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Original Research Article

Effect of Cinnamon Extract on the Inflammatory Response in the LPS-shock Rat

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Abstract - This study measured the plasma and liver concentrations of cytokines, the distribution of blood lymphocyte subpopulations (CD4 and CD8), plasma levels of nitrite (NO_3^-) and nitrate (NO_2^-), intercellular adhesion molecule 1 (ICAM-1), cytokine-induced neutrophil chemoattractant 1 (CINC-1), prostaglandin E2 (PGE2), and peritoneal lavage fluid (PLF) levels of monocyte chemotactic protein 1 (MCP-1) and CINC-1 in order to examine the anti-inflammatory activity of the cinnamon extract in lipopolysaccharide (LPS)-exposed rats. The plasma concentrations of interleukin (IL)-1β, IL-6, and tumor necrosis factor α (TNF-α) were lower in the cinnamon extract groups than in the control group at both 2 and 5 h after LPS injection. Furthermore, the liver concentrations of IL-1β, IL-6, and TNF-α were lower in the cinnamon extract groups than in the control group at 5 h after LPS injection. Plasma IL-10 concentrations were higher in the cinnamon extract groups than in the control group at both 2 and 5 h after LPS injection, and liver concentrations of IL-10 did not differ significantly among all treatment groups at 5 h after LPS injection. The distribution of CD4 tended to increase, and that of CD8 tended to decrease in the cinnamon extract groups. The CD4/CD8 ratio was increased in the cinnamon extract groups. The plasma concentrations of NO_3^-/NO_2^-, ICAM-1, CINC-1, and PGE2 and the PLF concentrations of MCP-1 and CINC-1 exhibited a tendency to decrease in the cinnamon extract groups. These results indicate that cinnamon extract can exert functional anti-inflammatory effects.

Key words - Cinnamon extract, Lipopolysaccharide, Anti-inflammatory, Cytokine, Lymphocyte subpopulations

Introduction

Under inflammatory conditions, macrophages, and neutrophils secrete several mediators, including eicosanoids, oxidants, cytokines, and lytic enzymes, that are responsible for the initiation, progression, and persistence of an acute or chronic state of inflammation (Lefkowitz *et al*., 1999). Prostaglandin E2 (PGE2) is an eicosanoid that induces the production of chemoattractants and proinflammatory cytokines (Harris *et al*., 2002). The oxidant nitric oxide (NO) is an expander, and increases the vascular permeability and edema formation at the site of inflammation (Moncada *et al*., 1991). Monocyte chemotactic protein 1 (MCP-1) is a chemotactic and activating factor for mononuclear phagocytes; it is also involved in the recruitment of peripheral blood leukocytes to the peritoneal cavity (Matsukawa *et al*., 1999). Inflammation shock causes the induction of a series of proinflammatory cytokines, such as interleukin (IL)-1β, tumor necrosis factor (TNF-α), IL-8 or IL-6, and anti-inflammatory cytokines such as the IL-1 receptor antagonists (RAs) and IL-10 (Hudson *et al*., 1995; Gabby and Kushner, 1999). Lipopolysaccharides (LPS) are structural components of the outer membranes of Gram-negative bacteria and are associated with tissue injury and fatal outcome in inflammation shock. Pro-inflammatory cytokines such as IL-1β, TNF-α, IL-8 or IL-6, and anti-inflammatory cytokines, such as IL-1 RAs and IL-10, are produced in response to LPS (Luster *et al*., 1994; Aono *et al*., 1997; Ayala *et al*., 1994).

While numerous traditional oriental medicines (natural compounds) have been investigated for their anti-inflammatory effects, such as san-huang-xie-tang (a combination of coptis and rhubarb) (LO *et al*., 2005), *Scutellariae radix* (Lee, 2007), *Clematis mandshurica* Rupr (Park *et al*., 2006), *Quercus infectoria* (Gurpreet Kaur *et al*., 2004), *Morus alba* L. (Cho and An, 2008), and *Torilis japonica* (Kim, 1993), no satisfactory results have been reported. Anti-inflammatory medicines with fewer adverse effects and better curative properties are

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required.

