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Research Article

SCHIFF BASE METAL COMPLEXES AS ANTIOXIDANTS – A REVIEW

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ABSTRACT
Damage to cells caused by free radicals is believed to play a central role in the aging process and in disease progression. Antioxidants are our first line of defense against free radical damage, and are critical for maintaining optimum health and wellbeing. The need for antioxidants becomes even more critical with increased exposure to free radicals. Pollution, cigarette smoke, drugs, illness, stress, and even exercise can increase free radical exposure. Because so many factors can contribute to oxidative stress, individual assessment of susceptibility becomes important. Many experts believe that the Recommended Dietary Allowance (RDA) for specific antioxidants may be inadequate and, in some instances, the need may be several times the RDA. As part of a healthy lifestyle and a well-balanced, wholesome diet, antioxidant supplementation is now being recognized as an important means of improving free radical protection.This review summarizes the recent advances in the use of Schiff base metal complexes as antioxidants.

Key Words: *Antioxidant, Free Radical, Schiff Base, Cells*

INTRODUCTION

An antioxidant is any compound, whether vitamin, mineral, nutraceutical, or herb that protects against cellular damage from reactive oxygen species, including free radicals, single oxygen atoms and hydrogen peroxide. Some of the more well-known antioxidants include ascorbic acid (Vitamin C), alpha-tocopherol (Vitamin E), beta-carotene, and enzymes such as catalase, superoxide dismutase and glutathione peroxidase.

Damage to cells caused by free radicals is believed to play a central role in the aging process and in disease progression. Antioxidants are our first line of defense against free radical damage, and are critical for maintaining optimum health and wellbeing. The need for antioxidants becomes even more critical with increased exposure to free radicals. Pollution, cigarette smoke, drugs, illness, stress, and even exercise can increase free radical exposure. Because so many factors can contribute to oxidative stress, individual assessment of susceptibility becomes important. Many experts believe that the Recommended Dietary Allowance (RDA) for specific antioxidants may be inadequate and, in some instances, the need may be several times the RDA. As part of a healthy lifestyle and a well-balanced, wholesome diet, antioxidant supplementation is now being recognized as an important means of improving free radical protection.

Weglicki *et al.,* (1992) evaluated the antioxidant properties of a number of cardiovascular drugs and emphasized the importance of lipophilicity as a property contributing to antioxidant potency. They found that the specific chemical moieties of various drugs may participate in the antioxidant mechanism of action.

Murakami and Yoshino *et al.,* (2005) analyzed antioxidant action of eugenol compounds in relation to the role of transition metal Antioxidant properties of eugenol compounds can be explained by forming complexes with reduced metals. Potent inhibitory effect of isoeugenol on lipid peroxidation may be related to the decreased formation of perferryl ion or the iron-oxygen chelate complex as the initiating factor of lipid peroxidation by keeping iron at a reduced state. Inhibition of LDL oxidation by eugenol compounds is due to the suppression of free radical cascade of lipid peroxidation in LDL by reducing copper ion.

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Gacche *et al.*, (2006) evaluated in-vitro antioxidant activity of Coumarin schiff-bases (CSB) possessing different substituents on the 4-methyl-2-substituted phenyl imino-2H-chromene-7-ol molecule. The antioxidant studies of selected CSB were carried out by determining their reducing power, OH* radical scavenging activity, scavenging of stable 2, 2-diphenyl-l-picrylhydrazine (DPPH*) radical and inhibition of the polyphenol oxidase (PPO) enzyme. All the CSBs under study showed significant reducing effects. The majority of the tested CSB were found to be effective scavengers of DPPH* radical with moderate to low OH* scavenging ability and significantly inhibited the activity of PPO.

Tian-Rong *et al.*, (2007) prepared a new ligand, naringenin-2-hydroxy benzoyl hydrazone (H (5) L), by condensation of naringenin with 2-hydroxy benzoyl hydrazine. Its Cu (II), Ni (II), Zn (II) complexes had also been synthesized. In addition, in vitro antioxidant activities (superoxide and hydroxyl radical) of the free ligand and its complexes were determined. These compounds were found to possess potent antioxidant activity and be better than standard antioxidants like vitamin C and mannitol. In particular, the Cu (II) complex displayed excellent activity on the superoxide radical.

Alkan *et al.,* (2008) prepared 3-Methyl-4-(4-diethylaminobenzylideneamino)-4,5-dihydro-1H-1,2,4-triazol-5-one, 3-Ethyl-4-(4-diethylaminobenzylideneamino)-4,5-dihydro-1H-1,2,4-triazol-5-one, 3-Benzyl-4-(4-diethylaminobenzylideneamino)-4,5-dihydro-1H-1,2,4-triazol-5-one, 3-(4-Methylbenzyl)-4-(4-diethylaminobenzylideneamino)-4,5-dihydro-1H-1,2,4-triazol-5-one, 3-(4-Chlorobenzyl)-4-(4-diethylaminobenzylideneamino)-4,5-dihydro-1H-1,2,4-triazol-5-one,3-Phenyl-4-(4-diethylaminobenzylideneamino)-4,5-dihydro-1H-1,2,4-triazol-5-one,3-Cyclopropyl-4-(4-diethylaminobenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-one and 1-Acetyl-3-alkyl(aryl)-4-(4-diethylaminobenzylideneamino)- 4,5-dihydro-1H-1,2,4-triazol-5-ones.These compound were tested for their anti oxidant activity by DPPH using the method of Blois. The results exhibited that the newly synthesized compounds showed moderate activities as a radical scavenger, indicating that it has good activities as hydrogen donors.

