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***SPECTROSCOPIC INVESTIGATIONS
OF SOME COMPLEXES WITH
BIOLOGICAL AND PHARMACEUTICAL
INTEREST***

PhD thesis summary

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THE CONTENTS OF THE THESIS

Introduction

I. Coordinative compounds of transitional metals

- I.1 The biological role of the transitional metals
- I.2 The geometry of the coordination compounds of the transitional metals
- I.3 The action of the ligand fields on the symmetry of the metallic complexes
- I.4 The molecular orbital theory for high symmetry metallic compounds

II. Structural investigations of metallic complexes by spectroscopical methods

- II.1 Vibrational spectroscopy
- II.2 Ultraviolet and visible spectroscopy (UV- VIS)
- II.3 Electron spin resonance (ESR)

III. Dinuclear clusters incorporated in polyoxotungstates

- III.1 Molecular complexes of heteropolyoxometalate type
- III.2 Investigation of the heteropolyoxometalates' structure by spectroscopic methods
- III.3 Spectroscopic investigation of the dinuclear clusters incorporated in polyoxotungstates

IV. Copper (II) complexes with theophylline ligand containing ethylenediamine derivatives as coligands

- IV.1. The complexes of the theophylline with transitional ions
- IV.2. IR and ESR studies of the copper (II) complexes with theophylline containing ethylenediamine derivatives as ligand

V. Metallic complexes with aminoacids

- V.1 The aminoacids' complexes with biometals
- V.2 Spectroscopic investigations of the Cu(II), Co (II) and Zn (II) complexes having the leucine as ligand
- V.3 Spectroscopic investigations of the Cu(II), Co (II) and Zn (II) complexes having the phenylalanine as ligand
- V.4 Spectroscopic investigations of the Cu(II), Co (II) and Zn (II) complexes having the methionine as ligand

VI. Structural investigation of the ranitidine molecule by vibrational spectroscopy and theoretical methods

- VI.1 Spectroscopical and theoretical investigation methods of the ranitidine molecule
- VI. 2 Theoretical and experimental study of the ranitidine hydrochloride

Conclusions

Bibliography

INTRODUCTION

The scientific research focusing on the synthesis and the characterization of biological compounds of the metallic ions has a special interest due to its applicability in pharmacy, medicine, agronomy and nutrition. The studies made on complexes of the transitional metals having as ligands molecules with biological interest have evidenced an increase of their biological activity in comparison with the pure ligands.

The introduction of the transitional metals into the human organism is indicated in the form of complexes, frequently as chelate complexes. The efficiency and the action of some well-known substances in pharmacy, such as the theophylline and the ranitidine, may be improved by the formation of some complexes with ions of major biological interest, like the Ca, Mg, or the ions of the transitional metals.

The compounds of the transitional metals with different molecules of biological interest are strongly implied in catalytic, functional and structural processes in living organisms. The biological activity of the complexes depend on the local structure around the metallic ions, on the type and strength of the chemical bonds.

The present work, entitled ***SPECTROSCOPIC INVESTIGATIONS OF SOME COMPLEXES WITH BIOLOGICAL AND PHARMACEUTICAL INTEREST*** presents the results of some spectroscopical investigations done on Cu, Co and Zn complexes, having as ligands the leucine, the theophylline or the sandwich-like Keggin structure formed by heteropolyoxotungstates. Finally, the thesis deals with the study of the rantidine molecule using vibrational spectroscopy.

For the optimal characterization of these complexes both *physico-chemical methods* (elemental anaysis, atomic mass absorbtion, differential calorimetric analysis) and *spectroscopic techniques*, such as infrared spectroscopy (FT-IR), ultraviolet and visible (UV-VIS) and electron spin resonance (ESR), were used.

The obtained data provided us with information about the coordination mode of the metallic ion, about the participating atoms at the bonds between the central ion and ligands, about chelating mode and the coordination number of the central ion, about the symmetry of the molecule, the nature of the chromophore and the character of the bonds in the complex. Finally, based on the data, a formula for the structure and the geometry of the molecule is proposed.

The first chapter, entitled **Coordinative compounds of transitional metals** presents some examples of compounds of the transitional metals implied in biochemical processes in live systems, emphasizing the importance of the Cu, Zn and Co ions contained in biomolecules in the functioning of animal and vegetal organisms.

The coordinative compounds of the transitional metals are symmetric structures, influenced by the action of the ligand field (crystal field).

The second chapter, entitled **Structural investigations of metallic complexes by spectroscopical methods**, presents how different spectroscopic methods (FT-IR, FT-Raman, UV-VIS, ESR), completed with chemical analysis, lead to the identification of the molecular structure.

The third chapter, entitled **Dinuclear clusters incorporated in polyoxotungstates**, presents the synthesis and characterization by spectroscopical methods (FT-IR, UV-VIS, ESR) of four new metallic dimer complexes, having as ligand a sandwich-type complex formed by two B-Keggin trilacunar structures: $K_{10}[M_2Bi_2W_{20}O_{70}] \cdot xH_2O$ (M = Mn(II)(1), Co(II)(2), Ni(II)(3), Cu(II)(4)).

The fourth chapter, entitled **Copper (II) complexes with theophylline ligand containing ethylenediamine derivatives as coligands**, presents the case of coordination of the copper ion aside with the deprotonated theophylline molecule and of some coligands derived from ethylenediamine, considered to be N,N donor chelating agents. The IR and ESR studies of the $[Cu(th)_2(dmen)] \cdot 2H_2O$ (1), $[Cu(th)_2(tmeda)(H_2O)]$ (2) and $[Cu(th)_2(pen)(H_2O)] \cdot 5H_2O$ (3) compounds indicate the monodentate coordination of the *theophylline* molecule to the copper ion through the nitrogen atom N(7). The coligands, such as *dmen*, *tmeda*, *dpheda*, act as bidentate ligands, bonding to the central ion through two nitrogen atoms.

Chapter five, entitled **Metallic complexes and aminoacids** presents the investigations on new combinations of some transitional metals of major biological interest (Cu, Co, Zn) with three α -aminoacids: leucine, phenylalanine and histidine.

Having at least two functional groups with donor potential (NH_3 , $COOH$), the aminoacids may show different coordination modes to the metallic centres, forming strong chelates with high thermodynamical stability. The divalent metals, such as Zn(II), Cu(II) and Co(II) may form coordinative compounds, in which the metal links two aminoacid molecules through nitrogen and oxygen, resulting in a ring-like structure of chelate, obtaining this way the $[Cu(L)_2] \cdot H_2O$, $[Co(L)_2] \cdot 2H_2O$ and the $[Zn(L)_2] \cdot H_2O$ complexes.

The last chapter, entitled **Structural investigation of the ranitidine molecule by vibrational spectroscopy and theoretical methods**, presents the methods for the determination of the geometrical, energetical and vibrational characteristics of the ranitidine hydrochloride molecule by DFT (density functional theory) calculations and experiments: FT-IR, Raman, Raman SERS, opening the way to the study of some metallic complexes, having the ranitidine as ligand.

The obtained results are useful to the studies of the metallic complexes' applicability in biochemistry and in the pharmaceutical industry.

Keywords: *microelements, transitional metals, coordinative compounds, metallic compounds, FT-IR spectroscopy, UV-VIS spectroscopy, ESR spectroscopy, Keggin-type polyoxometalate, dinuclear clusters, sandwich-type complex, theophylline, N,N – dimethyl ethylenediamine, meso-1,2 diphenyl-ethylenediamine, N,N,N'N'- tetramethyl-ethylenediamine, leucine, phenylalanine, methionine, ranitidine, Raman-SERS spectroscopy.*

I. COORDINATIVE COMPOUNDS OF THE TRANSITIONAL METALS

I.1 The biological role of the transitional metals

In general, metallic ions act in living organisms included in complexes. The biologically active complexes of the microelements are implied in electron transfer, metal and oxygen transport, cell redox reactions, energy transfer, the fixation of the nitrogen during photosynthesis, the synthesis and the degradation of fundamental biomolecules, blocking and the substitution of some functional groups. Beside the role of catalytic-enzymatic centres, the microelements have an important role in many metabolic processes.

I.2 The geometry of the coordination compounds of the transitional metals

The electronic structure of transitional metals $(n-1)d^{1-10} ns^2$ determines through a variety of oxidation states their disponibility of forming compounds with a large spectrum of ligands, such as complex cationic and anionics combinations, mono- or polynuclear, and chelate complexes. In general the metallic ion is tied to the ligands through donor atoms: nitrogen, oxygen or sulphur. In biological systems the transitional metallic ions usually participate in compounds with the coordination numbers 4, 5 or 6.

The geometry of the bioinorganic combinations, including the coordinative compound, obeys the principles of the hybridization theory for the central metallic ion's atomic orbitals (L. Pauling) and the principle of the repulsion of the electron pairs from the valence band (Gillespie).

I.3 The action of the ligand fields on the symmetry of the metallic complexes

The application of the group theory in molecular physics, in order to determine the energy levels and electronic transitions for some molecules, consists in performing a representation of the group, to which belongs the investigated molecule.

According to the *theory of the ligand field*, the molecular complex is modelled by a central metallic ion surrounded by a three-dimensional ligand arrangement. The *crystalline field* and the *coordination field theories* consider the effect of neighbours as a small perturbation upon the energy levels of the free ion. If on the spherical field of the ion is superimposed a field of different symmetry due to the ligands, the symmetry of the ion reduces. In the electrostatic field of the ligand the split of the 5-fold degenerated $(n-1)d$ level is produced, without the essential contribution of the ligand to the formation of the molecular

orbitals. The five *d* orbitals are considered as basis for the irreducible representation of the point groups corresponding to the system.

