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REVIEW ARTICLE

Review on the Antioxidant Effect of Schiff Base Metal Complexes

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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.

KEYWORDS

Antioxidant, Schiff Base, Free Radical

INTRODUCTION

An antioxidant is a molecule capable of inhibiting the oxidation of other molecules. Oxidation is a chemical reaction that transfers electrons from a substance to an oxidizing agent. Oxidation reactions can produce free radicals. In turn, these radicals can start chain reactions. When the chain reaction occurs in a cell, it can cause damage or death. When the chain reaction occurs in a purified monomer, it produces a polymer resin, such as a plastic, a synthetic fiber, or an oil paint film. Antioxidants terminate these chain reactions by removing free radical intermediates, and inhibit other oxidation reactions.

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They do this by being oxidized themselves, so antioxidants are often reducing agents such as thiols, ascorbic acid or polyphenols. Although oxidation reactions are crucial for life, they can also be damaging; hence, plants and animals maintain complex systems of multiple types of antioxidants, such as glutathione, vitamin C, and vitamin E as well as enzymes such as catalase, superoxide dismutase and various peroxidases. Low levels of antioxidants, or inhibition of the antioxidant enzymes, cause oxidative stress and may damage or kill cells. As oxidative stress appears to be an important part of many human diseases, the use of antioxidants in pharmacology is intensively studied, particularly as treatments for stroke and neurodegenerative diseases. However, it is unknown whether oxidative stress is the cause or the consequence of disease. Antioxidants are widely used as ingredients in dietary

supplements and have been investigated for the prevention of diseases such as cancer, coronary heart disease and even altitude sickness. Although initial studies suggested that antioxidant supplements might promote health, later large clinical trials did not detect any benefit and suggested instead that excess supplementation is harmful. In addition to these uses of natural antioxidants in medicine, these compounds have many industrial uses, such as preservatives in food and cosmetics and preventing the degradation of rubber and gasoline.

Antioxidants and Free radicals

Antioxidants are intimately involved in the prevention of cellular damage -- the common pathway for cancer, aging, and a variety of diseases. The scientific community has begun to unveil some of the mysteries surrounding this topic, and the media has begun whetting our thirst for knowledge. Athletes have a keen interest because of health concerns and the prospect of enhanced performance and/or recovery from exercise. The purpose of this article is to serve as a beginners guide to what antioxidants are and to briefly review their role in exercise and general health. What follows is only the tip of the iceberg in this dynamic and interesting subject.

It's the Radicals, Man

Free radicals are atoms or groups of atoms with an odd (unpaired) number of electrons and can be formed when oxygen interacts with certain molecules. Once formed these highly reactive radicals can start a chain reaction, like dominoes. Their chief danger comes from the damage they can do when they react with important cellular components such as DNA, or the cell membrane. Cells may function poorly or die if this occurs. To prevent free radical damage the body has a defense system of antioxidants. Antioxidants are molecules which can safely interact with free radicals and terminate the chain reaction before vital molecules are damaged. Although there are several enzyme systems within the body that scavenge free radicals, the principle micronutrient (vitamin) antioxidants are vitamin E, beta-carotene, and vitamin C. Additionally, selenium, a trace metal that is required for proper function of one of the body's antioxidant enzyme systems, is sometimes included in this category. The body cannot manufacture these micronutrients so they must be supplied in the diet.

(Zhanyong Guo et. al., 2005) synthesized five kinds of Schiff bases of chitosan and carboxymethyl chitosan (CMCTS). The antioxidant activity was studied using an established system, such as superoxide and hydroxyl radical scavenging. Differences between the Schiff bases of chitosan and CMCTS were observed, which might be related to contents of the active hydroxyl and amino groups in the molecular chains.

(Tang et. al., 2007) assessed antioxidant capacities of two hydroxyl-substituent Schiff bases, 2-((o-hydroxylphenylimino)-methyl)-phenol (OSAP) and 2-((p hydroxylphenylimino)methyl)phenol (PSAP) either used alone or in combination with some familiar water-soluble antioxidants i.e. 6-hydroxyl-2,5,7,8-tetramethylchroman-2-carboxylic acid (Trolox) and L-ascorbic acid (VC), and lipophilic ones i.e.α-tocopherol (TOH) and L-ascorbyl-6-laurate (VC-12). 2,2'-Azobis(2-amidinopropane hydrochloride) (AAPH). Induced hemolysis of human erythrocytes functioned as the evaluation experimental system in this investigation. Present experiment showed that either OSAP or PSAP not only was an antioxidant with high activity in protecting erythrocytes against AAPH-induced hemolysis concentration-dependently, but can also protect erythrocytes by acting with Trolox, TOH, VC and VC-12 synergistically. Based on chemical kinetic deduction, the number of trapping peroxyl radicals, n, of the above-mentioned antioxidants were calculated in relation to Trolox which traps two peroxyl radicals. Present studied might be helpful in the pharmaceutical application of two Schiff bases.

(Krishnankutty et al., 2008) prepared two new Schiff bases containing olefinic linkages have been synthesized by condensing ortho-substituted aromatic amines with dicinnamoylmethane under specified conditions. The existence of these compounds predominantly in the intramolecularly hydrogen bonded keto-enamine form has been well demonstrated from their IR, 1H NMR and mass spectral data. Details on the formation of their complexes with Ni(II), Cu(II) and Zn(II) and their nature of bonding are discussed on the basis of analytical and spectral data.

