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Comparison of Protective Effects between Cultured *Cordyceps militaris* and Natural *Cordyceps sinensis* against Oxidative Damage

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The Chinese herb DongChong-XiaCao originating from *Cordyceps sinensis* is widely used as a traditional medicine in China for treatment of a wide variety of diseases. The extracts of *Cordyceps sinensis* (CSE) and *Cordyceps militaris* (CME) are well-known for their biological effects. In the present study, the antioxidant efficiency of CME and CSE in protecting lipid, protein, and low-density lipoprotein (LDL) against oxidative damage was investigated. CME and CSE showed weakly inhibitory effect on liposome oxidation, that of CME being superior to that of CSE. As for the protein oxidation model system, the inhibitory effect of CME on protein oxidation was inferior to that of CSE. CME and CSE at 1.0 mg/mL showed 50.5 and 67.1% inhibition of LDL oxidation, respectively. The contents of bioactive ingredients cordycepin and adenosine in CME are higher than those of CSE; however, both cordycepin and adenosine showed no significant antioxidant activity as determined by the Trolox equivalent antioxidant capacity method. Polyphenolic and flavonoid contents are 60.2 and 0.598 μg/mL in CME and 31.8 and 0.616 μg/mL in CSE, respectively, which may in part be responsible for their antioxidant activities. In addition, a polysaccharide present in CME and CSE displayed antioxidant activity, which suggested that the activity might be derived partly from polysaccharides of CME and CSE. The tendency to scavenge the $ABTS^{\bullet+}$ free radical and the reducing ability of CME and CSE display concentration-dependent manners, suggesting that CME and CSE may be potent hydrogen donators. On the basis of the results obtained, the protective effects of CME and CSE against oxidative damage of biomolecules are a result of their free radical scavenging abilities.

KEYWORDS: Oxidative damage; *Cordyceps militaris*; *Cordyceps sinensis*; low-density lipoprotein; cordycepin; adenosine; scavenging free radical

INTRODUCTION

Oxidative stress attributed to free radicals and reactive oxygen species (ROS) has been broadly recognized as a contributor to cellular necrosis and a variety of pathological conditions such as cancer, degenerative disease in neurons, hepatopathies, atherosclerosis, and even aging (*1*). Numerous epidemiology studies have shown an inverse association between diets rich in fruits and vegetables and several degenerative diseases (*2*); possible reasons for this observation are the fact that polyphenolics and bioactive compounds possessing biological effect are present in fruits and vegetables (*3*−*5*). In addition, herbs have been proven to contain polyphenolics and bioactive compounds (*6*). This has led to a number of investigations in the study of protective actions on free radicals and ROS. In particular, research on the dietary intake of antioxidative compounds and the assay of the natural antioxidant source has recently drawn much attention.

DongChong-XiaCao in Chinese translates as "winter worm and summer grass", which is derived from the larva of *Hepialus armoricanus* infected by entomopathogenic fungi such as *Cordyceps*, *Paecilomyces*, *Torrubiella*, and *Podonectria* (*7*). The fungus naturally grows and multiplies in the host by yeast-like budding in the autumn, killing the host. Following overwintering, the fungus ruptures the host body, forming a sexual sporulating structure, called a stroma, that is connected to the dead larva and grows upward to emerge above the ground the next summer. This stroma with or without larva is traditionally used as a therapeutic agent in oriental countries (*8*). Among the fungi infected in *Hepialus*, *Cordyceps sinensis* has received tremendous attention so far. It is used not only as a tonic food but also as a restorative drug (*7*). There are many reports in the

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literature about the biological actions of *C. sinensis* including aphrodisiac (*9*), analgesic (*10*), antitumor (*11*), and hypotensive and vasorelaxant activities (*12*), free radical scavenging (*13*), and immune modulation (*14*). Meanwhile, *Cordyceps militaris*, which is an entomogenous fungus, has received increased attention in recent years due to the recognition that it has biological effects with health-stimulating properties and medicinal effects. For example, *C. militaris* displayed antifibrotic action on fibrotic rats, enhanced the forced swimming capacity, and inhibited proliferation of cultured human glomerular mesangial cells (*15*−*17*). In addition, a polysaccharide isolated from *C. militaris* showed anti-inflammatory activity and suppressed the humoral immunity (*18*).