Due to the *Jahn-Teller effect* the molecule will be deformed in a way to reduce the symmetry of the crystalline field and to lift the degeneration of the fundamental energy level. This deformation appears through the elongation or compression of the metal-ligand bond.

II. STRUCTURAL INVESTIGATIONS OF METALLIC COMPLEXES BY SPECTROSCOPICAL METHODS

II.1 Vibrational spectroscopy

The spectroscopy in the infrared domain (IR) is based on the absorption phenomenon of the infrared radiation by molecules, resulting in the change of the interatomic bonds' vibrational energies. This is considered to be the most proper method for the identification of the functional groups from the structure of the molecules of organic compounds. For the structural analysis the strict infrared domain (characterized by the wave number between 4000-400 cm^{-1}) is used.

In the IR domain only those vibrations are observed which assume a change in the dipole momentum of the molecule.

The Raman spectroscopy differs significantly from the IR one, because it is based on the inelastic scattering of the incident radiation's photons on the molecule, resulting in the change of the energy, and consequently the wavelength of the photon. The Raman scattering occurs only if the *polarizability* of the molecule changes during its vibration.

The surface enhanced Raman spectroscopy – SERS is based on the electromagnetic amplification of the Raman effect, which assumes the attachment of the molecules to the surface of some metallic nanoparticles (gold, silver, copper) with dimensions between 20 – 300nm. This technique is very sensitive, it can evidence even nanomolar concentrations.

II.2 Visible and ultraviolet spectroscopy (UV- VIS)

The spectroscopy in the ultraviolet and visible domain implies the absorption of the close UV (200-400 nm) or visible (400-800 nm) radiations by the molecules of the substance, resulting in the transition of the electrons (being on bonding orbitals σ , π or on nonbonding orbitals n) from a low energy state (most often the ground state, the most populated at normal temperatures) to an excited state with higher energy. Because electronic transitions occur, the spectra obtained by the absorption of these radiations are called *electronic spectra*. The functional group which participates at the electronic transitions is called *chromophore*.

II.3 Electron spin resonance

Electron spin resonance (ESR) is a branch of magnetic resonance spectroscopy based on the absorption of the electromagnetic radiation in the *microwave domain* by the paramagnetic molecular systems placed in a static homogenous magnetic field.

The phenomenon of the electron spin resonance requires the presence of an angular momentum in the studied probe. The spin angular momentum is due to the unpaired electrons from the p, d or f orbitals of the atoms in gasous phase or of some molecules.

The ESR spectrum contains four types of informations: *intensity*, *line width*, *the value of the giromagnetic factor (g)* and *the multiplet structure* (defined by the coupling constant **A**). These parameters provide informations about the concentration of the complex, dynamic processes, spin-spin interactions, the energies of the spin states and about the interactions with the neighboring nuclei.

III. DINUCLEAR CLUSTERS INCORPORATED IN POLYOXOTUNGSTATES

III. 1 Introduction

Heteropolyoxometalates (HPOM) are metal oxide clusters with nanosize and abundant topologies of compounds, which have been studied very extensively for their potential applications in the fields of catalysis, biology, medicine, and various material sciences .

The HPOMs contain elements of the 5th group as heteroatoms, such as (X) As³⁺, Sb³⁺, and Bi³⁺. These molecules display interesting structures due to the stereochemical effect of the lone-pair electrons at the heteroatom bonded to three oxygen atoms constituting the XO₃ trigonal pyramid.

We have investigated the new $K_{10}[M_2Bi_2W_{20}O_{70}] \cdot H_2O$ (**M** = Mn(II)(**1**), Co(II) (**2**), Ni(II) (**3**), Cu(II) (**4**)) sandwich-type complex by spectroscopic (FT-IR, UV-VIS, EPR) methods. The main goal was to obtain information about the structure of the M₂W₂ dinuclear cluster encapsulated between two trilacunary B-β-Keggin units, as well as about metal ions coordination to the trilacunary ligands, the local symmetry around the metal ions and the presence of possible metal-metal couplings.

In *Figure 1* is depicted the polyhedral plot of this type of compounds. Two β-B-XW₉ trilacunary Keggin-type subunits are linked together by two corner-sharing WO₆ octahedra. Two transition-metal atoms are bonded through two oxygen atoms of one unit and one oxygen atom of the other unit to the tungsten-oxygen framework.

This unusual formation leads to three free coordination sites at the transition-metal atoms that are completed by water molecules.

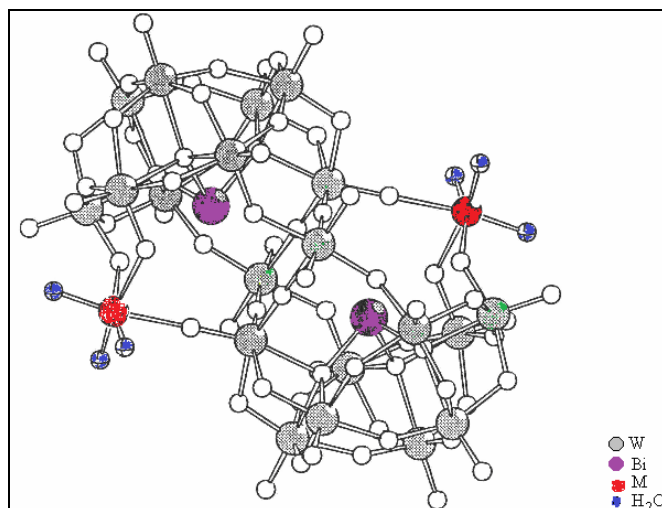


Fig. 1. Structure of the transition-metal substituted bis-decatungsto bismutates $[\text{Bi}_2\text{M}_2\text{W}_{20}\text{M}_2\text{O}_{70}(\text{H}_2\text{O})_6]^{(14-2n)-}$ anion.

$[\text{M}^{n+}_2\text{Bi}_2\text{W}_{20}\text{O}_{70}(\text{H}_2\text{O})_6]^{(14-2n)-}$ polyoxometalates are usually synthesized from their complete B- β - $[\text{Bi}_2\text{W}_{22}\text{O}_{74}(\text{OH})_2]^{12-}$, precursor structure by the removal of two WO_6 octahedra and have substituted with transition metal cations. They exhibit an increased reactivity towards metal ions, thus forming a broad variety of complexes in which the polyoxoanion framework remains unchanged.

III.2 Chemical and spectroscopic measurements

Synthesis of the Complexes

The Na_{12}L ligand was prepared as described previously. Then, 10 ml of an aqueous solution containing 0.55 g $\text{MnSO}_4 \cdot 7\text{H}_2\text{O}$, 0.58 g $\text{Co}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$, 0.56 g $\text{NiSO}_4 \cdot 7\text{H}_2\text{O}$ or 0.50 g $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (2 mmol) was added at 70 °C, under stirring, to a 40 ml aqueous solution containing 6.74 g Na_{12}L (1 mmol).

The mixture was subsequently stirred for 15 min (70 °C), and 0.2 g (2.8 mmol) of KCl was added. Next, the solutions were filtered, and cooled to room temperature.

Microcrystals of $\text{K}_{10}\mathbf{1}$ (yellow), $\text{K}_{10}\mathbf{2}$ (purple-red), $\text{K}_{10}\mathbf{3}$ (green-yellowish) or $\text{K}_{10}\mathbf{4}$ (green) precipitated after 3-4 days and were collected by filtration, then washed with KCl solution (2 mol dm^{-3}), ethanol and ether; eventually they were recrystallized from hot water.

Elemental Analysis

The results of elemental analysis and atomic absorption measurements confirm the formula obtained with theoretical calculation (*table 1*).

Complex	Color	Yield %	% Calculated / (Experimental)					
			K	Bi	W	M	H ₂ O Crist.	H ₂ O Coord.
1	Yellow	62	6.03 (6.08)	6.76 (6.70)	59.46 (59.30)	1.78 (1.82)	5.82 (5.85)	1.75 (1.77)
2	Purple-red	68	6.08 (6.12)	6.50 (6.45)	57.22 (57.18)	1.83 (1.85)	9.25 (9.28)	1.68 (1.70)
3	Green-yellow	65	6.28 (6.30)	6.71 (6.58)	59.04 (58.96)	1.89 (1.92)	6.36 (6.40)	1.74 (1.76)
4	green	64	6.32	6.62	58.28	2.01	7.43	1.71
			6.35	6.48	58.14	2.06	7.46	1.74

Table 1. Results of elemental analysis for the studied complexes

FT-IR Spectroscopy

FT-IR spectra of polyoxometalates generally exhibit contributions of the polyoxoanion framework.

The characteristic IR vibration bands of **1**, **2**, **3** and **4** complexes, compared to those of the Na₁₂ [Bi₂W₂₂O₇₄(OH)₂] ligand, are displayed in *Table 2*.

