International Journal of Pharmacology

ISSN 1811-7775

science alert

ansinet
Asian Network for Scientific Information

International Journal of Pharmacology 3 (6): 482-486, 2007
ISSN 1811-7775

Anti Oxidative Stress Potential of Cinnamon (*Cinnamomum zeylanicum*) in Operating Room Personnel; A Before/After Cross Sectional Clinical Trial

[1,2]Akram Ranjbar, [1]Sara Ghaseminejhad, [1]Hassan Takalu, [1]Akram Baiaty,
[2]Fatemeh Rahimi and [2]Mohammad Abdollahi
[1]School of Paramedical Sciences, Arak University of Medical Sciences, Arak
[2]Laboratory of Toxicology, Excellence Center of Toxicology and Food Chemistry,
Faculty of Pharmacy and Pharmaceutical Sciences Research Center,
Tehran University of Medical Sciences, Tehran, Iran

Abstract: Regarding role of oxidative stress in operating room personnel and the anti oxidative stress potential of *Cinnamon zeylanicum* (cinnamon) in healthy subjects, the present study aimed to examine anti oxidative stress potential of cinnamon in operating room personnel. A group of 18 operating room personnel was invited to drink cinnamon (100 mg/300 mL tea) once daily for 10 days. Blood samples were obtained before and after entering the study and plasma was measured for oxidative stress biomarkers including Lipid Peroxidation Level (LPO), Total Antioxidant Power (TAP) and Total Thiol Molecules (TTM). Treatment of subjects with cinnamon induced a significant reduction in plasma LPO (5.03±2.01 vs. 3.25±1.32 nmol mL^{-1}, p = 0.016). No statistically significant alteration was found for plasma TAP (1.24±0.12 vs. 1.28±0.12, p>0.05) and TTM (0.78±0.05 vs. 0.82±0.03, p>0.05) after 10 days treatment by cinnamon. In conclusion, reduction of cellular LPO by cinnamon as a dietary supplement can be a rational protocol to control source of hazards in operating room personnel.

Key words: Cinnamon, operating room personnel, oxidative stress, lipid peroxidation

INTRODUCTION

Oxidative stress arises when there is a marked imbalance between the production and removal of Reactive Oxygen Species (ROS). It has been known that exposure to anesthetic gases in operating room personnel is the source of formation of free radicals in living systems and oxidative damage to DNA, proteins and lipids (Malekirad *et al*., 2005a). Anesthetic gases are able to induce oxidative stress and their harmful chronic effects on reproductive, neurological, hematological, immunological, hepatic and renal systems and induction of cancer have been previously reported. Although the pathophysiology of these adverse effects of anesthetic gases is still unknown, one hypothesis is induction of oxidative stress in vital organs (Hoerauf *et al*., 1996, 1997; Cohen *et al*., 1980; Venables *et al*., 1983). Despite to the fact that anesthetic gases have low solubility in blood and tissues and thus are eliminated from the body rapidly, but they have been known to be neurotoxic, hepatotoxic and carcinogenic (Lucchini *et al*., 1996; Franco *et al*., 1991; Corbett *et al*., 1973).

Cinnamomum zeylanicum Blume, syn *C. verum*, form family Laureceae namely (cinnamon) is a widely used spice and have many applications in perfumery, flavoring and pharmaceutical industries. The chemical constituents of leaf and bark essential oil of cinnamon have been determined to have strong antioxidants (Raina *et al*., 2001; Simic *et al*., 2004; Jayaprakasha *et al*., 2002; Singh *et al*., 2007; Mancini-Filho *et al*., 1998; Javaprakasha *et al*., 2006; Jayaprakasha *et al*., 2003).

Cinnamon tea that is a mixture of regular tea and cinnamon that is traditionally used in Iran. Our recent cross sectional clinical trial for the first time showed that in individuals who drink cinnamon tea, their blood lipid peroxides decrease and total antioxidant capacity and total thiol molecules increase much more than those who drink regular tea (Ranjbar *et al*., 2006). Since oxidative stress has been introduced as the main hazard of exposure to anesthetetic gases in operating room personnel, the present cross-sectional before-after clinical trial was undertaken to explore possible protective effects of cinnamon.