Recently, naturally occurring compounds with antioxidant properties have received much attention as a result of their inhibition of oxidative stress. With respect to antioxidant activity in *Cordyceps*, *C. sinensis* has been shown to display antioxidant activity (*13*, *19*). However, the literature describing the antioxidant activity of *C. militaris* is limited. Thus, the antioxidant action of *C. militaris* remains largely unknown. Moreover, natural *C. sinensis* is scarce in nature and high in price; therefore, DongChong-XiaCao derived from fermentation with *C. militaris* is found in markets. Therefore, the aim of the present study was to compare the antioxidant actions of *C. militaris* and *C. sinensis*, which is well-known as a folk tonic food and high in price.

MATERIALS AND METHODS

Chemicals. Lecithin, tocopherol (Toc), and Trolox were purchased from Merck (Darmstadt, Germany). Butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) were purchased from Aldrich (Los Angeles, CA).

Sample Preparation. *C. sinensis* and *C. militaris* were kindly donated by the Iso-Green Biotechnology Co. Ltd., Danshui Town, Taiwan. Samples of *C. sinensis* (CS) and *C. militaris* (CM) were dried at 50 °C for 48 h and pulverized. Approximately 5.0 g of the samples was mixed with 100 mL of 60 °C water for 30 min, respectively. Then the filtrate was freeze-dried and weighed. These final freeze-dried samples (1.98 and 2.79 g for CS and CM, respectively) were designated water extracts of *C. sinensis* (CSE) and *C. militaris* (CME), respectively.

Determination of Protective Effect on Liposome and Low-Density Lipoprotein (LDL) Oxidation. Lecithin (580 mg) was sonicated in an ultrasonic cleaner (Branson 8210, Branson Ultrasonic Corp., Danbury, CT) in 58 mL of 10 mM phosphate buffer (pH 7.4) for 2 h in an ice-cold water bath. The sonicated solution (10 mg of lecithin/mL), $FeCl_3$, ascorbic acid, and samples (0−1.5 mg/mL) were mixed to produce a final concentration of 100 μM $FeCl_3$, and 100 μM ascorbic acid. The mixture was incubated at 37 °C for 1 h.

Human LDL (d = 1.02−1.06 g/mL) was prepared from fasting plasma, routinely pooled from healthy normolipemia individuals. Lipoproteins were isolated by sequential preparative ultracentrifugation and dialyzed overnight as previously described (*20*). Freshly prepared native LDL (0.1 mg/mL) was treated with 10 μM $CuSO_4$ and in the presence of samples (0−1.0 mg/mL) or not for up to 24 h at 37 °C; oxidation was stopped by the addition of BHT.

After incubation, the oxidation of both liposome and LDL was analyzed according to the thiobarbituric acid (TBA) method (*21*). The absorbance of the samples was read at 535 nm against a blank, which contained all reagents except lecithin and LDL, respectively. The results were expressed as percentage inhibition of liposome and LDL oxidation.

Determination of Protective Effects on Protein Oxidation. The effects of samples on protein oxidation were carried out according to the previously described method (*22*). The reaction mixture (1.2 mL), containing samples (0−400 μg/mL), phosphate buffer (20 mM, pH 7.4), bovine serum albumin (20 mg/mL), $FeCl_3$ (400 μM), H_2O_2 (3 mM), and ascorbic acid (400 μM), was incubated for 1 h at 37 °C, and 1 mL of 20 mM dinitrophenyl hydrazine (DNPH) in 2 M HCl was added to the reaction mixture. A total of 1 mL of cold trichloroacetic acid (20%, w/v) was added to the mixture and centrifuged at 3000*g* for 10 min. The protein was washed three times with 2 mL of ethanol/ethyl acetate (1:1, v/v) and dissolved in 2 mL of 6 M guanidine−HCl (pH 6.5). The absorbance of the sample was read at 370 nm.

