

## Abstract (En) / HABILITATION THESIS

This habilitation thesis presents the scientific activity of the candidate after he got the doctoral degree at the University of Bucharest, in 2008. The present habilitation thesis is entitled "**COMPLEX COMBINATIONS OF A NUMBER OF TRANSITIONAL METALS WITH SCHIFF BASE CLASS LIGANDS**". The thesis contains 2 chapters.

The **first chapter** describes the essential results concerning the synthesis, characterization and testing of Schiff base class ligands, as well as their complex combinations with various transitional metal ions.

**Subchapter 1.1.** contains data on "*Complex combinations with Schiff bases derived from aroylhydrazine*"; in this section metal complexes with two types of ligands are studied:

Isonicotinoylhydrazone and Benzoylhydrazone; Complex combinations with Isonicotinoylhydrazone-2,4,6-trimethylbenzaldehyde; Complex combinations with Isonicotinoylhydrazone-4-diphenylaminobenzaldehyde; Complex combinations with a Schiff-bases derived from benzoylhydrazine-*p*-substituted and 2-hydroxybenzaldehyde.

The complexes of Cu(II), Ni(II), Co(II), Mn(II), and Zn(II) with isonicotinoylhydrazone-2,4,6-trimethylbenzaldehyde (INHTB) are reported. The complexes have been characterized by analytical data, IR, UV-Vis, NMR spectra, magnetic susceptibility, thermal analysis and for the Cu(II) complex the ESR spectrum has been recorded [1].

A series of complexes of Cu(II), Ni(II), Co(II), Mn(II) and Cd(II) with isonicotinoylhydrazone-4-diphenylaminobenzaldehyde (INHDA) has been reported. The complexes have been characterized by analytical data, IR, UV-Vis, NMR spectra, magnetic susceptibility values, thermal analysis and for the Cu(II) complex the ESR spectrum has been registered [16].

A new Schiff base ligand from 2-[(1,3-benzothiazol-2-yl)sulfanyl]-N-[4-(hydrazinecarbonyl)phenyl]acetamide (BHA) and its five metal complexes with transition metal ions [Mn(II), Co(II), Ni(II), Cu(II) and Zn(II)] have been synthesized. The resulting compounds were subsequently characterized by FT-IR, UV-Vis, AAS, <sup>1</sup>H NMR, <sup>13</sup>C NMR and mass spectrometry [33].

**Subchapter 1.2.** contains results on "*Complex combinations with Schiff bases derived from 4-aminoantipyrine (4AA)*"; Complex combinations with a Schiff base derived from (4-AA), 3-hydroxy-4-nitrobenzaldehyde and acetylacetone; Complex combinations with a Schiff base derived from (4-AA), benzaldehyde and 2-amino-3-methylbutanoic acid; Schiff-based complex combinations derived from (4-AA), 3,4-dimethoxybenzaldehyde and 2-amino-benzoic acid; Complex combinations with a Schiff base derived from (4-AA) and 2-carb-aldehydefuran / 2,2'-bipyridine coligand.

A new series of transition metal complexes of Cu(II), Ni(II), Zn(II) and VO(IV), were synthesized from the Schiff base (L) derived from 4-aminoantipyrine, 3-hydroxy-4-nitrobenzaldehyde and acetylacetone. The structural features were arrived from their elemental analyses, magnetic susceptibility, molar conductance, Mass, IR, UV-Vis., <sup>1</sup>H NMR and ESR spectral studies. The nuclease activity of the above metal complexes shows that the copper and nickel complexes cleave DNA through redox chemistry, whereas other complexes are not effective [26].

The paper presents the synthesis of complex combinations of Cu(II) and Zn(II) with Schiff base obtained by the condensation reaction of 4-aminoantipyrine with benzaldehyde and 2-amino-3-methylbutanoic acid. Structural features of synthesized compounds were determined by analytical and spectral techniques. Binding of synthesized complexes with calf thymus DNA (CT DNA) was studied by spectroscopic methods and viscosity measurements [61].

A novel Schiff base has been designed and synthesized using the bioactive ligand obtained from 4-aminoantipyrine, 3,4-dimethoxybenzaldehyde and 2-aminobenzoic acid. Its Cu(II), Co(II), Ni(II), Zn(II) complexes have also been synthesized in ethanol medium. The structural features have arrived from their elemental analyses, magnetic susceptibility, molar conductance, mass, IR, UV-Vis, <sup>1</sup>H NMR and ESR spectral studies. The metal complexes have been found to promote cleavage of pUC19 DNA from the super coiled form I to the open circular form II [76].

Mn(II), Co(II), Ni(II), Cu(II), and Zn(II) mixed-ligand complexes were synthesized using 4-[(furan-2-ylmethylene)amino]-1,2-dihydro-1,5-dimethyl-2-phenyl-3Hpyrazol-3-one as the main ligand and 1,10-phenanthroline/2,2'-bipyridine as co-ligand(s). The DNA-cleavage activities of the complexes were also assessed using supercoiled pUC19 DNA and gel electrophoresis, and the results revealed that the hydroxyl radical is likely to be the reactive species responsible for the cleavage of pUC19 DNA by the synthesized complexes [91].