MATERIALS AND METHODS

Chemicals: Dithiobis-2-nitrobenzoic acid (DTNB), tris base, tetraethoxypropane, malonedialdehyde (MDA), 2-

Corresponding Author: Mohammad Abdollahi, Laboratory of Toxicology, Excellence Center of Toxicology and Food Chemistry, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 14155-6451, Iran

Table 1: Basic characteristics of the study subjects

	Gender	
Characteristics	Female 11 (61.1%)	Male 7 (38.9%)
Sport	6 (33.3)	12 (66.7)
History of disease	3 (16.7)	15 (83.3)
Mean daily work hours	8.0	8.0
Use of drug	5 (27.7)	13 (72.7)

Values in parenthesis show percentage

hiobarbituric acid (TBA), trichloroacetic acid (TCA), n-butanol and 2,4,6-tripyridyl-S-triazine (TPTZ) were used in this study. Cinnamon powder was obtained from local market.

Subjects: A comparative cross-sectional before after study was designed with 18 subjects in a University Hospital in Arak in summer 2006. Subjects were 11 female and 7 male in the age range of 22 to 53 years working as operating room nurse. The demographic characteristics of the subjects are shown in Table 1. None of these subjects was exposed in workplace to any hazardous agents other than anesthetic gases. They were active in work shifts weekly, starting 7:30 a.m and ending 4 p.m The subjects were asked to drink cinnamon tea containing 100 mg cinnamon in 30 mL boiling water daily (morning) for 10 days. Cinnamon powder is commercially available in Iran markets. Heparinized blood sample was obtained before and after treatment. The blood was centrifuged at 1700 g for 10 min and the plasma was separated and stored at -70°C until analysis.

All participants were provided with specific written information about the aims of the study before written consent was obtained, in accordance with the Declaration of Helsinki. The protocol of the study was approved by Institutional Review Board. Prior to blood collection, all subjects completed a structured questionnaire specifying date of birth, smoking and dietary habits, consumption of vitamin supplements and other antioxidants and use of therapeutic drugs. They were instructed not to take any multivitamin supplements or traditional herbs during the study.

Measurement of plasma total antioxidant power (TAP): The ability of plasma in reducing Fe^{3+} to Fe^{2+} is the principle of the method used. In brief, the medium is exposed to Fe^{3+} and the antioxidants present in the medium start to produce Fe^{2+}. The reagent included 300 mmol L^{-1} acetate buffer, pH 3.6 and 16 mL acetic acid as buffer solution, 10 mmol L^{-1} TPTZ in 40 mmol L^{-1} HCl and 20 mmol L^{-1} $FeCl_3 . 6H_2O$. The working reagent was prepared as required by mixing 25 mL acetate buffer, 2.5 mL TPTZ solution and 2.5 mL $FeCl_3 . 6 H_2O$ solution. Ten microliter of H_2O diluted sample was then added to 300 μL freshly prepared reagent warmed at 37°C. The complex between Fe^{2+} and TPTZ gives a blue color with absorbance at 593 nm (Benzie and Strain, 1999).

Measurement of lipid peroxidation (LPO): For measuring the rate of lipid peroxidation, the TBA-reactive substances (TBARS) were measured. In this method plasma samples were mixed with TCA (20%) and the precipitate was dispersed in H_2SO_4 (0.05 M). TBA (0.2% in sodium sulfate 2M) was added and heated for 30 min in boiling water bath. TBARS adducts were extracted by n-butanol and the absorbance was measured at 532 nm. In this method, the reaction products are reported as TBARS because in addition to MDA other aldehydes react with TBA. This reaction is formed in acidic pH and high temperature and gives a maximum absorbance with a pink color at 532 nm (Satho, 1978).