Determination of Antioxidant Ability by Trolox Equivalent Antioxidant Capacity (TEAC) Method. The total antioxidant activities of samples was measured using the TEAC assay as described by Miller et al. (*23*) with minor modification. The TEAC value is based on the ability of samples to scavenge the blue-green $ABTS^{\bullet+}$ radical cation relative to the ability of the water-soluble vitamin E analogue 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (Trolox). $ABTS^{\bullet+}$ is generated by the interaction of ABTS (100 μM), H_2O_2 (50 μM), and peroxidase (4.4 units/mL). After 1 mL of $ABTS^{\bullet+}$ was added to samples (0−4000 μg/mL) or Trolox, the absorbance at 734 nm was recorded after 10 min of incubation. The radical-scavenging capacity was plotted as a function of concentration, and the TEAC was calculated against a Trolox calibration curve. The higher the TEAC value of a sample, the stronger the antioxidant activity.

Determination of Total Phenolic Compounds. The concentration of total phenolic compounds was measured according to the method of Taga et al. (*24*) and calculated using gallic acid as standard. A sample (0.2 mL) was added to 2 mL of 2% Na_2CO_3. After 2 min, 0.1 mL of Folin−Ciocalteu reagent (50%) was added to the mixture, which was then left for 30 min. Absorbance was measured at 750 nm and compared to a gallic acid calibration curve.

Determination of Flavonoid Content. The spectrophotometric assay for the quantitative determination of flavonoid content was carried out as described by Hairi et al. (*25*). The samples (1 mL, 4 mg/mL) were incubated with 100 μL of 1% 2-aminoethyl diphenylborate solution for 20 min. The absorption was measured at 404 nm, and the amount of flavonoids in samples (in rutin equivalents) was calculated.

Determination of Polysaccharide Content. The isolation of polysaccharides was done as previously described (*26*). In brief, dried pulverized CS and CM (25 g) were defatted by using a Soxhlet apparatus with ether (250 mL) and then extracted with aqueous 80% alcohol (250 mL) for 24 h. After filtration, the residues were mixed with 80 °C water (500 mL) for 2 h and re-extracted under the same condition. The combined filtrates were evaporated to a final volume of 100 mL. These concentrated filtrates were then mixed with 4:1 v/v chloroform/isopentanol (100 mL) to deproteinize. After filtration, the filtrates were mixed with 4 volumes of absolute ethanol for 24 h to precipitate polysaccharide compounds. After centrifugation, the resulting precipitates were collected and washed with acetone. These final polysaccharide samples (0.25 and 0.74 g for CS and CM, respectively) were designated PCS and PCM.

Determination of Reducing Power. The reducing power of the samples was determined according to the method of Oyaizu (*27*). Samples (0−1.0 mg/mL) in phosphate buffer (1.0 mL, 0.2 M, pH 6.6) were added to potassium ferricyanide (1.0 mL, 10 mg/mL), and the mixture was incubated at 50 °C for 20 min. Then trichloroacetic acid (1.0 mL, 100 mg/mL) was added to the mixture, which was then centrifuged at 600*g* for 10 min. The supernatant (1.0 mL) was mixed with distilled water (1.0 mL) and ferric chloride (0.2 mL, 1.0 mg/mL), and then the absorbance was read at 700 nm. Higher absorbance of the reaction mixture indicated greater reducing power.

High Performance Liquid Chromatography. 3′-Deoxyadenosine (cordycepin), adenine, adenosine, uracil, and uridine in samples of CME and CSE were analyzed by HPLC (*28*). The HPLC analyses were conducted with a Hitachi HPLC system consisting of a pump (L-7100), a UV detector (L7420), an autosampling valve (L-7200) equipped with a sample loop of 10 μL used for sample injection, and Hitachi D-7000 HSM software for data analysis. The detection wavelength was set at 260 nm. The C18 column (5 μm, 250 × 4.6 mm i.d.) was a Thermo Hypersil ODS. The optimum resolution was obtained by using a linear isotonic elution. The mobile phase consisted of disodium hydrogen phosphate buffer (pH 6.0) and methanol in the ratio 85:15 (v/v). The flow rate was 1 mL/min.