(Hosakere et al., 2010) prepared a series of new compounds (3a-e) by condensation reaction of 3-amino-2-methyl- 4(3H) quinazolinone (AMQ) with different substituted aromatic aldehydes in methanol. The structures of the newly prepared compounds were confirmed by elemental analysis and spectrometric (IR, ^{1}H-NMR and MS) data. The compounds were also evaluated for their antioxidant activities. The result indicated that few of the synthesized compounds showed moderate to better scavenging activity.

(Shashikala et al., 2010) synthesized ethyl-3-nitronaphtho[2,1-b]furan-2-carboxylate from ethyl naphtha [2,1-b]furan-2-carboxylate. This nitro product on reactionwith hydrazine hydrate formed 3-nitronaphtho [2,1-b] furan-2-carbohydrazide. Various Schiff bases 3-nitro-N1(aryl-methylene)-substituted-naphtho [2,1-b]furan- 2-carbohydrazides were obtained by treating hydrazide with differentaldehydes. These Schiff bases on reaction with chloro acetyl chloride in presence oftriethylamine in dioxane yielded 3-nitro-N-(3-chloro-2-oxo-substituted-phenylazetidine-1-yl) naphtha [2,1-b]furan-2-carboxamides. The Schiff bases 3-nitro-N1 (aryl-methylene)-substituted-naphtho[2,1-b]furan-2- carbohydrazide, and azetidione derivatives3-nitro-N-(3-chloro-2-oxo-substituted-phenyl-azetidine-1-yl)naphtha [2,1-b]furan-2-carboxamide, had been studied for antioxidant and antimicrobial activities.

(Kumar and Rani 2011) evaluated antioxidant properties of schiff bases of nitrogen containing heterocyclic nucleus. The title compounds N1-(substituted benzilidine) – pyridin-3-yl-carbohydrazide (2a-n) were synthesized according to their standard procedures. The structures of the newly synthesized compounds have been confirmed on the basis of elemental analysis and spectral studies (IR, H^{1}NMR, C^{13}NMR and Mass). The synthesized compounds were screened for their antioxidant activity by using Nitric oxide (NO) radical scavenging. The synthesized compounds were demonstrated a significant dose dependent antioxidant activity comparable with ascorbic acid using as a standard.

(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.

(Karaoglan et al., 2010), synthesized D-π-D type Schiff base ligands and screened for their antioxidant capacity using several tests; reducing power, chelating ability on metal ions, scavenging capacity against the radicals 2,2-diphenyl-1-picrylhydrazyl, superoxide, hydroxyl, 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) and N,N-dimethyl-p-phenylenediaminedihydrochloride. The results were compared with synthetic antioxidants e.g.butylatedhydroxytoluene, butylatedhydroxy-anisole, α-tocopherol, trolox or ascorbic acid. The results indicate that the ligands have significant hydroxyl and free radical scavenging activity, metal chelating effect and reducing power against various antioxidant systems in vitro. One ligand (L2) showed excellent activity on scavenging the ABTS radical and superoxide radical. Therefore, these ligands may be a new kind of effective scavengers of reactive oxygen species.

(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.

(Liet et al., 2011) studied the antioxidant capacities of ferrocenyl Schiff bases including o-(1-ferrocenylethylideneamino)phenol (OFP), m-(1-ferrocenylethylideneamino)phenol (MFP), and p-(1-ferrocenylethylideneamino)phenol (PFP) were evaluated in 2,2′-azobis(2-amidinopropane hydrochloride) (AAPH), Cu^{2+}/glutathione (GSH), and hydroxyl radical ($^{\bullet}OH$)-induced oxidation of DNA, and in trapping 2,2′-diphenyl-1-picrylhydrazyl (DPPH) and 2,2′-azinobis(3-ethylbenzothiazoline-6-sulfonate) cationic radical ($ABTS^{+\bullet}$), respectively. OFP, MFP and PFP possessed similar activities to trap DPPH and $ABTS^{+\bullet}$. All the ferrocenyl Schiff bases employed herein behaved as prooxidants in Cu^{2+}/GSH- and $^{\bullet}OH$-induced oxidation of DNA except that OFP exhibited weak antioxidant activity in $^{\bullet}OH$-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

(Gwaram et al., 2012) synthesized some novel ketone derivatives of gallichydrazide-derived Schiff bases and examined for their antioxidant activities and in vitro and in silicoacetyl cholinesterase inhibition. The ferric reducing antioxidant power (FRAP) and 2,2-diphenyl-1-picrylhydrazyl (DPPH) assays revealed that all the compounds have strong antioxidant activities. N-(1-(5-bromo-2-hydroxyphenyl)-ethylidene)-3,4,5-trihydroxybenzohydrazide (2) was the most potent inhibitor of human acetylcholinesterase, giving an inhibition rate of 77% at 100 μM. Molecular docking simulation of the ligand-enzyme complex suggested that the ligand may be positioned in the enzyme's active-site gorge, interacting with residues in the peripheral anionic subsite (PAS) and acyl binding pocket (ABP). The current work warrants further preclinical studies to assess the potential for these novel compounds for the treatment of AD.

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