Vibration	L	1	2	3	4
$\nu_{as}(W=O_t)$	945	945	948	945	949
$\nu_{as}(Bi-O_i)$	832	825	826	828	836
$\nu_{as}(W-O_c-W)$	794	882	886	889	885
	749	760	762	763	763
$\nu_s(W-O_e-W)$	649	668	669	669	664
$\delta(W-O_{c,e}-W)$	508	515	510	512	505
			505		
$\nu_{as}(OH)$	3407	3431	3419	3420	3439
$\delta(HOH)$	1624	1626	1616	1625	1621

Table 2. Main vibration bands observed in the FT-IR spectra (cm⁻¹)

All asymmetric bonds frequencies involving tungsten atoms are shifted towards higher or lower frequencies (5-80 cm⁻¹) in the complexes spectra compared to the ligand spectrum. The tiny shift of the $\nu_{as}(W=O_t)$ stretching vibration in the spectra of the complexes, compared to the ligand, can be explained by the fact that terminal O_t atoms are not involved in the coordination of metal ions. The vibrational frequency of the Bi-O_i bond at ~ 830 cm⁻¹ are not involved in the coordination of metal ions, too.

On the other hand, the larger shift of the $\nu_{as}(W-O_{c,e}-W)$ stretching vibrations, for the bonds from the belt and cap areas, indicates the coordination of metal ions by O_c and O_e oxygen atoms from corner-sharing and edge-sharing octahedra. The shift of the frequencies for the tri-centric bonds in the FT-IR spectrum of the complex compared to the ligands suggests the coordination of the metal ions in the lacunary regions of the Keggin polyoxoanion structure.

Electronic Spectroscopy

The UV electronic spectra (Figure 2) are characteristic to the polyoxometalates and similar to the ligand. The lower energy band (ν_1) at ≈ 256 nm, split into two bands in both ligand and complexes, due to the $d_\pi-p_\pi-d_\pi$ electronic transitions from the tricentric $W-O_{c,e}-W$ bonds, was shifted to lower frequencies in complexes spectra compared to ligand and is due to the decrease of the symmetry as well as to the distortion of the WO_6 octahedra through complexation, which influences the electronic transfer from these bonds.

Visible spectra of complexes show the characteristic d-d electron transfer bands of Mn^{2+} , Co^{2+} , Ni^{2+} and Cu^{2+} ions in octahedral field (Figure 3). However, the expected transition bands are not found in the spectrum of complex 1. The very low intensity d-d transitions of the d^5 Mn^{2+} ion, forbidden by the Laporte and spin selection rules, are totally masked by the ν_5 charge transfer band, which extends from UV into the visible range. This indicates that Mn^{2+} ions are involved in the charge transfer in complex 1.

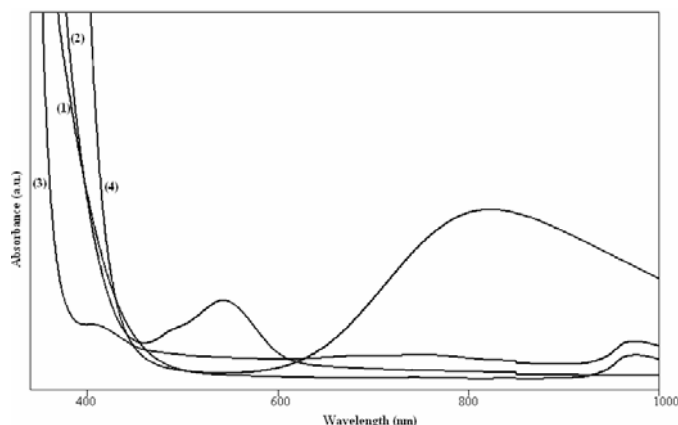


Figure 2. UV spectra of the polyoxotungstate complexes in $(5 \cdot 10^{-5} M)$ aqueous solution.

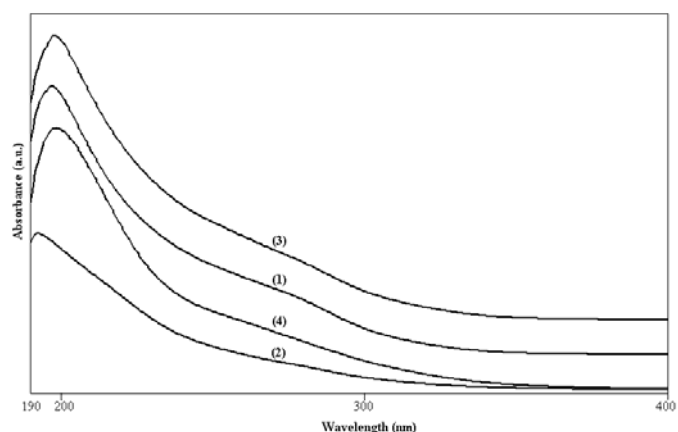


Figure 3. Vis spectra of the polyoxotungstate complexes in $(5 \cdot 10^{-3} M)$ aqueous solution

Electron spin resonance spectroscopy

The shape and ESR parameters for the **complexes 1** and **4**, represented on *Figures 4 and 5*, respectively, are typically for non-interacting species with octahedral distorted local symmetry around the metallic ion.

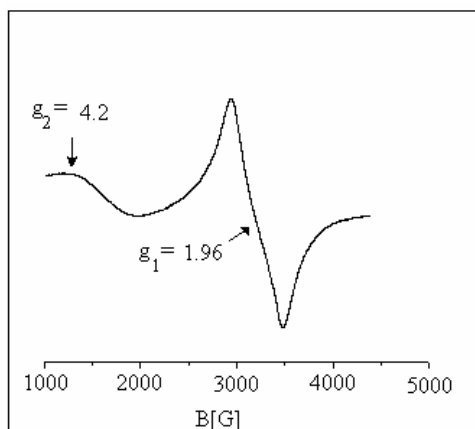


Figure 4. UV spectra of the polyoxotungstate complexes in ($5 \cdot 10^{-5}$ M) aqueous solution.

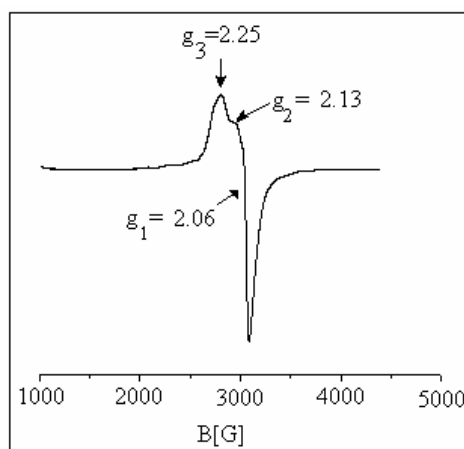


Figure 5. Vis spectra of the polyoxotungstate complexes in ($5 \cdot 10^{-3}$ M) aqueous solution

III.3. Conclusions

The FT-IR spectroscopic investigation of the investigated complexes indicate the coordination of the transition metal cations at corner-sharing and edge-sharing octahedra from each $[\text{Bi}_2\text{W}_{22}\text{O}_{74}(\text{OH})_2]^{12-}$ heteropolyanion.

UV spectra of the ligand and complexes are also very similar, evincing that the charge transfer inside the polyoxotungstate structure is not significantly affected by the coordination. The UV spectra show that in the studied complexes trilacunary Keggin anion plays the ligand role. They also reveal that the secondary heteroatoms are the manganese, cobalt, nickel and copper cations.

Visible electronic spectra indicate the *octahedral coordination* in distorted octahedron environment of the Mn^{2+} , Co^{2+} , Ni^{2+} , Cu^{2+} , cations in the $\text{K}_{10}[\text{M}^{2+}\text{Bi}_2\text{W}_{20}\text{O}_{70}(\text{H}_2\text{O})_6] \cdot x\text{H}_2\text{O}$ complexes. Visible spectra of complexes show the characteristic d-d electron transfer bands of Mn^{2+} , Co^{2+} , Ni^{2+} and Cu^{2+} ions in octahedric field. ESR spectra of complex (1) and (2) are typically for *distorted octahedral local symmetry* around the metallic ion. No significant metal-metal coupling was observed.

The results prove that the complexes have a sandwich-type structure, with a (M_2) dinuclear cluster encapsulated between two trilacunary B- β -Keggin units. Three water molecules are linked to two M (metal) atoms.

IV. COOPER (II) COMPLEXES WITH THEOPHYLLINE LIGAND CONTAINING ETHYLENEDIAMINE DERIVATES AS COLIGANDS

III.1 Introduction

Derivatives of nucleobases belonging to the xanthine group, like theophylline, have been known for a long time, and commonly used for their biologic effects. The coordination compounds of these molecules, may serve as model compounds for the interaction of metal ions with molecules of biologic interest.

The theophylline, *i.e.*, 1,3-dimethyl-2,6-dioxo-purine, in neutral or basic media act as monodentate ligand and coordinates through the N7 atom which is the preferred binding site in 6-oxopurines. The deprotonated theophylline may act as bidentate ligand forming N7/O6 chelates.

A series of novel mixed-ligand theophylline (th) complexes, **[Cu(th)₂(dmen)]·2H₂O (1)**, **[Cu(th)₂(tmeda)(H₂O)]·0.5H₂O (2)** and **[Cu(th)₂(dpen)(H₂O)]·5H₂O (3)**, were synthesized and investigated by means of infrared and EPR spectroscopic methods. As co-ligands the following ethylenediamine derivatives were used: N,N-dimethyl-ethylenediamine (**dmen**), N,N,N',N'-tetramethyl-ethylenediamine (**tmeda**) and *meso*-1,2-diphenyl-ethylenediamine (**dpen**). The geometry of complexes was optimized at B3LYP/LANL2DZ level of theory.