Statistical Analysis. Statistical analysis involved the use of the Statistical Analysis System software package. All data were recorded as means ± standard deviation (SD). Analysis of variance was

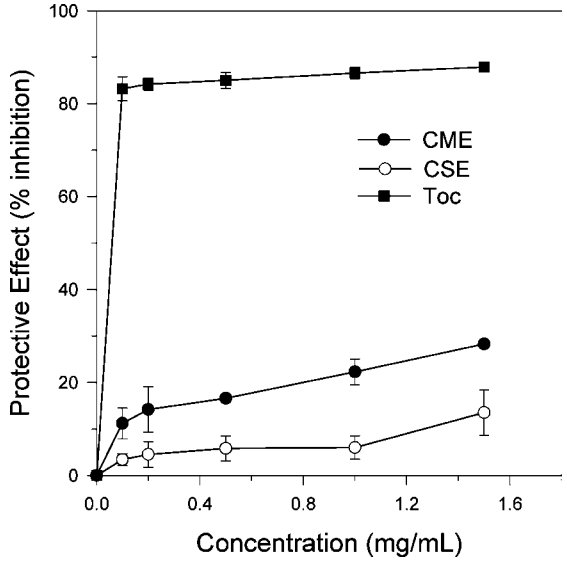

Figure 1. Inhibitory effect of water extracts of *C. militaris* (CME) and *C. sinensis* (CSE) and in liposome peroxidation. Tocopherol (Toc) was used as a positive control. The data are displayed as mean ± SD ($n = 3$). Results were analyzed by ANOVA ($p < 0.05$).

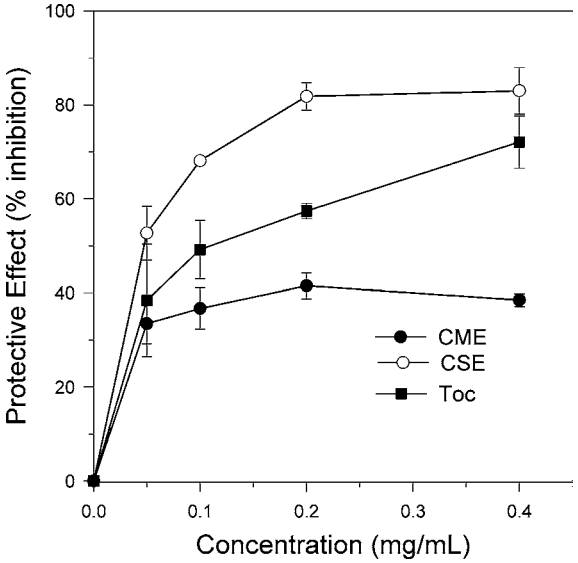

Figure 2. Inhibitory effect of water extracts of *C. militaris* (CME) and *C. sinensis* (CSE) on albumin oxidative damage. Tocopherol (Toc) was used as a positive control. The data are displayed as mean ± SD ($n = 3$). Results were analyzed by ANOVA ($p < 0.05$).

performed by ANOVA procedures. Significant differences between means were determined by Duncan's multiple-range tests at a level of $p < 0.05$.

RESULTS AND DISCUSSION

Lipid plays a crucial role in the metabolism of cells by providing a source of energy and reserved storage materials. As lipids oxidize, they form hydroperoxides, which are susceptible to further oxidation or decomposition to secondary reaction products (*29*). Subsequently, these compounds negatively affect nutritional value and are toxic to the cells. Therefore, protecting the lipid against oxidative damage draws much attention from investigators.

Figure 1 shows the inhibitory effect of CME and CSE in liposome peroxidation, as compared with tocopherol (Toc). CME and CSE in the range of 0−1.5 mg/mL showed weakly inhibitory effects on liposome peroxidation. CME and CSE, at 1.0 mg/mL, showed 22.3 and 6.0% inhibitory effects on liposome peroxidation, which are less than the same concentration of Toc (86.6%). Apparently, CSE displayed only a negligible effect on liposome peroxidation. The inhibitory effect of CME on liposome peroxidation was higher than that of CSE; however, CME and CSE showed relatively weak inhibition of liposome peroxidation as compared to Toc. Although the inhibitory effect of CME on liposome peroxidation was less than that of Toc, CME may be expected to protect against damage to cell membranes, because it reduces the level of lipid peroxides