Measurement of plasma Total Thiol Molecules (TTM): A volume of plasma (0.20 mL) was mixed in a 10 mL test tube with 0.6 mL of Tris-EDTA buffer (Tris base 0.25 M, EDTA 20 mM, pH 8.2) followed by the addition of 40 μL of 10 mM of DTNB in methanol. The final volume of the reaction mixture was made up to 4.0 mL by adding 3.16 mL of methanol. The test tube was capped and the color was developed for 15-20 min, followed by centrifugation at 3000 g for 10 min at ambient temperature. The absorbance of the supernatant was measured at 412 nm (Hu and Dillard, 1994).

Statistics: A detailed multiple variable database was formed. All data were collected either as dichotomous variables e.g., age and weight or as continuous variables e.g., laboratory measurements. All data were analyzed with StatsDirect version 2.6.2. Paired t-test was used to analyze the differences observed in plasma biomarkers after treatment by cinnamon. p-values greater than 0.05 were considered insignificant. Data were expressed as mean±SE.

RESULTS AND DISCUSSION

As shown in Table 2, TAP value was not different before and after using cinnamon tea ($p>0.05$, 1.24±0.12 vs. 1.28±0.12). A significant reduction in plasma LPO was observed after use of cinnamon tea ($p = 0.01$, 5.3±0.47 vs. 3.25±0.31 nmol mL^{-1}). TTM value was not different before and after use of cinnamon tea ($p>0.05$, 0.78±0.05 vs. 0.82±0.03).

The present results indicated the positive potential of cinnamon in decreasing plasma TBARS to an extent of 34%. This means that the level of free radicals and their damaging effects on the cells have been markedly

Table 2: Oxidative stress biomarkers before and after treatment by cinnamon tea

Biomarker	Before	After	p-value
TAP (μmol mL^{-1})	1.24±0.12	1.28±0.12	0.70
TBARS (nmol mL^{-1})	5.30±0.47	3.25±0.31	0.01
TTM (nmol mL^{-1})	0.78±0.05	0.82±0.03	0.60

reduced. In the meantime, the present results indicate that plasma TAP and TTM did not change by cinnamon meaning that other non-thiol antioxidants, such as uric acid, transferrin, ceruloplasmin, albumin and vitamin antioxidants e.g., α-tocopherol and ascorbic acid might have been stimulated to maintain antioxidant balance at normal state (Malekirad *et al*., 2005a; Rahimi *et al*., 2005; Shahriari *et al*., 2006).

As mentioned earlier, numerous substances have been suggested to act as antioxidants in cinnamon. Various phenolic antioxidants such as flavonoids, Rosmarinic Acid (RA), tannins, coumarins, xanthenes and more recently, procyanidins have been shown to scavenge radicals in a dose dependent manner (Czinner *et al*., 2000; D'Amelio, 1999). Flavonoids and RA have been introduced as the main constituents of Cinnamon (Altschuler *et al*., 2007). Diabetes is one of diseases that the balance of body oxidants/antioxidants is very important parameter in its pathophysiology and also complications of the disease (Rahimi *et al*., 2005). In a clinical trial in patients with poorly controlled type 2 diabetes, cinnamon lowered plasma glucose (Pham *et al*., 2007). In another study in diabetic patients, cinnamon reduced insulin resistance (Wang *et al*., 2007). In another clinical trial, intake of 6 g cinnamon with rice pudding in healthy subjects reduced postprandial blood glucose and delayed gastric emptying without affecting satiety (Hlebowicz *et al*., 2007). There is evidence that cinnamon moderately reduces fasting plasma glucose in diabetic patients with poor glycaemic control (Mang *et al*., 2006). The intake of 1, 3 or 6 g of cinnamon/day reduced serum glucose, triglyceride, low-density lipoprotein cholesterol and total cholesterol in people with type II diabetes (Khan *et al*., 2003). Animal studies indicate that dietary cinnamon inhibits hepatic HMG CoA-reductase activity, resulting in lower hepatic cholesterol content as well as suppressing lipid peroxidation via the enhancement of hepatic antioxidant enzyme activities (Shobana and Naidu, 2000; Lee *et al*., 2003).