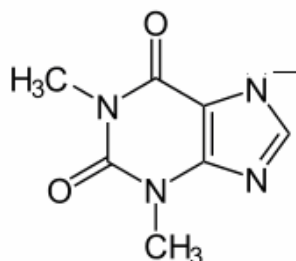


Figure 6.
Deprotonated theophylline structural formula

III.2 Chemical and spectroscopic measurement

Synthesis

The complexes **[Cu(th)₂(dmen)]·2H₂O (1)**, **[Cu(th)₂(tmeda)(H₂O)]·0.5H₂O (2)** and **[Cu(th)₂(dpen)(H₂O)]·5H₂O (3)** were synthesised from theophylline and appropriate copper(II) complexes in basic media according to published methods. Compounds 1–3 were isolated in good yield as microcrystalline solids and were characterized by elemental analyses, IR and ESR spectroscopy.

Elemental analysis

The theoretically calculated and experimentally obtained elemental analysis data are shown in *table 3*.

Complex	1	2	3
	$C_{18}H_{30}CuN_{10}O_6$	$C_{20}H_{32}CuN_{10}O_5$	$C_{28}H_{42}CuN_{10}O_{10}$
MW ($g \cdot mol^{-1}$)	545.78	556.08	742.25
Yield (%)	81	62	41
Experimental (calculated)			
C (%)	39.58 (39.56)	30.78 (43.20)	45.33 (45.31)
H (%)	5.54 (5.45)	3.98 (5.80)	5.18 (5.70)
N (%)	25.66 (25.41)	20.44 (25.19)	18.63 (18.87)

Table 3. Physico-chemical properties and elemental analysis data of the metal complexes (1–3)

FT-IR spectra

Spectra of all copper(II) complexes show the two strong bands of theophylline assigned to the stretching vibration of carbonyl groups shifted towards lower wavenumbers, due to the deprotonation of theophylline and participation of C(6)=O and C(2)=O groups in intra- or intermolecular hydrogen bond formation (*table 4*). The C=N vibrations of the theophylline are shifted to lower wave numbers in complexes suggesting that the ligand coordinates through one of the *imidazole's nitrogen atoms*, acting as *monodentate ligand*.

In all spectra of complexes the symmetric and antisymmetric stretching vibrations of coordinated NH_2 groups can be assigned in the $3285\text{--}3154\text{ cm}^{-1}$ region. There are significant changes in the bands assigned to N–H vibrations as consequence of the deprotonation of theophylline at N(7) atom and coordination of the amine type ligands. The *amine ligands* are coordinated as *bidentate ligands* through N atoms to the metal center.

Vibration	theophylline	1 [Cu(th) ₂ (dmen) ₂]	2 [Cu(th) ₂ (tmeda) (H ₂ O)]	3 [Cu(th) ₂ (dpen) (H ₂ O)]
v(N–H)	3122	3285m 3154m 3102m	–	3462m 3245m 3161m
v(C=O)	1717 1669	1686vs 1642vs	1690vs 1636vs	1690vs 1641vs
v(C=C)	1610	1580m	1528m	1591m
v(C=N)	1568	1527m	1528m	1530m

Table 4. Some IR absorption bands (cm^{-1}) for the theophylline and the metal complexes 1–3
(m – medium, vs- very strong)

The ν_{CH} vibrations of ligands appear at 2851–2954 cm^{-1} and 3027–3066 cm^{-1} for aliphatic CH_2 and aromatic CH, respectively.

The presence of strong broad bands in FTIR spectra of the complexes at 3500–3200 cm^{-1} may be assigned to various types of hydrogen bonds.

Electronic spin resonance spectroscopy

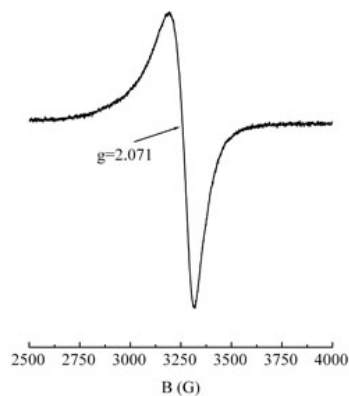


Figure 7. Powder ESR spectra of **$[\text{Cu}(\text{th})_2(\text{dmen})]\cdot 2\text{H}_2\text{O}$ (1)**

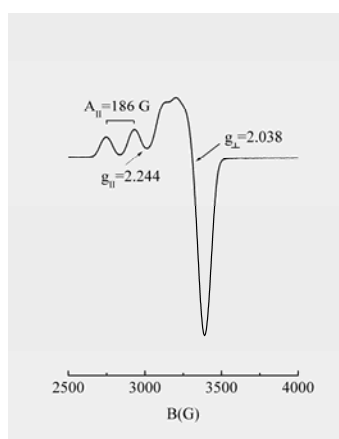


Figure 8. Powder ESR spectra of **$[\text{Cu}(\text{th})_2(\text{tmeda})(\text{H}_2\text{O})]\cdot 0.5\text{H}_2\text{O}$ (2)**

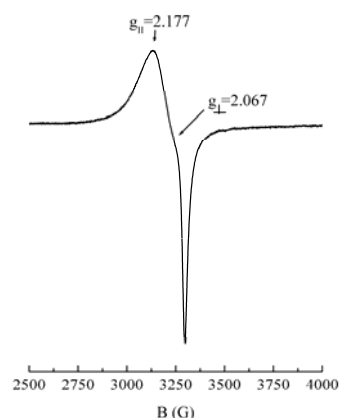


Figure 9. Powder ESR spectra of **$[\text{Cu}(\text{th})_2(\text{dpen})(\text{H}_2\text{O})]\cdot 5\text{H}_2\text{O}$ (3)**

The room temperature ESR powder spectrum of **$[\text{Cu}(\text{th})_2(\text{dmen})]\cdot 2\text{H}_2\text{O}$ (1)** as shown in *Figure 7* is typically for copper ions with *distorted tetrahedral local symmetry* ($g_0 = 2.071$) suggesting the $\{\text{CuN}_4\}$ chromophore.

Complexes 2 and 3 are monomer. The room temperature ESR powder spectrum of **$[\text{Cu}(\text{th})_2(\text{tmeda})(\text{H}_2\text{O})]\cdot 0.5\text{H}_2\text{O}$ (2)** exhibits four hyperfine lines in the g_{\parallel} region and a strong absorption signal in the g_{\perp} region (*figure 8*). The shape of the spectrum and the obtained values of ESR parameters ($g_{\parallel} = 2,244$ and $g_{\perp} = 2,038$, $A_{\parallel} = 186 \text{ G}$) correspond to a square pyramidal symmetry suggesting $\{\text{CuN}_4\text{O}\}$ environment for copper ion.

Complex **$[\text{Cu}(\text{th})_2(\text{dpen})(\text{H}_2\text{O})]\cdot 5\text{H}_2\text{O}$ (3)** presents square pyramidal symmetry suggesting $\{\text{CuN}_4\text{O}\}$ environment for copper ion, which is confirmed by ESR spectral

parameters ($g_{\parallel}=2,177$, $g_{\perp}=2,067$) (fig. 9). No hyperfine splitting because of the interaction of paramagnetic electron with nitrogen nuclei was observed.

IV.3 Computational details

Geometry optimizations were performed by using the density functional theory (DFT), and utilizing the unrestricted Becke three-parameter hybrid exchange functional, combined with the Lee–Yang–Parr correlation functional (B3LYP) and LANL2DZ basis sets. The *Gaussian09* electronic structure program package was used for calculations. The molecular structure of the complexes 1–3 was optimized in the gaseous phase. The optimized structures are displayed in *figures 10,11,12*.

The optimized structure of complexes 2 and 3 presents square pyramidal geometry around the pentacoordinated Cu^{II}, the base of distorted pyramid, consisting of four N atoms of the diamine type ligand and the N7 atom of each of the two theophyllinate moieties. One of the water molecules is positioned on the coordination axis, in axial position. For complex 1 the disordered tetrahedral geometry was chosen, based on the RES spectrum (*figure 10,11,12*).

IV.4 Conclusions

In summary, we have synthesized and characterized three new mixed-ligand theophyllinato coordination compounds. A combination of spectroscopic methods and density functional calculations has been used to describe the electronic structure of complexes. For the Cu(II)theophylline complexes with some amine ligands the local symmetry around the Cu(II) ion is strongly influenced by the nature of amines.

IR investigations show *monodentate coordination of the theophylline*, respectively the *bidentate coordination of the amine ligands* to central copper ion with N atoms. According to the ESR data, compound **1** contains $\{CuN_4\}$ *chromophore*, with a distorted tetrahedral symmetry around the copper ion, with bidentate bonding of neutral diamine dmen.

The data of dpheda and tmeda co-ligands containing complexes, **2** and **3**, confirm a $\{CuN_5O\}$ *chromophore*, with a square pyramidal coordination geometries around the central copper(II) ion. The theophylline coordinates *via* the N(7) nitrogen.

Theoretical investigations at B3LYP/LANL2DZ level of the theory revealed that the utilized technique is efficient in optimizing structural geometries of systems based on organic molecules and copper(II) ions.