The inhibitory effect of CME and CSE on albumin oxidative damage is shown in **Figure 2**. The inhibitory effect of CME and CSE in the range of 0−0.2 mg/mL on protein oxidation shows a concentration-dependent manner. No significant difference ($p > 0.05$) was found between 0.2 and 0.4 mg/mL of CME and CSE. Obviously, the protective effect of CME on protein oxidation was weaker than that of CSE. In addition, the protective effect of CSE on protein oxidation is higher than those of Toc and CME. This finding reveals that different components causing the different protective effects on protein oxidation may be present in CME and CSE. Protein oxidation may be an exothermic process; amino acid residues of proteins are susceptible to attack by free radical, subsequently leading to aggregation, fragmentation, and amino acid modification (*30*). In addition, higher levels of protein oxidation were found in the hippocampus of Alzheimer's patients (*31*). Spina and Cohen (*32*) noted that an increase of H_2O_2 production in striatal neurous leads to increased protein oxidation in this region. Felton (*30*) reported that all amino acid residues of protein are susceptible to ROS, and therefore their structure and function can be altered. In addition, during aging or under conditions of oxidative stress, lipofuscin (a peroxidized lipid−protein aggregate) is accumulated as a result of declines in antioxidant defenses or loss of repair function (*33*). In other words, the more antioxidants contained in the diet, the greater is the protective efficiency against oxidative stress. According to the data in **Figure 2**, CME and CSE have inhibitory effects on oxidative damage and stabilize protein against oxidation. This finding implies that CME and CSE may be used as resources in attempts to protect against oxidative stress in human disease.

Figure 3 shows the protective effect of CME and CSE on LDL oxidation. The inhibitory effect of samples was compared at the same concentrations (200 and 1000 μg/mL). At 200 μg/mL, Toc and CSE had negligible effects on LDL oxidation; however, CME showed 19.2% inhibition of LDL oxidation. When evaluated at addition levels of 1000 μg/mL, there was no significant difference ($p > 0.05$) between Toc and CME, but significant differences ($p < 0.05$) were found between CSE and both Toc and CME in the inhibition of LDL oxidation. LDL is the main cholesterol-carrying lipoprotein in plasma. The rich level of unsaturated fatty acid in LDL is very susceptible to oxidative degeneration under oxidizing conditions in the circulation. Consequently, several clinical and experimental investigations have firmly shown a correlation between raised levels of oxidized LDL and the onset of atherosclerosis (*34*, *35*). In the present study, CME and CSE showed comparable inhibitory effects on LDL oxidation, indicating that CME and CSE are potent inhibitors of LDL oxidation. Therefore, we suggest that CME and CSE are likely to attenuate the attack of atherogenicity as a result of protective effect on LDL oxidation. In other words, CME and CSE that protect LDL against oxidation may help to prevent atherosclerosis and coronary heart disease.

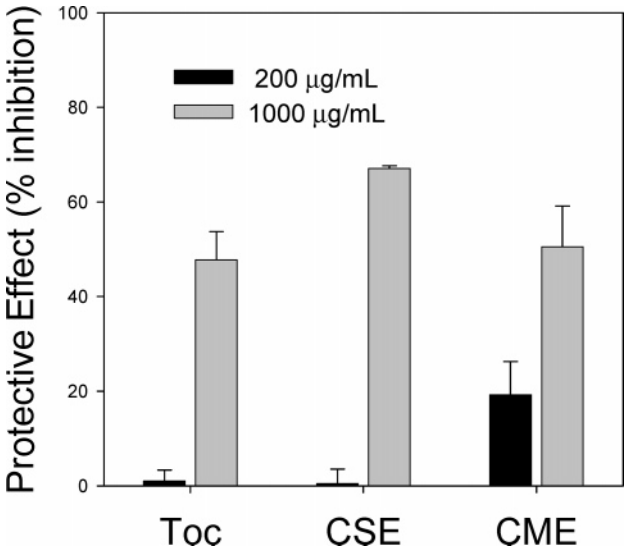

Figure 3. Protective effect of water extracts of *C. militaris* (CME) and *C. sinensis* (CSE) on copper-induced low-density lipoprotein (LDL) oxidation. Tocopherol (Toc) was used as a positive control. The data are displayed as mean ± SD ($n = 3$). Results were analyzed by ANOVA ($p < 0.05$).

