TABLE 3 : Magnetic and electronic spectral data and ligand field parameters of nickel(II) complexes

Compound	μ_{eff}	Electronic transitions [a] (ε)[b]	10Dq	B	β
$[Ni(INAP)(Hist)(H_2O)_{2]}]$	2.25	12000(10) 16490(30) 26906(240)	12000	499	0.48
$[Ni(INAP)(Phen)(H_2O)_2]$	2.43	12100 (18) 16580(11) 27777(150)	12100	531	0.51
$[Ni(INAP)(Tryp)(H_2O)_2]$	1.94	12200(10) 16980(25) 28200(175)	12200	572	0.55

[a]wave number in cm^{-1}; [b]absorption molar coefficient in l.cm-1.mol-1

Full Paper

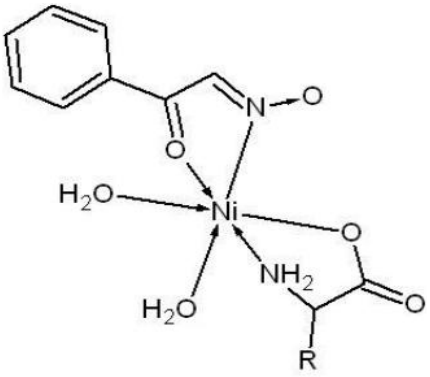
^{1}HNMR

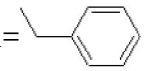
The ^{1}H NMR spectra of ligands and the corresponding Nickel(II) complexes were recorded in DMSO d_6 show broad signals due to their paramagnetic nature.

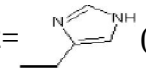
The signal attributed to the proton of the =NOH group observed at 9 ppm, disappeared in the NMR spectra of ternary Nickel(II) complexes. This is due to the participation of the –OH (oxime) with the displacement of a hydrogen atom. The spectra also do not reveal a proton signal due to –COOH group of the 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. This 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 Nickel complexes are found to be octahedral with two coordinated water molecules probably in cis position. The proposed structures are given in Figure. 3.



R1=  (Phenylalanine)

R2=  (Histidine)

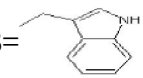
R3=  (Tryptophan)

Figure 3 : Proposed structure of mixed nickel(II) complexes

Cyclic voltammetry

The electrochemical behavior of the present Nickel(II) complexes are illustrated by cyclic voltammograms which were obtained in DMSO solution from +1.5 to -1.5 (vs SCE). Coulometric measurements revealed that in each of the processes involves one electron transfer.

The cyclic voltammogram of $NiCl_2$ exhibits the beginning of a cathodic wave at the limit of the cathodic potential used and its associated anodic peak was observed at Epa =-0.17V.

The cyclic voltammogram of each complex exhibits one irreversible reduction process. The electrochemical results on reduction of the complexes at a sweep rate of 0.1 V.s-1 are given in TABLE 4.

TABLE 4 : Electrochemical data for the reduction of the ligands, $NiCl_2$ and the Ni(II) complexes[a] in DMSO (0.1 M TBAP)

Compound	Epc(V)	Epa(V)	ΔE(mV)
HINAP	-0.756	- 0.554	202
Histidine	-0.466	0.936	1402
Phenylalanine	-0.542	0.914	1452
Tryptophan	-0.524	0.722	1246
$NiCl_2$	<-1.600	-0.170	--
[Ni(INAP)(Hist)$(H_2O)_2$]	-0.527	-0.344	183
	-0.889	-0.808	81
[Ni(INAP)(Phen)$(H_2O)_2$]	-0.926	-0.09	836
	<-1.250	-0.935	82
[Ni(INAP)(Tryp)$(H_2O)_2$]	-0.538	0.545	1083
	<-1.5	-0.602	618

[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

By comparing the cyclic voltammograms of the complexes to those of ligands and that of $NiCl_2$, $6H_2O$ taken as references, the cathodic process could be assigned to the reduction of Ni(II) to Ni(I).

In all of Nickel(II) complexes, the metal based reduction agrees with an irreversible electron transfer[30].

Further, in the negative potential range and on the cathodic scan the waves observed for the complexes are of medium intensity. Also on the reverse sweep, the anodic waves related with the cathodic peaks are of medium intensity. This indicates that chemical reactions occur after the cathodic reduction and anodic oxidation of the complexes.

It was observed in this study that reduction potentials of the Ni(II/I) couple are sensitive to the electronic effect of the R group of the amino acid. These potentials shift cathodically from histidine to tryptophan.

As the substituent R in the amino acid is varied from histidine to tryptophan, the electron density on the metal ion increases.

The addition of the secondary ligand increases the difficulty to reduce the metal center and stabilize high oxidation state for the metal ion[31,32]. This is probably due to the high stability of the ternary complexes of Nickel(II), where the power of ligand field increases on going from histidine to phenylalanine to tryptophan.