Cinnamon, which is the dried bark of the *Cinnamomum cassia* tree, is used in oriental medicine prescriptions to treat headache, fever, anorexia, palpitations, and cold therapy (Chang *et al*., 1998; Youk, 1990). The major components of cinnamon, compounds of cinnamon aldehyde, are currently used in beverages, toothpaste, cosmetics, and as a remedy for bad breath. Cinnamon is known to possess antiulcer (Shigeo *et al*., 1989), anticancer (Chung *et al*., 1999), antibacterial (Bang *et al*., 1997; Jeong *et al*., 1998; Yang *et al*., 2001), and antiallergy properties (Park *et al*., 2001), and to induce the expression of immune-enhancing antibodies (Lee *et al*., 1999). These properties suggest that cinnamon could affect immune function.

Therefore, the aim of this research was to determine whether cinnamon could be used a basis for developing a new anti-inflammatory medicine by determining the anti-inflammatory effects of cinnamon extract. To this end, the anti-inflammatory effects of cinnamon extract were assessed in rats with LPS.

Materials and Methods

Animals and treatment

Thirty-two male, Sprague-Dawley rats with a body weight of 207.39 ± 7.25 g (mean ± SD, 8 weeks) were used in this study. They were housed in a temperature- and humidity-controlled environment and were allowed free access to a basal diet for 1 week before the experiment, and had free access to water ad libitum throughout the experiment. The rats were randomly assigned to one of the following four groups (n = 8/group) according to the administered concentration of cinnamon extract (or normal saline): (1) control group, normal saline at 100 ㎎/㎏; (2) cinnamon extract 100 ㎎/㎏; or (3) cinnamon extract 200 ㎎/㎏; cinnamon extract 300 ㎎/㎏.

Experimental diet and water

The diet (Table 1) and water were provided ad libitum for the 4-week experimental period.

Cinnamon extract

Cinnamon (dried weight: 500 g) was divided and extracted three times for 5 h each time in a cooling water reflux cistern, concentrated through decompression, and produced as an ethanol extract (137 g). Cinnamon extract was administered orally using a Jones tube at 5 p.m. every day. The control group was given normal saline in the same manner.

Table 1. Composition of experimental diet

Ingredients (%)	experimental diet
Casein	20.0
α-Corn starch	35.0
Sucrose	11.0
Lard	4.0
Corn oil	1.0
Mineral mix[z]	3.5
Vitamin mix[y]	1.0
Cellurose powder	23.5
DL-methione	0.3

[z]Mineral mix. (g/㎏ diet): $CaCO_3$, 29.29; $CaHPO_4 \cdot 2H_2O$, 0.43; KH_2PO_4, 34.30; NaCl, 25.06; $MgSO_4 \cdot 7H_2O$, 9.98; Feric citrate hexahydrate, 0.623; $CuSO_4 \cdot 5H_2O$, 0.516; $MnSO_4 \cdot H_2O$, 0.121; $ZnCl_2$, 0.02; KI, 0.005; $(NH_4)_6\ MO_7O_{24} \cdot 4H_2O$, 0.0025.

[y]Vitamin mix (㎎/㎏ diet): Thiamine-HCl, 12; Riboflavin, 40; Pyrodoxin-HCl, 8; Vitamin-B_{12}, 0.005; Ascorbic acid, 300; D-biotin, 0.2; Menadione, 52; Folic acid, 2; D-calcium pantothenate, 50; P-aminobenzoic acid, 50; Nicotinic acid, 60; Cholin choloride, 2000 (IU/㎏ diet); Rethinyl acetae, 5000 (IU/㎏ diet); Cholecalciferol, 250 (IU/㎏ diet).

LPS injection

After 4 weeks of cinnamon extract administration, LPS (concentration: 5 ㎎/㎏) was injected into the abdominal cavity of every rat (Marriot *et al*., 1998).

Tissue sampling

Blood samples were taken from all rats under ether anesthesia and using the cardiac puncture method at three time points: the end of the 4 weeks of daily cinnamon extract administration, just before LPS injection, and 2 and 5 h thereafter. At 5 h after the LPS injection, a midabdominal incision was made in the animal, and 10 ㎖ of phosphate-buffered saline was injected intraperitoneally to elute the peritoneal cells. The peritoneal lavage fluid (PLF) and liver were harvested simultaneously from all of the animals.