Adenosine and cordycepin isolated from *Cordyceps* have shown biological activity (*36*). Adenosine has merit as a cardioprotective and therapeutic agent against chronic heart failure (*37*). Cordycepin displays antileukemic activity against terminal deoxynucleotidyl transferase-positive (TdT+) leukemic cells (*38*). Besides these, little information is available about the antioxidant activity of the bioactive components in CSE and CME. In the present study, the bioactive components were determined. The analytical plot is shown in **Figure 4**. Five components were identified as uracil, uridine, adenine, adenosine, and cordycepin. As can be seen in **Figure 4**, adenosine and cordycepin are present as major compounds. **Table 1** shows the levels of adenosine and cordycepin in CME and CSE. Obviously, trace amounts of cordycepin and adenosine were present in CSE; however, the levels of cordycepin and adenosine in CME were 29.4- and 7.7-fold higher as compared to those in CSE, respectively.

The literature is replete with studies on the biological activities of adenosine and cordycepin. However, little information about their antioxidant activities has been found so far. The antioxidant activities of the bioactive components uracil, uridine, adenine, adenosine, and cordycepin in CSE and CME in an aqueous system were determined according to the TEAC method. At 400 μg/mL, the TEAC values (μg/mL) for uracil, uridine, adenosine, and cordycepin were 1.8 ± 0.6, 2.0 ± 0.9, 2.5 ± 1, and 2.1 ± 0.8, respectively. The TEAC (μg/mL) value for 100 μg/mL of adenine was 4.2 ± 1.1, and adenine at higher concentration was unable to dissolve in the TEAC test system. Apparently, these samples showed nearly no scavenging effect on ABTS radicals, indicating that the bioactive components mentioned above are unable to contribute to the antioxidant activities of CME and CSE.

Polyphenolics are commonly called hydrogen-donating antioxidants because they donate hydrogens in the active hydroxyl groups to form resonance-stabilized phenoxyl radicals. In addition, polyphenolics exhibited antioxidant activity and other biological activities due to scavenging of ROS and chelating of metal ions. To explore the mechanism of antioxidative action of CME and CSE, the contents of flavonoids and polyphenolics in CME and CSE were determined. The contents of flavonoids and polyphenolics are 0.598 and 60.2 μg/mL in CME and 0.616 and 31.8 μg/mL in CSE, respectively. The level of flavonoid in CSE is slightly higher than that in CME; however, the level of polyphenolics in CME is 1.9-fold compared to that in the CSE. Flavonoids and polyphenolics are present in CME and CSE; the levels of both compounds in samples are relatively small compared to the results of our previous studies, which showed levels of polyphenolics at 415.3, 229.5, 164.5, 21.6, 17.2, and 238.7 mg/mL for green tea (*39*), pu-erh tea (*39*), black tea (*39*), roasted coffee (*40*), flower of *Chrysanthemun morifolium* Ramat. (*41*), and water extracts of Hsian-tsao (*Mesona procumbens* Hemsl.) (*42*). Although polyphenolics possess antioxidant activity, the protective effect of CME and CSE on oxidative damage could not be solely attributed to their phenolic content due to the low level of polyphenolics in CME and CSE. In addition, the levels of polyphenolics in CME are higher than