It is well known that people working in hospital-operating theaters are often exposed to anesthetic gases (Abdollahi *et al*., 2003). Starting from the 1960s, adverse health effects were observed in medical personnel, mainly nurses, who had been working with anesthetic gases particularly nitrous oxide and halothane (Lopez, 2005). The present study confirmed existence of oxidative stress in blood of operating room personnel and radiology staff (Malekirad *et al*., 2005a,b). Genotoxicity is one of the key outcomes of oxidative stress (Abdollahi *et al*., 2004; Shadnia *et al*., 2005). In the body, antioxidants act as free radical scavengers and thus protect cells from being exposed to free radicals and further cellular damage. This is the mechanism by which they protect the human body from several diseases attributed to the reactions of radicals. Genotoxic effects such as micronuclei formation, sister chromatid exchange, or chromosome aberrations of occupational exposure to volatile anaesthetics have been shown to increase in operating room personnel. In addition, increased frequencies of spontaneous abortion and birth defects have been reported in operating room personnel (Nilsson *et al*., 2005; Abdollahi *et al*., 2003). In conclusion, exposure to anesthetic gases in the operating room personnel cannot be neglected and therefore reduction of cellular LPO can be a rational protocol to control source of hazards that is free radicals. Supporting this idea, a recent clinical trial showed that occupational exposure to anaesthetic gases induces oxidative DNA damage and supplementation of them with vitamin C and vitamin E for 12-weeks resulted in a significant decrease in the DNA damage (Sardas *et al*., 2006). Regarding existence of flavonoids in cinnamon, it should be noted that flavonoids existing in herbal products have equal potential to vitamin E in reduction of oxidative stress *in vivo* (Mehdipour *et al*., 2006). Taking all findings collectively, the present study indicates that cinnamon can protect body from increased LPO. Further studies with higher doses and higher duration of treatment are proposed to elucidate this effect more efficiently. At this stage, use of cinnamon as a dietary supplement for operating room personnel is a rational recommendation.

REFERENCES

Abdollahi, M., M. Akhgari and A. Etemadi-Aleagha, 2003. A brief review on adverse effects of anesthetic agents in operating room personnel. Mid East Pharmacy, 11 (4): 6-7.

Abdollahi, M., A. Ranjbar, S. Shadnia, S. Nikfar and A. Rezaiee, 2004. Pesticides and oxidative stress: A review. Med. Sci. Monit., 10: RA141-RA147.

Altschuler, J.A., S.J. Casella, T.A. MacKenzie and K.M. Curtis, 2007. The effect of cinnamon on A1C among adolescents with type 1 diabetes. Diabetes Care, 30 (4): 813-816.

Benzie, I.F. and J.J. Strain, 1999. Ferric reducing/antioxidant power assay: Direct measure of total antioxidant activity of biological fluids and modified version for simultaneous measurement of total antioxidant power and ascorbic acid concentration. Methods Enzymol., 292: 15-27.

Cohen, E.N., H.C. Gift, B.W. Brown, W. Greenfield, M.L. Wu and T.W. Jones *et al*., 1980. Occupational disease in dentistry and chronic exposure to trace anesthetic gases. J. Am. Dent. Assoc., 101: 21-31.

Corbett, T.H., R.G. Cornell, K. Lieding and J.L. Endres, 1973. Incidence of cancer among Michigan nurse-anesthetists. Anesthesiology, 38: 260-263.

Czinner, E., K. Hagymasi, A. Blazovics, A. Kery, E. Szoke and E. Lemberkovics, 2000. *In vitro* antioxidant properties of *Helichrysum arenarium* (L.) Moench. J. Ethnopharmacol., 73: 437-443.

D'Amelio, F.S., 1999. Botanics: A Phytocosmetic Desk Reference. CRC Press, London, pp: 36.