Valentina *et al.,* (2009) prepared a series of schiff's bases of 3-substituted 1, 2, 4 triazo -5 thione (4a-e) from the ester of methyl paraben. All the compounds were evaluated for its antioxidant activity by hydrogen peroxide scavenging method. The result shows that all the compounds have good bio availability and have significant antioxidant activity. The activity was shown as IC50 value which lies between 20 to 60 μg/ml. The antioxidant activity revealed that all the tested compounds have good antioxidant activity which may be due to the presence of – SH group in the 5^{th} position.

Hossain *et al.*, (2010) synthesized nitrogen containing heterocyclic compounds such as oxindoles especially isatins (*β*-lactams). Their derivatives were investigated for their antioxidant activity by DPPH method with respect to ascorbic acid. To determine the antioxidant activity, a number of methyl/chlorinated isatins, their Schiff-bases, *spiro*-thiadiazolines and optically active phenolics of different isatins were synthesized by both microwave and conventional heating methods.

Asadia *et al.,* (2010) synthesized oxovanadium (IV) binary complexes from condensation of salicylaldehyde with aniline and its derivatives which contain schiff bases. The complexes screened for antioxidant activity, but these compounds were not able to showed antioxidant activity.

Rajasekaran *et al.*, (2011) prepared a series of some coumarinyl and chromen sulfanyl derivatives by conventional methods. The title compounds were subjected for *in vitro* antioxidant activity by 1, 1-Diphenyl-2, 2-picryl hydrazyl free radical (DPPH) method.

Kavitha *et al.*, (2011) synthesized 2- amino (4- chloro phenyl) thiazoles by brominating p-chloroaceto phenone to give p-chloro phenacyl bromide which was then reacted with thiourea in microwave synthesizer to give 2- amino (4- chloro phenyl) thiazoles (II). Later the compund II was treated with ten different substituted aryl aldehydes to yield ten new Schiff bases (III). Investigation on the antioxidant activity of these compounds was determined by DPPH assay method. Among the compounds tested, Drug SMK IIf with 4-chlorosubstitution showed better antioxidant activity with lower IC50 value 487.50 μg/ml. Drug SMK IIe with 4-hydroxy substitution and SMK IIg with 4-chlorosubstitution showed moderate activity with IC50 values 625.00 and 800.00 μg/ml, respectively.

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Zarrelli *et al.*, (2011) evaluated the antioxidant properties of the compounds in a cellular model *in vivo* and they displayed an antioxidant activity comparable to or higher than silybin and DHS, being able to prevent H_2O_2-induced generation of intracellular reactive oxygen species (ROS). Most of the derivatives also displayed a better hydrophilicity while retaining the biological activities of silybin and they might broaden the *in vivo* applications of this class of natural compounds.

Li *et al.*, (2010) evaluated the antioxidant capacities of ferrocenyl Schiff bases including *o*-(1-ferrocenylethylideneamino)phenol (OFP), *m*-(1-ferrocenylethylideneamino)phenol (MFP), and *p*-(1-ferrocenylethylideneamino)phenol (PFP) in 2,2′-azobis(2-amidinopropane hydrochloride) (AAPH), Cu^{2+}/glutathione (GSH), and hydroxyl radical (•OH)-induced oxidation of DNA, and in trapping 2,2′-diphenyl-1-picrylhydrazyl (DPPH) and 2,2′-azinobis(3-ethylbenzothiazoline-6-sulfonate) cationic radical ($ABTS^{+}$•), respectively. All the ferrocenyl Schiff bases employed herein behaved as pro oxidants in Cu^{2+}/GSH- and OH-induced oxidation of DNA except that OFP exhibited weak antioxidant activity in OH-induced oxidation of DNA. PFP, OFP and MFP can terminate about 15.2, 11.3, and 9.4 radical-chain-propagations in AAPH-induced oxidation of DNA. Especially, the introduction of ferrocenyl group to Schiff base increased the antioxidant effectiveness more remarkably than benzene-related Schiff bases.

(Kadhum et al., 2011) synthesized 3-Aminocoumarin (L) and used as a ligand for the formation of Cr (III), Ni (II), and Cu (II) complexes. The elemental analyses revealed that the complexes where M=Ni(II) and Cu(II) have the general formulae [ML(2)Cl(2)], while the Cr(III) complex has the formula [CrL(2)Cl(2)]Cl.. The free radical scavenging activity of metal complexes have been determined by measuring their interaction with the stable free radical DPPH and all the compounds have shown encouraging antioxidant activities.

Amiery *et al.*, (2012) synthesized metal complexes of (Z)-2-(pyrrolidin-2-ylidene)hydrazinecarbothioamide (L) with Cu(II), Co(II), and Ni(II) chlorides. The free-radical-scavenging ability of the metal complexes was determined by their interaction with the stable free radical 2, 2’’-diphenyl-1-picrylhydrazyl, and all the compounds showed encouraging antioxidant activities

Amiery *et al.*, (2012) synthesized, 2-(2-imino-1-methylimidazolidin-4-ylidene) hydrazinecarbothioamide (IMHC by the reaction of creatinine with thiosemicarbazide.. The free radical scavenging ability of the IMHC was determined by it interaction with the stable-free radical 2,2"-diphenyl-1-picrylhydrazyl (or nitric oxide or hydrogen peroxide) and showed encouraging antioxidant activities.

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