(Color code: C – grey, N – blue, O – red, H – white, Cu – cyan)

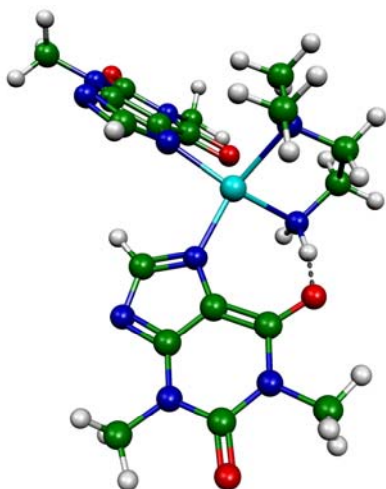


Figure 10. A view of
B3LYP/LANL2DZ optimized structures
of the copper(II) complex
[Cu(th)₂(dmen)]·2H₂O (1)

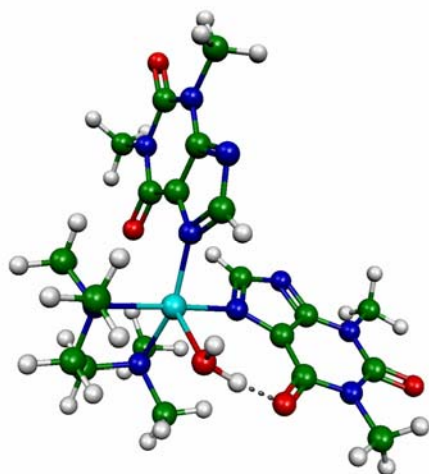


Figure 11. A view of
B3LYP/LANL2DZ optimized structures
of the copper(II) complex
[Cu(th)₂(tmeda)(H₂O)]·0.5H₂O (2)

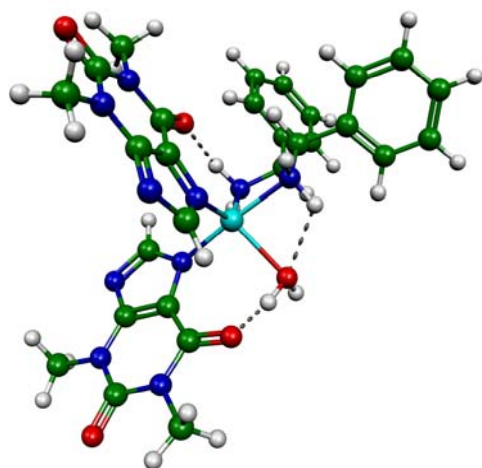


Figure 12. A view of
B3LYP/LANL2DZ optimized structures
of the copper(II) complex
[Cu(th)₂(dpen)(H₂O)]·5H₂O (3)

V. METALLIC COMPLEXES WITH AMINOACIDS

V.1 Introduction

Amino acids are the “building blocks” of the body. Besides building cells and repairing tissue, they form antibodies to combat invading bacteria and viruses; they are part of the enzyme and hormonal system, they build nucleoproteins and carry oxygen throughout the body and participate in muscle activity.

A simple amino acid anion is a potential bidentate ligand which may coordinate to a transition metal ion through the *amino* lone pair of electrons and the *carboxylate* oxygen lone pair of electrons. The metallic complexes with amino acids as ligands were deeply investigated due to their capacities of forming chelates, which are used in various domains like: medicine, chemistry, pharmacy, biology, nutrition and physics.

Complexes of transition metals with amino acids in proteins and peptides are utilized in numerous biological processes, such as oxygen conveyer, electron transfer and oxidation. Metal (II) complexes present antibacterial and antifungal activity.

The metallic complexes with amino acids as ligands were deeply investigated due to their capacities of forming chelates, which are used in various domains like: medicine, chemistry, pharmacy, biology, nutrition and physics.

New complexes of α -aminoacids, $[\text{Cu}(\text{L})_2] \cdot \text{H}_2\text{O}$ (**1**), $[\text{Co}(\text{L})_2] \cdot 2\text{H}_2\text{O}$ (**2**) and $[\text{Zn}(\text{L})_2] \cdot \text{H}_2\text{O}$ (**3**) have been investigated by physical-chemical methods. Here we present some spectroscopic methods of molecular structure investigation, like FTIR, UV-Vis and ESR. (L represents the aminoacid ligands: *leucine*, *phenylalanine*, *methionine*).

V.2 Spectroscopic investigation of metallic Cu(II), Co(II), Zn(II) complexes with leucine as ligand

Leucine (Fig.13.) is an essential amino acid that is used as a source for the synthesis of blood sugar in the liver during starvation, stress, and infection to aid in healing [2].

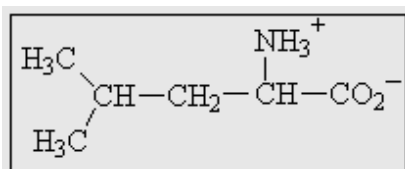


Fig. 13. Structural formula for leucine

Synthesis of the complexes

The complexes were prepared as described previously: 2 mmol of the leucine (0.262 g) were dissolved in 20 ml warm distilled water. For the amino acid deprotonation 0.33 ml 30% NaOH was added. The precipitation of the leucine complexes were instantaneous, and a blue-green precipitate was obtained ($\eta=69.6\%$) for **1**, a pink one for **2** ($\eta=69.6\%$) and a white one for **3** ($\eta=58.6\%$). The complexes were filtered, washed with ethanol and dried in

desiccators under P₄O₁₀. Afterward, the complexes were recrystallized on methanol, dried and weight to establish the percent of complexation.

Elemental analysis and atomic absorption spectroscopy

The elemental analysis and atomic absorption spectroscopy measurements confirm the metal ion: leucine ratio of 1:2 for composition of the complexes.

Complex	Molecular weight	% Calculated/ Found			
		C	H	N	Metal
[Cu(L) ₂].H ₂ O	323.5	43.51 (42.71)	8.65 (9.22)	7.41 (6.38)	19.40 (19.36)
[Co(L) ₂].2H ₂ O	319	44.14 (43.2)	8.77 (9.32)	7.52 (8.25)	21.35 (22.15)
[Zn(L) ₂].H ₂ O	325	44.25 (43.75)	8.60 (9.10)	7.37 (6.80)	18.00 (17.98)

Table 5. Elemental analysis results of the metal-leucine complexes

FT-IR spectra

Complex	$\nu(\text{O-H})$	$\nu(\text{N-H})$	$\nu(\text{C=O})$	$\delta(\text{N-H})$
Leu	-	3052	1608	1577 1511
Cu- Leu	3421	3319 3245	1619	1561
Co- Leu	3475	3223 3107	1639	1578
Zn- Leu	-	3325 3268	1654	1608

Table 6. FT-IR spectral data (cm⁻¹) metal-leucine complexes

In the spectrum of the ligand, the $\nu_s(\text{N-H})$ stretching vibration appears at 3052 cm⁻¹ and is shifted in the complexes spectra at: 3319 cm⁻¹, 3245 cm⁻¹ (**1**), 3223 cm⁻¹, 3107 cm⁻¹ (**2**) 3325 cm⁻¹ 3268 cm⁻¹ (**3**) proving the involvement of the -NH₂- group in the complex formation.

The absorption band at 1608 cm⁻¹ was attributed to the $\nu(\text{C=O})$ stretching vibration in the spectrum of the ligand and appears to be shifted toward higher wave numbers with 11 cm⁻¹, 31 cm⁻¹ and 46 cm⁻¹ in the spectra of **1**, **2** respectively **3** proving the involvement of the carboxylic group in the covalent bonding to the metal ion.

The $\nu(\text{O-H})$ stretching vibrations does not appear in the spectra of the ligand and complex **3** but emerge in spectra of complexes (**1**) and (**2**) at 3421 cm⁻¹ and 3475 cm⁻¹, respectively, suggesting the presence of the crystal water in these compounds[11]. Due to

the $\delta(\text{N-H})$ bending vibration shifting in the complexes spectra the involvement of the $-\text{NH}_2-$ group to the metal bonding formation was confirmed.

Electronic spectra

Compound	$n \rightarrow \pi^*$ transition	$d-d$ transition
Leucine	277 nm	-
Cu-leu	270 nm	600-650 nm
Co-leu	276 nm	450-540 nm
Zn-leu	268 nm	-

Table 7. UV and visible spectral data

The $n \rightarrow \pi^*$ characteristic band assigned to the C=O bond appears at 277 nm in the ligand spectrum and is shifted toward UV domain with 7 nm, 1nm and 11 nm in the complex **1**, **2** and **3** spectra , proving the presence of the ligand within the complex and the covalent nature of the metal-ligand bond.

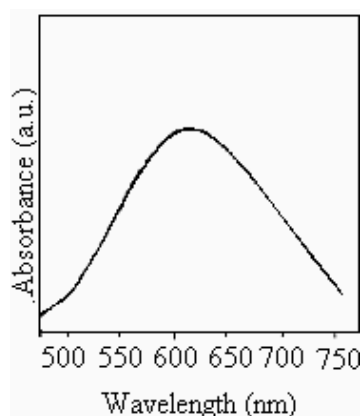


Fig. 14. Visible spectrum of $[\text{Cu}(\text{L})_2] \cdot \text{H}_2\text{O}$ (**1**) in DMSO (10^{-3}M)

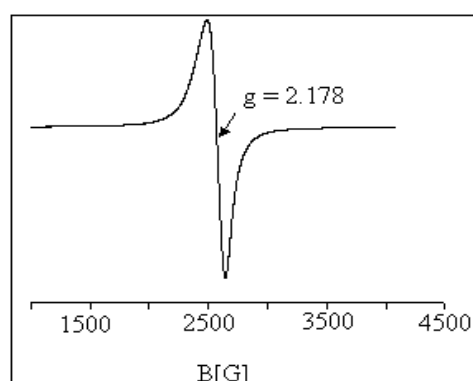


Fig. 15. Powder EPR spectrum of $[\text{Cu}(\text{L})_2] \cdot \text{H}_2\text{O}$ (**1**) at room temperature

The metal-ligand charge transfer band appears below at 250nm in the spectrum of complex **2** and between 290- 320 nm in the spectrum of complex **3**.