Franco, G., P. Marraccini, G. Santagostineo, P. Filisetti and I. Preseglio, 1991. Behavior of urinary D-glucaric acid excretion in surgical patients and anaesthesiology staff acutely exposed to isoflurane and nitrous oxide. Med. Lav., 82: 527-532.

Hlebowicz, J., G. Darwiche, O. Bjorgell and L.O. Almer, 2007. Effect of cinnamon on postprandial blood glucose, gastric emptying and satiety in healthy subjects. Am. J. Clin. Nutr., 85: 1552-1556.

Hoerauf, K.H., C. Koller, W. Jakob, K. Taeger and J. Hobbhahn, 1996. Isoflurane waste gas exposure during general anaesthesia: The laryngeal mask compared with tracheal intubation. Br. J. Anaesth., 77: 189-193.

Hoerauf, K., M. Harth, K. Wild and J. Hobbhahn, 1997. Occupational exposure to desflurane and isoflurane during cardiopulmonary bypass: Is the gas outlet of the membrane oxygenator an operating theater pollution hazard? Br. J. Anaesth., 78: 378-380.

Hu, M.L. and C.J. Dillard, 1994. Plasma SH and GSH measurement. Meth. Enzymol., 233: 385-387.

Jayaprakasha, G.K., L.J. Rao and K.K. Sakariah, 2002. Chemical composition of volatile oil from *Cinnamomum zeylanicum* buds. Z Naturforsch [C], 57: 990-993.

Jayaprakasha, G.K., L. Jagan Mohan Rao and K.K. Sakariah, 2003. Volatile constituents from *C. zeylanicum* fruit stalks and their antioxidant activities. J. Agric. Food Chem., 51: 4344-4348.

Javaprakasha, G.K., M. Ohnishi-kameyama, H. Ono, M. Yoshida and L. Jaganmohan Rao, 2006. Phenolic constituents in the fruits of *Cinnamomum zeylanicum* and their antioxidant activity. J. Agric. Food Chem., 54: 1672-1679.

Khan, A., M. Safdar, M.M. Ali Khan, K.N. Khattak and R.A. Anderson, 2003. Cinnamon improves glucose and lipids of people with Type 2 diabetes. Diabetes Care, 26: 3215-3218.

Lee, J.S., S.M. Jeon, E.M. Park, T.L. Huh, O.S. Kwon, M.K. Lee and M.S. Choi, 2003. Cinnamate supplementation enhances hepatic lipid metabolism and antioxidant defense systems in high cholesterol-fed rats. J. Med. Food, 6: 183-191.

Lopez, V., 2005. Commentary on: Health risks and occupational exposure to volatile anaesthetics: A review with a systematic approach. J. Clin. Nurs., 14: 1160-1161.

Lucchini, R., D. Placidi, F. Toffoletto and L. Alessio, 1996. Neurotoxicity in operating room personnel. Working with gaseous and nongaseous anesthesia. Int. Arch. Occup. Environ. Health, 68: 188-192.

Malekirad, A.A., A. Ranjbar, K.2. Rahzani, M. Kadkhodaee, A. Rezaie, B. Taghavi and M. Abdollahi, 2005a. Oxidative stress in operating room personnel: Occupational exposure to anesthetic gases. Hum. Exp. Toxicol., 24: 597-601.

Malekirad, A.A., A. Ranjbar, K. Rahzani, A.A. Pilevarian, A. Rezaie, M.J. Zamani and M. Abdollahi, 2005b. Oxidative stress in radiology staff. Environ. Toxicol. Pharmacol., 20: 215-218.

Mancini-Filho, J., A. Van-Koiij, D.A. Mancini, F.F. Cozzolino and R.P. Torres, 1998. Antioxidant activity of cinnamon (*C. zeylanicum*, Breyne) extracts. Boll. Chim. Farm., 137: 443-447.

Mang, B., M. Wolters, B. Schmitt, K. Kelb, R. Lichtinghagen, D.O. Stichtenoth and A. Hahn, 2006. Effect of a cinnamon extract on plasma glucose, HbA and serum lipids in diabetes mellitus type 2. Enr. J. Clin. Invest., 36: 340-344.