The separation between the anodic and the cathodic peak potentials, ΔEp is large, ranging from 183mV to 1083mV for the Ni(II)/Ni(I) redox couple. This indicates an irreversible reduction processes[33].

Antibacterial activity

The results of the bacterial screening of the synthesized compounds are recorded in TABLE 5. As expected, no growth inhibition was observed for DMSO

TABLE 5 : Results of antibacterial activity screening of ligands and nickel 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	---
Ni-INAP-Hist	11	12	---	10	13	---	---
Ni-INAP-Phen	11	14	11	10	17	---	---
Ni-INAP-Tryp	15	25	---	11	18	16	---
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

and metal salts.

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

The best activity is observed with the mixed complexes of tryptophan and phenylalanine against *Streptococcus pyogenes*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*.

The nickel complex of histidine was less sensitive for all the tested bacterial strains. The [Ni(INAP)(tryp)(H_2O)$_2$], displayed the highest inhibitory effect against the four bacteria (Streptococcus, Pseudomonas aeruginosa, Proteus mirabilis and Staphylococcus aureus. It was less active against, *Bacillus subtilis*, *Escherichia coli* and the yeast *Candida albicans.*

We conclude that Nickel complexes have no antifungal activity.

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

The increased activity of the metal chelates can be explained on the basis of chelation theory[34].

Chelation considerably reduces the polarity of the metal ion because of the positive charge of the metal is partially shared with the donor atoms present in the ligand, and there may be π-electron delocalization over the whole chelating space[35,36].

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

Antioxidant activity

The reaction of DPPH with numerous antioxidants has been published before. Therefore, in our study we

have tested the antioxidant power of ligands, metal salts and nickel mixed complexes with the DPPH method described before.

The model of the scavenging of the stable DPPH radical is extensively used to evaluate antioxidant activity in less time than other methods[37-39].

The reducing activity of the tested compounds is lower than the one of the ligands (TABLE 6).

TABLE 6 : Results of antioxidant activity of nickel(II), ligands and complexes

Compounds	Eq. Trolox	AA%
HINAP	129.62	16
Histidine	130.6	19
Phenylalanine	132.65	22.4
Tryptophan	136.7	23
$NiCl_2.6H_2O$	2.02	3.4
Ni-INAP-His	50.63	18
Ni-INAP-Phe	111.39	20.56
Ni-INAP-Tryp	121.52	22.58
Chlorogenic acid	51	17

Where AA% = % scavenging effect

The results are compared with chlorogenic acid, a powerful antioxidant which is founded in many vegetables like carrot, potatoes and particularly bean of coffee.

By examining the trend of AA% values obtained, it may be seen that the antioxidant power of Ni(II) complexes increases in the order of the amino acids, from histidine to tryptophan.

This order satisfactorily correlates with the cathodic potentials which shift towards more negative values on going from histidine to tryptophan.

Ni(II) complexes with tryptophan have the higher antioxidant power. It can be explain on the basis of the indole, the aromatic heterocycle that terminates the tryptophan sidechain, which is both electron rich and posses an H-bond donor[40].

The reference standard and the antioxidant activity are expressed in Trolox equivalent.

The antioxidant power of chlorogenic acid is equal to 51 eq. Trolox. We can consider that the sample has an antioxidant activity if the antioxidant powerful is higher than 50 eq. Trolox. The results are summarized in TABLE 6.

ACKNOWLEDGEMENT

The authors are thankful to the doctor Christelle HUREAU (CNRS, Laboratory of Coordination Chemistry, Toulouse, France) for the microanalysis and the magnetic measurements. We gratefully acknowledge NASSI Ouassila (Microbiological Laboratory of University of El Khemis, Algeria) for assistance with biological activities.