Measurements of cytokines in the blood and liver

The blood samples were immediately centrifuged at 3000

rpm for 10 min, and the serum collected, frozen, and maintained at -80℃ until required for analysis. Liver cytokine samples were prepared by homogenizing 1 g of liver particles on ice in 5 ㎖ of cold phosphate-buffered saline (PBS; pH 7.4) containing a protease inhibitor cocktail (Tablete Complete, Roche, Germany). The samples were then centrifuged at 15,000 rpm for 15 min at 4℃. The supernatants were filtered through a 0.45-㎛ filter (Millex-HA, Millipore, Molsheim, France) and again centrifuged at 15,000 rpm for 15 min at 4℃. The liver extracts were removed, frozen, and kept at -80℃ until cytokine analysis was performed. Plasma and hepatic cytokine (IL-1β, TNF-α, IL-6, and IL-10) concentrations were determined by enzyme-linked immunosorbent assay (ELISA), using commercial kits (BioSource International, USA). The minimum detectable concentration of TNF-α was 0.7 pg/㎖, and that of the remaining cytokines was 3-8 pg/㎖. The hepatic levels of cytokines were calculated per 1 g of wet tissue in 5 ㎖ of PBS. Plasma and hepatic cytokine concentrations are expressed as picograms per milliliter and picograms per milligram of tissue, respectively.

Distribution of lymphocyte subpopulations

The proportions of CD4 and CD8 in the blood were determined by flow cytometry. Briefly, blood was incubated for 15 min at 4℃, and fluorescein-conjugated mouse-anti-rat CD8 and phycoerythrin-conjugated mouse-anti-rat CD4 (Serotec, Oxford, UK) to identify T-helper cells and cytotoxic T cells, respectively. Red blood cells were lysed with lysing buffer (Serotec). Fluorescence data were collected on 5×10^4 viable cells and analyzed by flow cytometry (Coulter, Miami, FL, USA).

Determination of stable nitrite and nitrate

The plasma concentrations of nitrite (NO_2^-) and nitrate (NO_3^-) were measured using a commercial kit (Assay Designs, Ann Arbor, MI, USA) following the manufacturer's instructions.

Measurement of plasma concentrations of intercellular adhesion molecule 1, cytokine-induced neutrophil chemoattractant 1, and PGE2

The plasma concentrations of intercellular adhesion molecule 1 (ICAM-1) and cytokine-induced neutrophil chemoattractant 1 (CINC-1) concentrations were measured using commercially available ELISA microtiter plates, with antibodies specific for rat ICAM-1 (R&D Systems, Minneapolis, MN, USA) and CINC-1 (Amersham Pharmacia Biotech, Buckinghamshire, UK). The detection limits for ICAM-1 and CINC-1 were <17 pg/㎖ and 1.3 pg/㎖, respectively. Measurements of PGE2 concentrations were also made by ELISA. Acetylcholinesterase covalently coupled to PGE2 was used as the enzymatic tracer (R&D Systems). The sensitivity of the PGE2 assay was <8.3 pg/㎖.

MCP-1 and CINC-1 in peritoneal lavage fluid (PLF)

The concentrations of MCP-1 and CINC-1 were measured using a quantitative sandwich enzyme immunoassay kit (Biosource International), the detection limit for which was < 8 pg/㎖.

Statistical analysis

The data were analyzed by one-way ANOVA by using an SPSS package, and the significance of differences between the groups was determined using Duncan's multiple-range test. The threshold for statistical significance was set at $P < 0.05$.

Results

Plasma cytokine

The plasma concentrations of IL-1β (Table 2) and IL-6 (Table 3) exhibited a tendency to increase 2 h and 5 h after LPS injection in all of the experimental (i.e., cinnamon) groups. However, the values for the 200 ㎎/㎏ and 300 ㎎/㎏ cinnamon extract groups were lower than for the control and 100 ㎎/㎏ groups.

Plasma TNF-α concentrations (Table 4) peaked at 2 h after LPS injection, and then plateaued to 5 h postinjection. The plasma TNF-α values of the 200 ㎎/㎏ and 300 ㎎/㎏ cinnamon-extract groups were significantly lower than those of the control group and at both 2 h and 5 h postinjection. The concentration of plasma IL-10 (Table 5) increased 2 h postinjection, and reached a peak at 5 h. The IL-10 values of the 200 ㎎/㎏ and 300 ㎎/㎏ cinnamon extract groups were

Table 2. Effect of Cinnamon ext. on plasma IL-1β concentration in lipopolysaccharide-exposed rats

Treatment	IL-1β (pg/ml), Time (h)[z]		
	0 h	2 h	5 h
Control (saline, 100 mg/kg)	16.92 ± 2.37[NSy]	81.59 ± 7.18[bx]	371.59 ± 32.51[b]
Cinnamon ext. (100 mg/kg)	17.12 ± 2.58[NS]	79.33 ± 8.43[b]	311.62 ± 37.15[b]
Cinnamon ext. (200 mg/kg)	17.31 ± 2.29[NS]	52.19 ± 7.61[ax]	235.18 ± 29.32[a]
Cinnamon ext. (300 mg/kg)	16.75 ± 3.11[NS]	49.27 ± 7.57[a]	214.36 ± 30.47[a]

[z]: 0 h, 2 h and 5 h after LPS injection.
[y]NS: Not significantly different (P > 0.05).
[x]a,b: Means in the same column with different superscripts are significantly different (p < 0.05).