In the visible domain the spectrum of complex **1** (Fig.14) show a large shoulder at 620 nm, assigned to the ${}^2\text{T}_{2g} \rightarrow {}^2\text{E}_g$ transition, specific to Cu (II) complexes with tetragonal distortion due to the Jahn-Teller effect. Yet again in visible domain, the spectrum of complex **2** illustrates two bands at 360 nm and 525 nm, also ascribed to the $d-d$ transition, the last band within the spectrum was assigned to the ${}^4\text{T}_{1g}(\text{P}) \rightarrow {}^4\text{T}_{1g}(\text{F})$ transition, expected for an octahedral symmetry of cobalt ion.

ESR Spectra

Powder ESR spectrum of complex **1** (Fig. 15) measured at room temperature is quasi-isotropic ($g = 2.178$) and is characteristic for pseudotetrahedral symmetry around the copper ion. The shape and the value of the g tensor correspond to a $\{CuN_2O_2\}$ chromophore.

The powder ESR spectrum of complex **2** revealed the presence of monomeric compounds, with octahedral symmetry around the cobalt ion, the g tensor value is $g = 2.195$.

V.3 Spectroscopic investigation of metallic Cu(II), Co(II), Zn(II) complexes with phenylalanine as ligand

Phenylalanine (Fig. 16) is used by the brain to produce norepinephrine, a chemical that transmits signals between nerve cells and the brain; keeps you awake and alert; reduces hunger pains; functions as an antidepressant and helps improve memory.

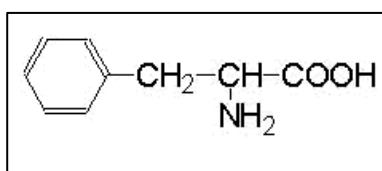


Figure 16. Structure formula for phenylalanine

Synthesis of the complexes: the complexes were prepared as described previously.

Elemental analysis

The elemental analysis and atomic absorption spectroscopy measurements confirm the metal ion: phenylalanine ratio of 1:2 for the composition of the complexes.

Symbolic formula	Molecular weight	%C		%H		%N	
		Meas.	Calc.	Meas.	Calc.	Meas.	Calc.
Cu(L) ₂	391.5	54.79	55.1	7.31	7.66	6.92	7.15
Co(L) ₂	389.4	51.42	55.46	8.59	8.2	8.28	7.59
Zn(L) ₂	395	51.85	54.69	9.07	8.10	6.57	7.08

Table 8. Elemental analysis results for metal- phenylalanine complexes

FT-IR spectroscopy

Information about the metal ions coordination was obtained by comparing the IR frequencies of the ligand with those of the copper, cobalt and zinc complexes.

The $\nu(OH)$ stretching vibration does not appear in the spectra of the ligand and complex 3, but emerges in the spectra of complexes 1 and 2 complexes at 3454 cm^{-1} respectively 3453 cm^{-1} and 3359 cm^{-1} suggesting the presence of the crystal water in these compounds.

Compound	$\nu(\text{O-H})$ (cm^{-1})	$\nu(\text{N-H})$ (cm^{-1})	$\nu(\text{C=O})$ (cm^{-1})	$\delta(\text{N-H})$ (cm^{-1})
Phenylalanine	-	3078 3030	1623	1557
Cu-phe	3454	3320 3256	1629	1567
Co-phe	3453 3359	3220	1633	1586
Zn-phe	-	3334 3256	1614	1531

Table 9. FT-IR spectral data (cm^{-1}) for metal- phenylalanine complexes

Electronic spectroscopy

Information about local symmetry of metal ions was obtained by comparing the ligand spectra with those of complexes with amino acids.

Compound	$n \rightarrow \pi^*$	$\pi \rightarrow \pi^*(\text{arom})$	$d-d$
Phenylalanine	231 nm	260 nm	-
Cu-phe	225 nm	275 nm	600-650 nm
Co-phe	235 nm	280 nm	500-540 nm
Zn-phe	220 nm	260-270 nm	-

Table 10. UV and visible spectral data for metal- phenylalanine complexes

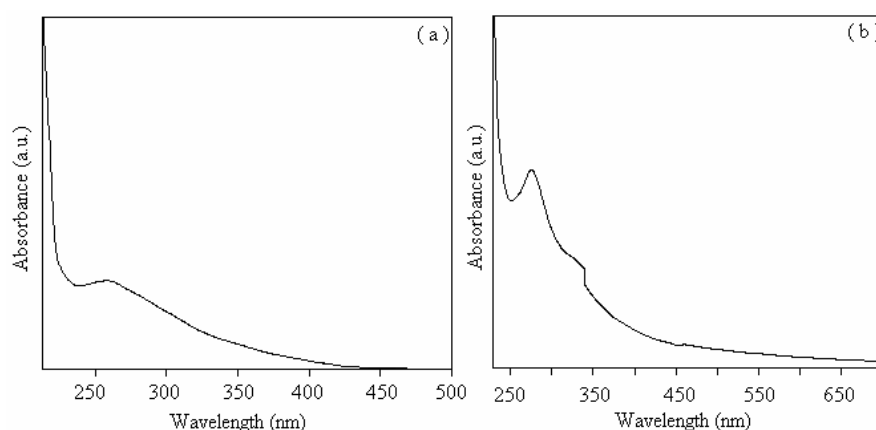


Figure 17. UV spectra of phenylalanine (a) and Cu-L (b)

The $n \rightarrow \pi^*$ characteristic band in the UV spectra assigned to the C=O bond appear at 231nm for phenylalanine (Fig.17.a) and is shifted toward higher wave lengths at 225nm (1), 235nm (2) and 220 nm (3) confirming the presence of the ligand in the complex and the

covalent nature of the metal-ligand bond. In the UV spectrum of the ligand the $\pi \rightarrow \pi^*$ characteristic band appears at 260nm, and is shifted in the complexes spectra with 15nm (1), 20nm (2) and 7nm (3), being assigned to conjugated systems.

In the visible domain (Fig.17) a d–d transition points out at 615 nm in the copper complex spectrum and was assigned to the ${}^2T_{2g} \rightarrow {}^2E_g$ transition, specific for Cu (II) complexes with tetragonal distortion owing to the Jahn–Teller effect. In the visible domain, the cobalt complex spectrum shows a band at 540nm attributed to the d–d transition of cobalt electrons.

Electron spin resonance spectroscopy

Powder ESR spectra (Fig.18.a.) at room temperature are typical for monomeric species with pseudotetrahedral symmetry around the copper ion ($g = 2.009$). The ESR spectrum of complex 1 in DMF solution at room temperature (Fig.18.b.) exhibit the copper hyperfine structure with the isotropic parameters: $g_0 = 2.124$, $A_0 = 82G$. The powder ESR spectrum of complex 2 revealed the presence of monomeric compounds, with octahedral symmetry around the cobalt ion, the g tensor value is $g = 2.185$.

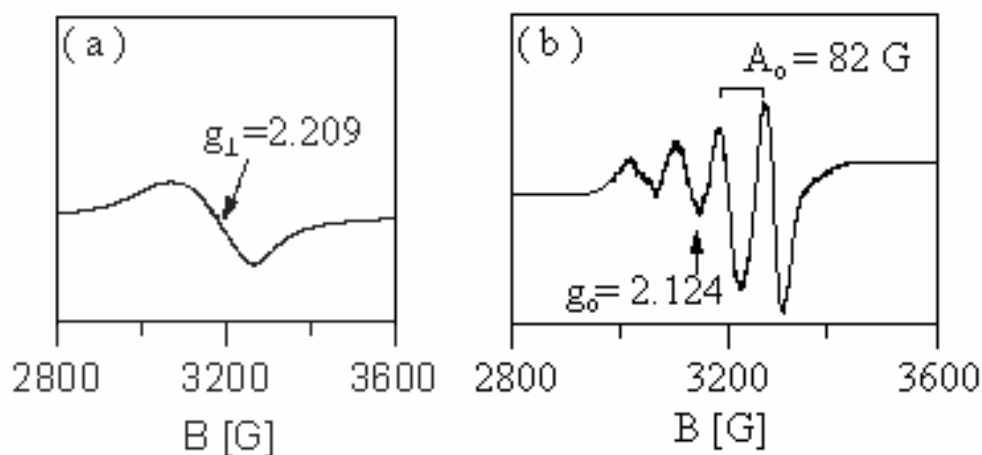


Figure 18. ESR spectra of complex 1 in powder (a) and DMF solution (b)

V.4 Spectroscopic investigation of metallic Cu(II), Co(II), Zn(II) complexes with methionine as ligand

Methionine (Fig.19) is the only sulfur-containing amino acid that is essential for mammals and must therefore be derived entirely from the diet.

Methionine is synthesized by plants and most micro organisms after the initial steps of inorganic sulfate assimilation and cysteine or homocysteine syntheses .