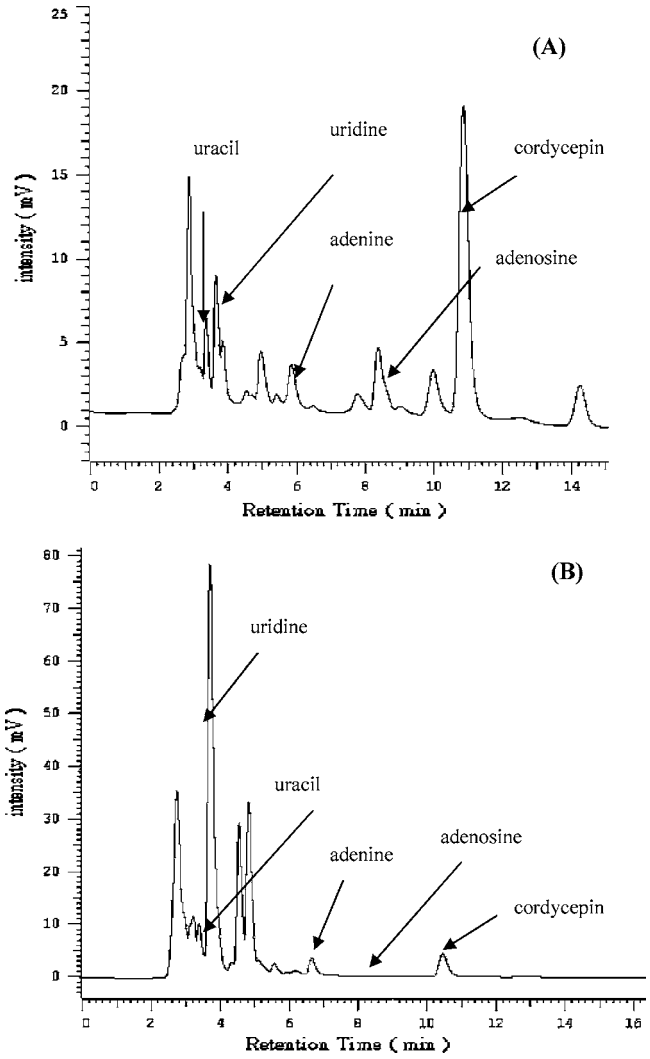

Figure 4. HPLC chromatogram of water extract of (**A**) *C. militaris* (CME) and (**B**) *C. sinensis* (CSE).

Table 1. Contents of Adenosine and Cordycepin in Water Extract of *C. militaris* (CME) and *C. sinensis* (CSE)[a]

sample	adenosine (mg/g of extract)	cordycepin (mg/g of extract)
CME	1.385 ± 0.09a	7.652 ± 0.88a
CSE	0.180 ± 0.016b	0.260 ± 0.04b

[a] The data are displayed as mean ± SD ($n = 3$). Values with different letters in a column are significantly different ($p < 0.05$).

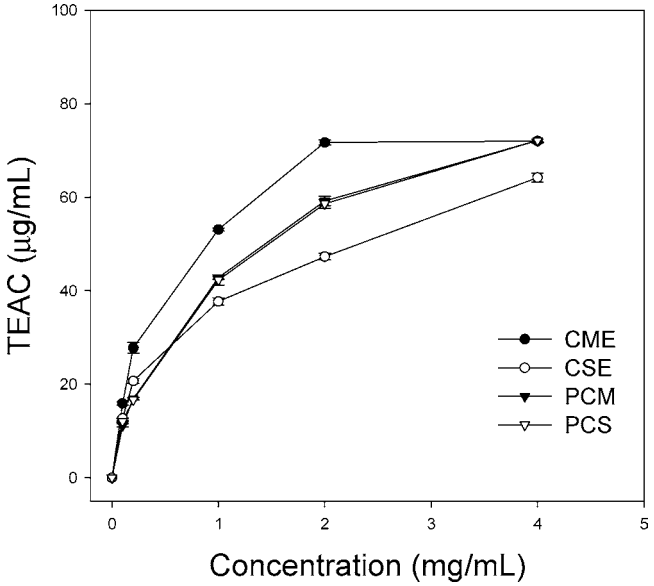

Figure 5. Total antioxidant activity of water extract of *C. militaris* (CME) and *C. sinensis* (CSE), polysaccharide in CM (PCM) and CS (PCS), determined by TEAC method. TEAC is the concentration of Trolox solution (μg/mL) having the antioxidant capacity equivalent to a μg/mL solution of the sample under investigation. The data are displayed as mean ± SD ($n = 3$). Results were analyzed by ANOVA ($p < 0.05$).

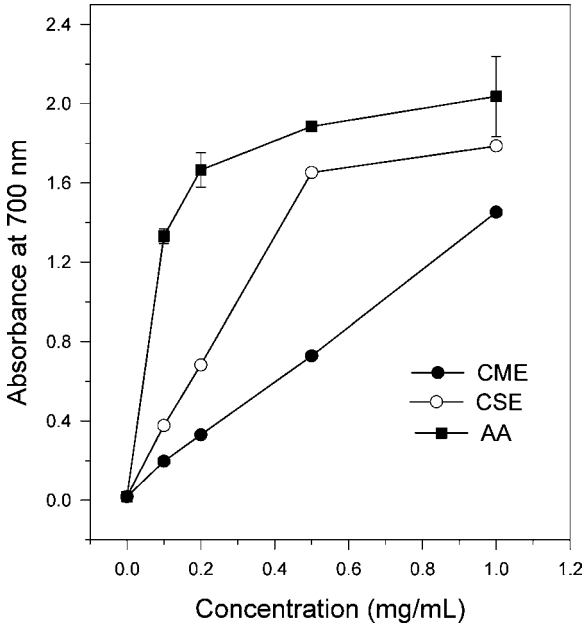

Figure 6. Reducing ability of water extracts of *C. militaris* (CME) and *C. sinensis* (CSE). Ascorbic acid (AA) was used as a positive control. The data are displayed as mean ± SD ($n = 3$). Results were analyzed by ANOVA ($p < 0.05$).