Table 3. Effect of Cinnamon ext. on plasma IL-6 concentration in lipopolysaccharide-exposed rats

Treatment	IL-6 (pg/ml), Time (h)[z]		
	0 h	2 h	5 h
Control (saline, mg/kg)	25.18 ± 3.57[NSy]	187.55 ± 21.94[bx]	847.29 ± 51.17[b]
Cinnamon ext. (100 mg/kg)	22.73 ± 3.11[NS]	171.39 ± 21.48[b]	725.52 ± 49.34[b]
Cinnamon ext. (200 mg/kg)	24.25 ± 3.15[NS]	125.51 ± 21.15[a]	517.93 ± 51.09[a]
Cinnamon ext. (300 mg/kg)	24.17 ± 3.47[NS]	122.62 ± 23.87[a]	532.13 ± 48.66[a]

[z]: 0 h, 2 h and 5 h after LPS injection.
[y]NS: Not significantly different (P > 0.05).
[x]a,b: Means in the same column with different superscripts are significantly different (p < 0.05).

Table 4. Effect of Cinnamon ext. on plasma TNF-α concentration in lipopolysaccharide-exposed rats

Treatment	TNF-α (pg/ml), Time (h)[z]		
	0 h	2 h	5 h
Control (saline, mg/kg)	11.39 ± 3.57[NSy]	724.95 ± 52.61[cx]	709.59 ± 57.32[b]
Cinnamon ext. (100 mg/kg)	12.14 ± 3.25[NS]	675.83 ± 46.94[bc]	691.44 ± 42.98[b]
Cinnamon ext. (200 mg/kg)	12.87 ± 3.31[NS]	598.29 ± 43.52[ab]	563.52 ± 42.15[a]
Cinnamon ext. (300 mg/kg)	12.45 ± 3.63[NS]	532.57 ± 41.54[a]	527.11 ± 52.63[a]

[z]: 0 h, 2 h and 5 h after LPS injection.
[y]NS: Not significantly different (P > 0.05).
[x]a,b,c: Means in the same column with different superscripts are significantly different (p < 0.05).

Table 5. Effect of Cinnamon ext. on plasma IL-10 concentration in lipopolysaccharide-exposed rats

Treatment	IL-10 (pg/ml), Time (h)[z]		
	0 h	2 h	5 h
Control (saline, 100 mg/kg)	21.17 ± 4.53[NSy]	44.59 ± 4.73[ax]	71.22 ± 8.95[a]
Cinnamon ext. (100 mg/kg)	23.57 ± 4.81[NS]	52.12 ± 5.25[a]	69.47 ± 11.21[a]
Cinnamon ext. (200 mg/kg)	21.89 ± 4.67[NS]	63.41 ± 4.89[b]	92.57 ± 8.12[b]
Cinnamon ext. (300 mg/kg)	22.68 ± 4.31[NS]	67.34 ± 4.27[b]	95.11 ± 9.15[b]

[z]: 0 h, 2 h and 5 h after LPS injection.
[y]NS: Not significantly different (P > 0.05).
[x]a,b: Means in the same column with different superscripts are significantly different (p < 0.05).

significantly higher than those of the control and 100 mg/kg groups at both 2 and 5 h post-LPS injection.

Liver cytokines

Liver concentrations of cytokine were measured only at 5 h after the LPS injection (Table 6). The concentrations of liver

IL-1β in all of the cinnamon extract groups were lower than in the control group. However, the difference between the values for the control and 100 ㎎/㎏ cinnamon extract groups was not statistically significant. The liver concentrations of IL-6 in all of the cinnamon extract groups were lower than in the control group. However, the difference was significant only between the control and 300 ㎎/㎏ cinnamon extract groups. There were no differences in the liver concentrations of TNF-α and IL-10 among any of the treatment groups.