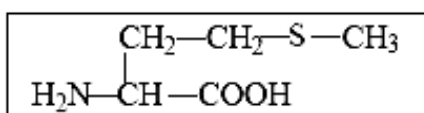


Fig.19. Methionine structural formula.

Synthesis of the complexes: the complexes were prepared as described previously.

FT-IR spectroscopy

The CH₂-S and CH₃-S stretching vibrations appear as a sharp band at 2915 cm⁻¹ in the ligand spectrum and are insignificantly shifted in the spectra of the complexes confirming the non involvement of these groups in the coordination.

Compound	$\nu(\text{O-H})$	$\nu(\text{N-H})$	$\nu(\text{C=O})$	$\delta(\text{N-H})$	$\nu(\text{C-C})$
Met	-	3146	1610	1580 1563 1508	1352 1316
Cu- Met	-	3229	1649	1568 1616	1334
Co- Met	3419	3175	1640	1584	
Zn- Met	3383	3170	1586	1502 1558	1385

Table 11. FT-IR spectral data (cm⁻¹) for metal-methionine complexes

Electronic spectroscopy

Compound	$n \rightarrow \pi^*$ transition	$d-d$ transition
Methionine	267 nm	-
Cu-Met	275 nm	600-650 nm
Co-Met	274 nm	450-550 nm
Zn-Met	265 nm	-

Table 12. UV and visible spectral data for metal- methionine complexes

The $n \rightarrow \pi^*$ characteristic band assigned to the C=O bond appears at 267 nm in the ligand spectrum and is shifted toward UV domain with 8 nm, 7nm in the complex **1** and **2** spectra, proving the presence of the ligand within the complex and the covalent nature of the metal-ligand bond.

In the visible domain the spectrum of complex **1** show a large shoulder at 625 nm, assigned to the $2T_{2g} \rightarrow 2E_g$ transition, specific to Cu (II) complexes with tetragonal distortion due to the Jahn-Teller effect. Yet again in visible domain, the spectrum of complex **2** illustrates a band at 512 nm, also ascribed to the $d-d$ transition.

The position of the band maxima and respective assignment for Co(II) complex with methionine is typical for octahedral geometries.

Electron spin resonance spectroscopy

The powder EPR spectrum of the copper(II) complex measured at room temperature is characterized by the presence of an isotropic signal centered at $g = 2.094$, which can be assigned to a pseudotetrahedral symmetry around the copper ion. The shape and the value of the g tensor correspond to a $\{CuN_2O_2\}$ chromophore. The powder EPR spectrum of complex **2** revealed the presence of monomeric compounds, with octahedral symmetry around the cobalt ion, the g tensor value is $g = 2.201$.

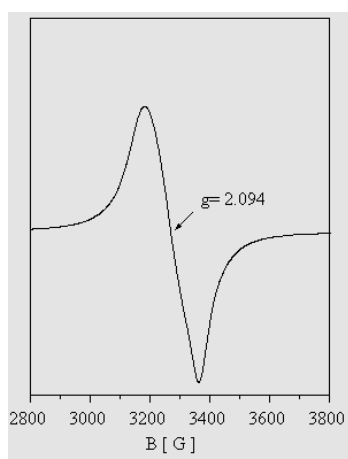


Fig. 20. Powder EPR spectrum of complex Cu- **Met**.

V.5 Conclusions

New metallic complexes with α -aminoacids as ligand were synthesised and investigated by spectroscopic means: $[Cu(L)_2] \cdot H_2O$ (**1**), $[Co(L)_2] \cdot 2H_2O$ (**2**) și $[Zn(L)_2] \cdot H_2O$ (**3**). A metal amino acid chelate is composed of an amino acid that has two donor groups combined with the metal so that one or more rings are formed, with the metal being the closing component of this heterocyclic ring.

The elemental analysis and atomic absorption spectroscopy measurements confirm the metal ion: aminoacid ratio of 1:2 for the composition of the complexes.

Information about the metal ions coordination was obtained by comparing the IR frequencies of the ligand with those of the copper, cobalt and zinc complexes.

The FT-IR spectra show that the amino acid is acting as *bidentate ligands* with the coordination involving the *carboxyl oxygen* and the *nitrogen atom* of amino group.

UV-VIS and ESR spectroscopies confirm the *pseudotetrahedral local symmetry* around the copper and zinc ions and the *octahedral symmetry* around the cobalt ion.

The obtained structural data allow us to propose the molecular formulae for the studied metal complexes which are shown in *Figure 7*.

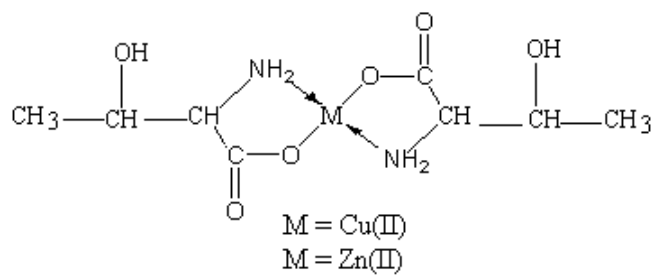


Fig. 21. Structural formulae proposed for the synthesized complexes of leucine (1)

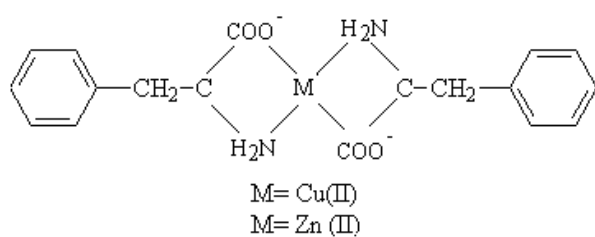
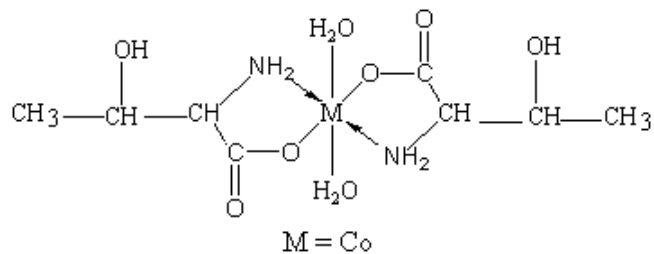


Fig.22. Structural formulae proposed for the synthesized complexes of phenylalanine(2)

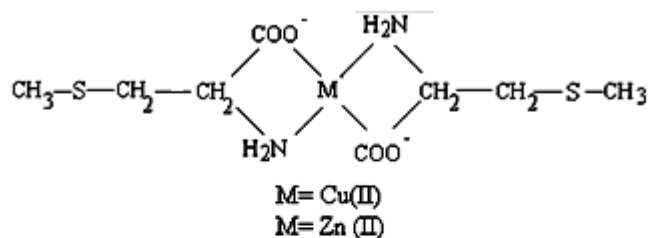
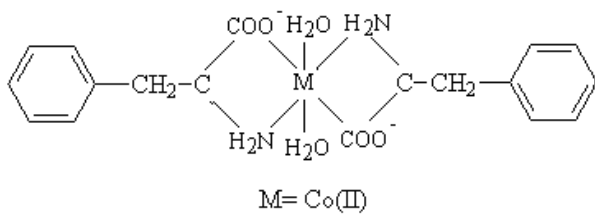
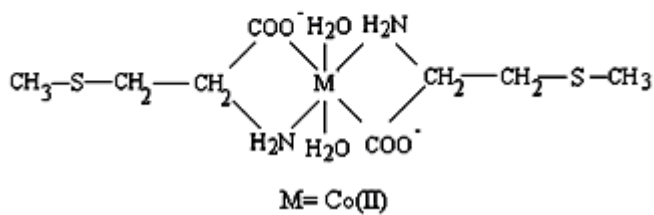


Fig. 23. Structural formulae proposed for the synthesized complexes of methionine (3)



VI. STRUCTURAL INVESTIGATION OF RANITIDINE MOLECULE BY VIBRATIONAL SPECTROSCOPIC METHODS AND THEORETICAL CALCULATION

VI.1 Introduction

Ranitidine hydrochloride is widely used for more than 20 years in the treatment of duodenal and gastric ulceration, as well as gastro-esophageal reflux disease. This molecule is effective as blocker of H₂ histamine receptors located in parietal cells of gastric mucosa.

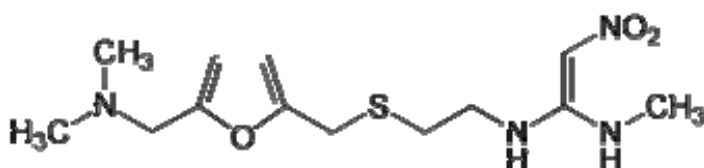


Fig. 24. Structural formula of ranitidine

A variety of analytical techniques have been successfully used for quantitative solid-state analysis including scanning electron microscopy, X-ray powder diffraction (XRPD), differential scanning calorimetry (thermal analysis), Raman and FT IR spectroscopy, nuclear magnetic resonance. XRPD gives fundamental structural information, while Raman spectroscopy provides molecular specific information.

Ranitidine serve as an effective ligand towards metal ions with very strong coordination ability.

In the present study IR and Raman spectra of ranitidine hydrochloride were assigned using DFT calculations based on the hybrid B3LYP exchange-correlation functional, coupled with the standard 6-31G(d) basis set. The adsorption geometry of the ranitidine hydrochloride molecule on colloidal silver surface was deduced from the SERS selection rules and the analysis of the calculated molecular electrostatic potential (MEP).