REFERENCES

[1] J.R.Lancaster Jr; The bioinorganic chemistry of Nickel, VCH, Weinheim, **(1988)**.
[2] J.Costamagna, J.Vargas, R.Latorre; Coord.Chem. Rev., **67**, 119 **(1992)**.
[3] H.Seigel; Metal ions in biological systems, New York **(1973)**.
[4] G.L.Bichorn; Inorganic Biochemistry, Elsevier, Amsterdam, **(1973)**.
[5] G.Wilkinson; Comprehensive Coordination Chemistry, Pergamon Press Oxford, 2, 751, 4, 634, 5,687, 6,166, 494, 638 **(1987)**.
[6] N.E.Dixon, T.C.Gazzolo, R.L.Blakely, B.Zermer; J.Am.Chem.Soc., **97**, 4131 **(1975)**.
[7] T.Nowak, A.S.Mildvan, G.L.Kenyon; Biochemistry, **(1973)**.
[8] X.Zhang, H.Yun, M.Ding; J.Chromatogr.B, **877**, 1678 **(2009)**.
[9] J.D Schaechte, R.J.Wurtman; Brain Res., **532**, 203 **(1990)**.
[10] Özlen Altun, Selin Bilcen; Spectrochim.Acta Part A, **75**, 789 **(2010)**.
[11] Sergio R.de Antrade leite, Marco A.Couto dos Santos, Célia R.Carubelli, Ana M.Galindo Massabni; Spectrochim.Acta Part A, **55**, 1185 **(1999)**.
[12] J.A.Cowan; Inorg.Biochem., An Introduction, VCH, New York, **(1993)**.
[13] Renata Francik, Grzegorz Kazek, Marek Cegla, Marek Stepniewski; Acta Poloniae Pharmaceutica-drug Research, **68**, 185 **(2011)**.
[14] K.Marxen, K.H.Vanselow, S.Lippemeier; Sensors, **7**, 2080 **(2007)**.
[15] D.Mitic, M.Milenkovic, S.Milosavljevic, D.Godevac; Eur.J.Med.Chem., **44**, 1537 **(2008)**.
[16] M.Shebl, Saied M.E.Khalil, Faizah S.Al-Gohani; J.Mol.Struct., **78**, 980 **(2010)**.
[17] Cristina Popovici, I.Saykova, B.Tylkowski; Revue de Génie industriel, **25**, 4 **(2009)**.
[18] M.A.Zayed, F.A.Nour El-dien, Djehad G.Mohamed;

Spectrochim.Acta.Part A, **4**, 216 **(2006)**.
[19] S.Nigam, M.M.Patel, A.Ray; J.Phys.and Chem. Solids, **61**, 1389 **(2000)**.
[20] Ramazan Gup, E.Giziroglu; Spectrochimica Acta Part A, **65**, 719 **(2006)**.
[21] S.Z.Jadhao, R.D Rant, B.D.Saraf; Asian J.Chem., **17**, 1059 **(2005)**.
[22] A.Stanila, A.Marcu, D.Rusu, M.Rusu, L.David; J.Mol.Struct., **834**, 364 **(2007)**.
[23] R.Carballo, A.Castifieiras, W.Hiller, Strahlej; Polyhedron, **12**, 1083 **(1993)**.
[24] B.Bosnich; J.Amer.Chem.Soc., **90**, 627 **(1968)**.
[25] M.S.Surendra Babu, P.G.Krishna, K.H.Reddy; Indian J.Chem., **47A**, 1661 **(2008)**.
[26] P.V.Anantha Lakshni, P.Saritha Reddy; Spectrochim.Acta Part A, **74**, 52 **(2009)**.
[27] S.Chandra, A.K.Sharma; Spectrochim.Acta Part A, **72**, 851 **(2009)**.
[28] A.B.P.Lever; Inorganic Electronic Spectroscopy, Elsevier Amsterdam, **(1984)**.
[29] H.Hamrit, S.Djebbar, O.Benali-Baitich, M.A.Khan, G.Bouet; Synth.React.Inorg.Met.-Org.Chem., **30**, 1835 **(2000)**.
[30] S.Djebbar, O.Benali-Baitich, M.Khan, Bouet; Synth.React.Met-Org.Chem, **27**, 1219 **(1997)**.
[31] N.Tidjani-Rahmouni, S.Djebbar, N.Chenah, O.Benali-Baitich; Synth.React.Met-Org.Chem., **29**, 979 **(1999)**.
[32] E.Pereira, L.Gomes, B.de Castro; Inorg.Chim. Acta, **271**, 83 **(1998)**.
[33] A.Adkhis, S.Djebbar, O.Benali-Baitich, A.Kadri, M.A.Khan, G.Bouet; Synth.React.Met-Org.Chem., **33**, 35 **(2003)**.
[34] S.K.Gupta, O.P.Pandey, B.K.Srivastava; Transition Met.Chem., **23**, 349 **(1998)**.
[35] A.Rohaya., A.Abdul Manaf, A.Dand; Life Sci, **76**, 1953 **(2005)**.
[36] Mehmet Tümer, Duygu Ekinci, Ferhan Tümer; Spectrochim.Acta Part A, **67**, 916 **(2007)**.
[37] S.Birjees Bukhari, Shahabuddin Memon, M.Mahroof-Tahir; Spectrochim.Acta Part A, **71**, 1901 **(2009)**.
[38] A.Colak, Ü.Terzi, Melek Col, S.Alpay; Eur.J.Med. Chem., **45**, 5169 **(2010)**.
[39] P.C.Christidis, Z.D.Georgousis, D.Hadjipovlou-Litina; J.Mol.Struct., **73**, 872 **(2008)**.
[40] G.W.Gokel; International Congress Series, **1**, 1304 **(2007)**.