Blood lymphocyte subpopulation

The findings regarding the distributions of blood lymphocyte subpopulations are given in Table 7. There was a tendency toward an increase in CD4 in the cinnamon extract groups compared to the control group, but the difference was only significant for the 300 ㎎/㎏ cinnamon extract group. The distribution of CD8 tended to decrease in the cinnamon extract groups compared to the control group, but again, the difference was only significant for the 300 ㎎/㎏ cinnamon extract group. The CD4/CD8 ratio exhibited a tendency to increase in the cinnamon extract groups.

Plasma concentrations of NO_3^-/NO_2^-, ICAM-1, CINC-1, and PGE2

The plasma concentrations of NO_3^-/NO_2^-, ICAM-1, CINC-1, and PGE2 are listed in Table 8. Although the concentrations of NO_3^-/NO_2^- and ICAM-1 exhibited a tendency to decrease in the cinnamon extract groups compared to the control, only the value for the 300 ㎎/㎏ cinnamon extract group was significantly lower than that of the control group. The plasma CINC-1 concentration did not differ significantly among all treatment groups. The concentration of PGE2 in all of the

Table 6. Effects of Cinnamon ext. on liver cytokines concentration in lipopolysaccharide-exposed rats[z]

Treatment	IL-1β (pg/㎎)	IL-6 (pg/㎎)	TNF-α (pg/㎎)	IL-10 (pg/㎎)
Control (saline, 100 ㎎/㎏)	23.11 ± 3.51[cy]	8.52 ± 1.12[b]	1.92 ± 0.51[NSx]	1.53 ± 0.47[NS]
Cinnamon ext. (100 ㎎/㎏)	22.75 ± 3.69[bc]	8.14 ± 1.08[ab]	1.74 ± 0.53[NS]	1.47 ± 0.59[NS]
Cinnamon ext. (200 ㎎/㎏)	17.44 ± 3.27[ab]	7.24 ± 1.15[ab]	1.75 ± 0.62[NS]	1.78 ± 0.52[NS]
Cinnamon ext. (300 ㎎/㎏)	15.91 ± 3.38[a]	6.81 ± 1.17[a]	1.61 ± 0.58[NS]	1.84 ± 0.43[NS]

[z]: 0 h, 2 h and 5 h after LPS injection.
[y]a,b,c: Means in the same column with different superscripts are significantly different ($p < 0.05$).
[x]NS: Not significantly different ($P > 0.05$).

Table 7. Effects of Cinnamon ext. on lymphocyte subpopulation composition in lipopolysaccharide-exposed rats

Treatment	CD4 (%)	CD8 (%)	CD4/CD8 (%)
Control (saline, 100 ㎎/㎏)	33.81 ± 5.38[az]	26.1 ± 3.91[b]	1.29
Cinnamon ext. (100 ㎎/㎏)	42.57 ± 5.15[ab]	22.58 ± 3.37[ab]	1.89
Cinnamon ext. (200 ㎎/㎏)	43.49 ± 6.25[ab]	19.79 ± 3.04[ab]	2.20
Cinnamon ext. (300 ㎎/㎏)	48.31 ± 5.53[b]	17.33 ± 3.75[a]	2.79

[z]a,b: Means in the same column with different superscripts are significantly different ($p < 0.05$).

Table 8. Effects of Cinnamon ext. on the concentration of NO_3^-/NO_2^-, ICAM-1, CINC-1 and PGE_2 in plasma of lipopolysaccharide-exposed rats

Treatment	NO_3^-/NO_2^- (μM)	ICAM-1 (ng/㎖)	CINC-1 (pg/㎖)	PGE_2 (pg/㎖)
Control (saline, 100 ㎎/㎏)	53.94 ± 3.27[b]	95.16 ± 7.24[by]	273.11 ± 67.58[NSz]	871.25 ± 72.43[b]
Cinnamon ext. (100 ㎎/㎏)	51.17 ± 3.38[b]	94.47 ± 7.58[b]	259.21 ± 54.88[NS]	695.35 ± 77.12[a]
Cinnamon ext. (200 ㎎/㎏)	47.12 ± 4.05[ab]	87.35 ± 8.31[ab]	247.39 ± 55.26[NS]	681.58 ± 69.24[a]
Cinnamon ext. (300 ㎎/㎏)	42.38 ± 3.19[a]	79.21 ± 7.36[a]	232.44 ± 61.23[NS]	635.31 ± 64.59[a]

[z]NS: Not significantly different ($P > 0.05$).
[y]a,b: Means in the same column with different superscripts are significantly different ($p < 0.05$).