VI.2 IR, Raman, SERS and DFT study of ranitidine

Raman and infrared (IR) spectroscopies provide information about the vibrational and vibrational-rotational modes of molecules. In solid or liquid phases only vibrational frequencies of the sample can be observed.

Surface-enhanced Raman scattering (SERS) is a phenomenon resulting in strongly increased Raman signals when molecules are attached to nanometer sized metallic structures.

All chemicals used were of analytical reagent grade. The silver colloidal SERS substrate was prepared by reducing Ag⁺ with hydroxylamine. Briefly, 0.017 g silver nitrate was solved in 90 ml double distilled water. In a separate recipient, 0.017 g of hydroxylamine hydrochloride were solved in 10 ml water, followed by the addition of 1,15 ml sodium

hydroxide solution, 1%(v) to OH. The hydroxylamine/sodium hydroxide solution was then added rapidly to the silver nitrate solution under vigorous stirring. After few seconds a grey-brown colloidal solution resulted and it was further stirred for 10 min. The pH value of the silver colloid, measured immediately after preparation, was found to be 8.5.

Computational details

The molecular geometry optimization, molecular electrostatic potential (MEP) and vibrational spectra calculations were performed with the Gaussian 03W software package by using density functional theory (DFT) methods with B3LYP hybrid exchange-correlation functional and the standard 6-31G(d) basis set. No symmetry restriction was applied during geometry optimization.

After geometric optimization, vibrational frequencies were calculated for ranitidine hydrochloride.

The assignment of the experimental frequencies is based on the observed band frequencies and intensity pattern of the Raman spectra and confirmed by establishing a one to one correlation between the observed and theoretical calculated frequencies.

To aid in mode assignment, we based on the direct comparison between the experimental and calculated spectra by considering both, the frequency sequence and intensity pattern, and by comparisons with vibrational spectra of similar compounds.

As deduced from calculations of pKa values, of interest are two molecular forms of ranitidine, the neutral and protonated form of the N11 atom. Thus, molecular geometry optimization was carried out of these two forms using B3LYP functional with 6-31G basis set (d) (Fig.26). When comparing the experimental FTIR spectrum with the calculated spectra it has to be taken in consideration that the theoretical spectra are calculated for the gas phase of the substance and the experimental data were recorded for solid samples.

Figure 25 shows experimental Raman and SERS spectra of ranitidine, using the laser wavelengths 532 and 633 nm.

Most intense bands are due to stretching vibration of N-C-N group and the NO₂ group stretching vibration. From FT-Raman spectra of powder ranitidine and Raman calculated by DFT method in the N11 nitrogen atom protonated and neutral form, the following features were observed:

(a) The most intense band in the FT-Raman spectrum appears at 1552 cm⁻¹, being attributed to the symmetric C = C stretching vibration of the ring. This band is found in the calculated spectra at 1520 cm⁻¹ in the neutral form and 1512 cm⁻¹ in the protonated form, respectively.

(b) The group of intense bands at 1246 cm⁻¹ is attributed to CH deformation vibrations. Calculated wavenumbers have been scaled with the scaling factor (0.9614) proposed by Scott and Random

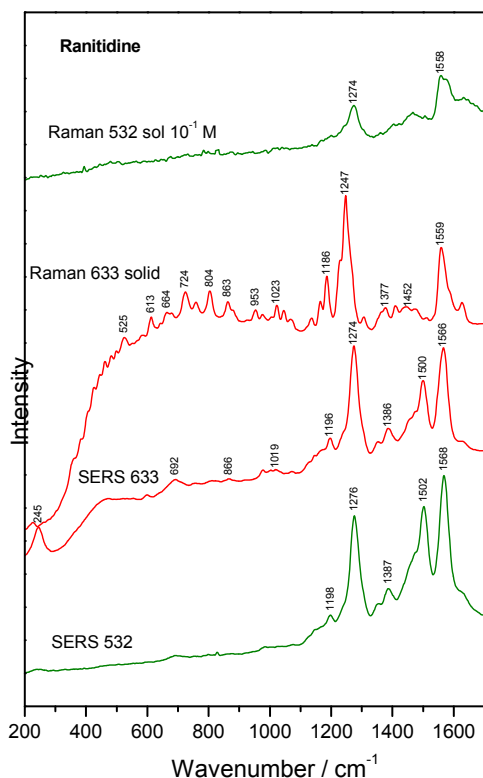


Fig. 25

Experimental Raman and SERS spectra of the ranitidine molecule

A new-band at 1500 cm^{-1} is observed in the SERS spectrum which is attributed to N=O stretching vibration, which shows an interaction of ranitidine molecule with the silver surface through the two oxygen atoms of the NO_2 group. *Figure 27* shows a high electronic density around the NO_2 group, so we can assume that this group will interact with the surface of colloidal silver nanoparticles. Thus, we deduce the geometry as shown schematically in *Figure 26*.

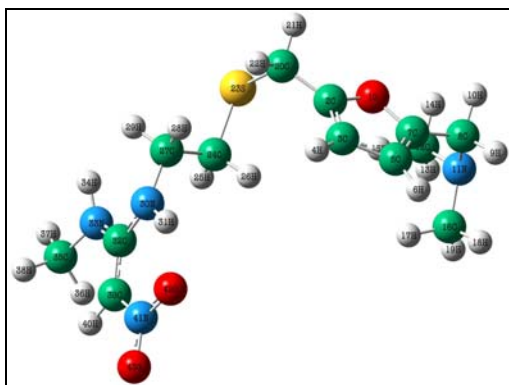


Fig. 26. Optimized geometry of neutral molecular forms of ranitidine

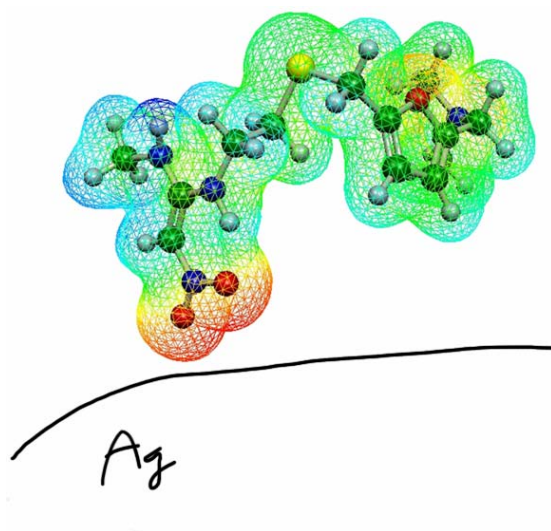


Fig. 27. Adsorption geometry of the ranitidine molecule on the silver surface

FINAL CONCLUSIONS

Three classes of metallic complexes have synthesised and characterised, having as ligands polioxotungstates, theophylline, ethylenediamine derivatives and amino acids.

The goal of the *metal–amino-acide compounds*' synthesis is their follow-up investigation regarding their antibacterian, antifungal and anticarcinogen effect. The *heteropolyoxometalates* may form complex combinations as ligands, with interesting structures and useful in the foundation of a structural physico-chemical theory. The research done in the metallic ions' complexes of pharmaceutical interest, like the *theophylline and ranitidine*, has a clear perspective regarding the growing of the efficiency and improving the action of some already known medications.

The structural characterization of these compounds with biological and pharmaceutical interest was realized by infrared spectroscopy (FT-IR), Raman spectroscopy, surface enhanced Raman spectroscopy, electronic spectroscopy in the ultraviolet and visible domain (UV-VIS) and by electron spin resonance (ESR). As confirmed both by the shape of the ESR spectra and by the values of the g parameters, we can state the followings:

- The cations **Mn²⁺**, **Co²⁺**, **Ni²⁺**, **Cu²⁺** are octahedrally coordinated in a distorted octahedral crystalline field of the $K_{10}[M^{2+}_2 Bi_2 W_{20} O_{70} (H_2O)_6] \cdot xH_2O$ complex.
- The **[Cu(th)₂(dmen)]·2H₂O (1)** compound contains the {CuN₄} chromophore with a distorted tetrahedral symmetry around the copper ion.
- The **[Cu(th)₂(tmeda)(H₂O)]·0.5H₂O (2)** and **[Cu(th)₂(dpheda)(H₂O)]·5H₂O (3)** present a pyramidal tetragonal symmetry for the {CuN₅O} chromophore.
- Pseudo-tetrahedral symmetry was observed around the Cu(II) and Zn(II) for **ML₂**, L being leucine, phenylalanine or methionine.
- Octahedral surrounding of the Co(II) was observed in case of the complexes with leucine, phenylalanine or methionine amino-acids.

The structure of the ranitidine molecule was studied by the FT-IR, FT-Raman and Raman-SERS methods. Theoretical calculations lead to different geometries for the two molecular forms of the ranitidine: neutral and protonated. From the analysis of the molecular electrostatic potential (MEP) is observed, that the negative charge is concentrated mainly on the oxygen atoms from the NO₂ group, indicating the adsorption of the molecule to the metallic surface through the oxygen atoms.

The obtained results encourage the continuation of the present research, mainly regarding the synthesis and the structural analysis of the theophylline's complexes with other transitional ions, and also of the ranitidine's complexes with Cu or Co, focusing on the improvement of the biological activity of the metallic complexes in comparison to the action of the ligand.

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