in CSE; however, the protective effect on protein oxidation and on LDL oxidation is somewhat less than that shown by CSE, indicating that the amount of phenolic compounds is not the only factor in the consideration of antioxidant activity.

To further explore the role of active components in the antioxidant activity of CME and CSE, a polysaccharide from CME and CSE was isolated. **Figure 5** shows the antioxidant activity of a polysaccharide isolated from CME and CSE, determined by using the TEAC method. The polysaccharide of CME and CSE in the range of 0−4.0 mg/mL showed antioxidant activity, which increased with increasing concentration of the samples. These findings implied that a polysaccharide in CME and CSE displayed antioxidant activity. This result is in agreement with the report of Li et al. (*43*), who noted that a polysaccharide containing glucose, mannose, and galactose isolated from *C. sinensis* showed antioxidant activity. Therefore, we suggest that the antioxidant activity of CME and CSE might be in part derived from polysaccharides in CME and CSE.

Moreover, to clarify how the extracts contribute to antioxidant activity, the TEAC method was selected for the present study as a model. **Figure 5** also shows the measurements of the antiradical capacity of CME and CSE in an aqueous system by measuring the scavenging ABTS radicals. CME and CSE in the range of 0−4.0 mg/mL displayed antiradical activity, and the antiradical activity of these samples increased with increasing concentration of the extracts, indicating that CME and CSE showed scavenging activity on free radicals. As can be seen in **Figure 5**, the scavenging activity of CME on free radical was superior to that of CSE. In addition, CME showed marked scavenging effect on free radicals determined through TEAC. However, Won and Park (*44*) noted that CME was weak in scavenging the DPPH radical, a stable hydrophobic free radical. In the present study, CME and CSE in aqueous system showed remarkable scavenging effects on the $ABTS^{\bullet+}$ free radical, a stable hydrophilic free radical. It is suggested that the reason for this is that CME and CSE in the hydrophilic system are more effective in scavenging free radicals than CME and CSE in the hydrophobic system. According to the TEAC method, CME and CSE acted as a direct free radical scavenger, indicating that CME and CSE had significant antiradical activity.

Figure 6 shows the reducing ability of CME and CSE. The reducing ability of CME and CSE increased with increased concentration of samples. Thus, CME and CSE are good electron donors and may terminate the radical chain reaction by converting free radicals to more stable products. Tanaka et al. (*45*) noted that the antioxidant property is concomitant with the development of reducing ability. The findings suggested that CME and CSE exhibited remarkable reducing abilities, which may be attributed to reductones present in CME and CSE, and reacted with free radicals to stabilize and terminate radical chain reactions. In general, on the basis of the data obtained, the antioxidant action of CME and CSE in a hydrophilic system (protein and reducing ability) is superior to that in a hydrophobic system (liposome and LDL oxidation).

Bioactive compounds and phytochemicals in natural substances such as fruits and vegetables have been recognized to possess multifunctional properties (*46*). Oxidative stress causes lipid, protein, and DNA peroxidation in all classes of organic molecules and results in degenerative disorders (*47*). Thus, diets rich in naturally occurring antioxidants and phytochemicals in fruit and vegetable agents may reduce the risk of oxidative stress-induced chronic diseases.

In conclusion, our results showed that the biological effect of CME in the inhibition of liposome oxidation was superior to that of CSE; however, its inhibition of protein oxidation was inferior to that of CSE. The levels of polyphenolics and bioactive components such as cordycepin and adenosine in CME were higher than those in CSE. Polyphenolics, polysaccharides, and some unknown bioactive compounds present in CME and CSE appear to be major contributors of antioxidant phytochemicals. This observation may partly be responsible for the biological effects of CME and CSE. Therefore, additional consumption of CME and CSE may increase the levels of phytochemicals and enhance therapeutic effects in human diseases related to oxidative stress.

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