Table 9. Effect of Cinnamon ext. on the concentration of PLF MCP-1 and PLF CINC-1 in lipopolysaccharide-exposed rats

Treatment	MCP-1 (pg/㎖)	CINC-1 (pg/㎖)
Control (saline, 100 ㎎/㎏)	135.92 ± 44.29^{NSz}	355.27 ± 78.44^{NS}
Cinnamon ext. (100 ㎎/㎏)	119.54 ± 31.75^{NS}	337.15 ± 67.49^{NS}
Cinnamon ext. (200 ㎎/㎏)	113.97 ± 47.88^{NS}	322.73 ± 71.52^{NS}
Cinnamon ext. (300 ㎎/㎏)	105.11 ± 35.23^{NS}	295.39 ± 69.18^{NS}

[z]NS: Not significantly different ($P > 0.05$).

cinnamon extract groups was significantly lower than that of the control group. However, this parameter did not differ significantly among the three cinnamon-treated groups.

PLF concentrations of MCP-1 and CINC-1

The PLF concentrations of MCP-1 and CINC-1 tended to decrease in the cinnamon extract groups compared to the control group, but the differences did not reach statistical significance (Table 9).

Discussion

This study investigated the anti-inflammatory activity of cinnamon extract by measuring the plasma and liver concentrations of cytokines, blood lymphocyte subpopulations (CD4, CD8), plasma concentrations of NO_3^-/NO_2^-, ICAM-1, CINC-1, and PGE2, and PLF levels of MCP-1 and CINC-1 in cinnamon-treated rats that were exposed to LPS. Although the plasma concentrations of IL-1β (Table 2), IL-6 (Table 3) and TNF-α (Table 4) tended to increase 2 h and 5 h after LPS injection in all of the experimental groups, the values of the cinnamon extract groups were lower than those of the control group. Furthermore, the liver concentrations of IL-1β, IL-6, and TNF-α in the cinnamon extract groups were lower than in the control group at 5 h after LPS injection. However, the liver TNF-α concentration did not differ significantly among all of the treatment groups (Table 6).

IL-1β, IL-6, and TNF-α are proinflammatory cytokines that have been implicated as mediators of LPS toxicity both in vivo and in vitro, and their similar biological properties and synergism of their effects is evident in several models (Mathiak *et al*., 2000). Proinflammatory cytokines are released in response to various stimuli, including bacterial LPS (Chamulitrat *et al*., 1995), and overproduction of these cytokines is associated with a wide range of pathologic conditions. This has led to many recent efforts to find ways of down-regulating their production or inhibiting their effects *in vivo* (Marriot *et al*., 1998). In the present experiment, the concentrations of these cytokines in the cinnamon extract groups were lower than in the control group, suggesting that cinnamon extract interferes with anti-inflammatory function.

The plasma concentration of IL-10 (Table 5) was increased after 2 h, and further increased at 5 h postinjection in all four animal groups. However, the values of the cinnamon extract groups were higher than that of the control group. The liver concentrations of IL-10 did not differ significantly between the treatment groups at 5 h after LPS injection (Table 6). IL-10 and IL-1 receptor RAs are anti-inflammatory cytokines (Hudson *et al*., 1995; Gabby and Kushner, 1999). In this experiment, the concentration of IL-10 in the cinnamon extract groups was higher than in the control group, and may have affected the concentrations of the other cytokines.

The numbers of T lymphocytes and CD4-positive cells, and the ratio of CD4-/CD8-positive cells (Chiu *et al*., 2008) significantly decreases in the inflammatory state (Lennard *et al*., 1985; Schander *et al*., 2002; Chiu *et al*., 2008). In the present study, the distribution of CD4 tended to increase, and that of CD8 tended to decrease in the cinnamon extract groups, and the CD4/CD8 ratio increased in the cinnamon extract groups. These results indicate that cinnamon extract has anti-inflammatory properties (Table 7).

Concentrations of NO, ICAM-1, CINC-1, and PGE2, which are involved in the response to inflammation, are markedly increased in the inflammatory condition (Moncada *et al*., 1991; Hogg, 1998; Weber, 2003; Harris *et al*., 2002). MCP-1 is a chemotactic and activating factor for mononuclear phagocytes, and is involved in the recruitment of peripheral blood leukocytes to the peritoneal cavity (Matsukawa *et al*.,

1999). In the present study, the plasma concentrations of NO_3^- /NO_2^-, ICAM-1, CINC-1, and PGE2 (Table 8), and of the PLF concentrations of MCP-1 and CINC-1 (Table 9) tended to decrease in the cinnamon extract groups. These findings indicate that cinnamon extract can exert functional anti-inflammatory effects.

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