Mehdipour, S., N. Yasa, G. Dehghan, R. Khorasani, A. Mohammadirad, R. Rahimi and M. Abdollahi, 2006. Antioxidant potentials of Iranian *Carica papaya* juice *in vitro* and *in vivo* are comparable to alpha-tocopherol. Phytother. Res., 20 (7): 591-594.

Nilsson, R., C. Bjordal, M. Andersson, J. Bjordal, A. Nyberg, B. Welin and A. Wilman, 2005. Health risks and occupational exposure to volatile anaesthetics: A review with a systematic approach. J. Clin. Nurs., 14: 173-186.

Pham, A.Q., H. Kourlas and D.Q. Pham, 2007. Cinnamon supplementation in patients with type 2 diabetes mellitus. Pharmacotherapy, 27: 595-599.

Rahimi, R., S. Nikfar, B. Larijani and M. Abdollahi, 2005. A review on the role of antioxidants in the management of diabetes and its complications. Biomed. Pharmacother., 59: 365-377.

Raina, V.K., S.K. Srivastava, K.K. Aggarwal, S. Ramesh and S. Kumar, 2001. Essential oil composition of *Cinnamomum zeylinicum* Blume leaves from little Andaman India. Flav. Fragr. J., 16: 374-376.

Ranjbar, A., S. Ghasmeinezhad, H. Zamani, A.A. Malekirad, A. Baiaty, A. Mohammadirad and M. Abdollahi, 2006. Antioxidative stress potential of *Cinnamomum zeylanicum* in humans: A comparative cross-sectional clinical study. Therapy, 3: 113-117.

Sardas, S., S. Izdes, E. Ozcagli, O. Kanbak and E. Kadioglu, 2006. The role of antioxidant supplementation in occupational exposure to waste anaesthetic gases. Int. Arch. Occup. Environ. Health, 80: 154-159.

Satho, K., 1978. Serum lipid peroxidation in cerebrovascular disorders determined by a new colorimetric method. Clin. Chim. Acta, 90: 37-43.

Shadnia, S., E. Azizi, R. Hosseini, S. Khoei, S. Fouladdel, A. Pajoumand, N. Jalali and M. Abdollahi, 2005. Evaluation of oxidative stress and genotoxicity in organophosphorus insecticide formulators. Hum. Exp. Toxicol., 24: 439-445.

Shahriari, S., N. Yasa, A. Mohammadirad, R. Khorasani and M. Abdollahi, 2006. *In vivo* antioxidant potentials of Rosa Damascene Petal extract from Guilan, Iran, comparable to α-tocopherol. Int. J. Pharmacol., 2 (6): 646-649.

Shobana, S. and K.A. Naidu, 2000. Antioxidant activity of selected Indian spices. Prostaglandins Leukot Essent Fatty Acids, 62: 107-110.

Simic, A., M.D. Sokovic, M. Ristic, S. Grujic-Jovanovic, J. Vukojevic and P.D. Marin, 2004. The chemical composition of some Lauraceae essential oils and their antifungal activities. Phytother. Res., 18: 713-717.

Singh, G., S. Maurya, M.P. Delampasona and C.A. Catalan, 2007. A comparison of chemical, antioxidant and antimicrobial studies of cinnamon leaf and bark volatile oils, oleoresins and their constituents. Food Chem. Toxicol., doi: 10.1016/j.fct.

Venables, H., N. Cherry, H.A. Waldron, L. Buck, C. Edling and H.K. Wilson, 1983. Effects of trace levels of nitrous oxide on psychomotor performance. Scand J. Work Environ. Health, 9: 391-396.

Wang, J.G., R.A. Anderson, G.M. Graham, M.C. Chu, M.V. Sauer, M.M. Guarnaccia and R.A. Lobo, 2007. The effect of cinnamon extract on insulin resistance parameters in polycystic ovary syndrome: A pilot study. Fert. Ster., 88: 240-243.