**Subchapter 1.3.** contains data on "*Complex combinations with Schiff bases derived from aromatic amines and thiosemicarbazine*"; Complex combinations with a Schiff base derived from 1,2-diaminobenzene and 3-benzylidenepentane-2,4-dione; Complex combinations with a Schiff base derived from *para*-dimethylaminobenzaldehyde and 1,2-diaminobenzene; Complex combinations with a Schiff base derived from 3-(2-hydroxybenzylidene)pentane-2,4-dione and 2-aminophenol; Complex combinations with a Schiff base derived from 4-morpholinacetophenone and 4-amino-5-cyanopyrimidine; Complex combinations with a Schiff base derived from curcumin and 2-aminobenzothiazole; Complex combinations with a Schiff base derived from 3-Bromo-5-Chlorosalicylaldehyde and N(4)-phenylthiosemicarbazine.

Novel Schiff base Cu(II), Ni(II), Co(II) and Zn(II) complexes have been designed and synthesized using the macrocyclic ligand derived from the condensation of diethylphthalate with Schiff base, obtained from benzene-1,2-diamine and 3-benzylidene-pentane-2,4-dione. Control experiments show inhibition of cleavage in the presence of singlet oxygen quencher like sodium azide and enhancement of cleavage in D<sub>2</sub>O, suggesting the formation of singlet oxygen as a reactive species in a type-II process [28].

Few N<sub>4</sub>O<sub>2</sub>-type mixed ligand complexes (metallointercalators) were synthesized using benzene-1,2-diamine derived Schiff base as primary ligand and 8-hydroxyquinoline as co-ligand. They were characterized by physicochemical and spectral techniques. Gel electrophoresis technique reveals that the complexes have been found to promote cleavage of pUC19 DNA from the supercoiled form to the open circular form in the presence of ascorbic acid [43].

New Schiff base complexes [Cu(L<sup>1</sup>)Cl] (1), [Ni(L<sup>1</sup>)Cl] (2), [Zn(L<sup>1</sup>)Cl] (3), and

[Fe(L<sup>2</sup>)(H<sub>2</sub>O)Cl] (4) {L<sup>1</sup> = (4E)-3-(2-hydroxybenzylidene)-4-(2-hydroxyphenylimino)pentan-2-one; L<sup>2</sup> = 2,2'-(1E,1'E)-(3-(2-hydroxybenzylidene)-pentane-2,4-diylidene)bis(azan-1-yl-1-ide)diphenol} have been synthesized and characterized by elemental analysis, UV-Vis, IR, FAB-mass, EPR, spectral studies and electrochemical studies, the ligands L<sup>1</sup> & L<sup>2</sup> were characterized by <sup>1</sup>H and <sup>13</sup>C NMR spectra. DNA cleavage studies of complexes (1) and (4) with pUC18 DNA were studied by gel electrophoresis and complex (4) cleaves supercoiled pUC18 DNA in an oxidative manner in the presence of H<sub>2</sub>O<sub>2</sub> and on photo-irradiation at 312 nm [149].

Novel Cu(II) (1) and Zn(II) (2) complexes with 4-(1-(4-morpholinophenyl)ethylideneamino)pyrimidine-5-carbonitrile (L) have been synthesized and characterized by various spectroscopic and analytical techniques. DFT (density functional theory) studies result confirms that, LMCT mechanism have been done between (L) and M(II) ions. The *in vitro* anticancer activities results show that complexes (1) & (2) have moderate cytotoxicity against cancer cell lines and low toxicity on normal cell line than ligand (L) [162].

An unique Schiff base ligand, formed by the condensation reaction of 2-aminobenzothiazole with curcumin and its Cu(II), Ni(II), Co(II) and Zn(II) complexes incorporating 2,2'-bipyridine as coligand were synthesised. They were characterized via analytical and spectroscopic methods. The gel electrophoresis results exhibit that the metal complexes cleave pBR322 plasmid DNA in presence of hydrogen peroxide effectively compared to the ligand. This exploration reveals that Cu(II) complex has a valued biological and photochemical profile [177].

Among the bio-metals, copper derivatives of O,N,S donor salicylaldehyde thiosemicarbazones have been obtained large interest due to their potential biological applications.

Multisubstituted thiosemicarbazone ligand (HL) derived, new ternary Cu(II) complexes of [Cu(L)(bpy)](1) and [Cu(L)(phen)](2) (where, bpy is 2,2'-bipyridine and phen is 1,10-phenanthroline) have been synthesized and characterized using different physico-chemical techniques. Complexes (1) and (2) are structurally characterized by single crystal X-ray diffraction analysis, which reveals the trigonal bipyramidal distorted square based pyramid geometry of both the complexes (1) and (2) [192].

**In the second chapter**, the candidate's main lines and directions concerning the development of his teaching and research career are briefly presented. From that angle, the new research topics are defined as a stimulating continuation of the studies conducted out so far.

The habilitation thesis contains, as its final part, the **bibliography**, which consists of 202 bibliographical references.