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Antioxidant Activity of Korean Rice Cake Added *Cicer arietinum* for Post-Menopausal Women

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Abstract: The symptoms caused by a decrease in hormone levels in women are referred to as menopause. These affect loss of femininity, cause estrogen-dependent disease and often develop into a personal as well as social issue. Menopausal women try to alleviate their symptoms by hormone injections and intake of functional health foods; however, many homemakers do not respond positively. Many soybean products include phytoestrogen similar to estrogen and *Cicer arietinum* also include phytoestrogen. For this reason, this study examined antioxidant activity of rice cakes supplemented with *C. arietinum*. The results were confirmed that antioxidant activity increased rice cakes supplemented with *C. arietinum* than normal rice cake. Above all, antioxidant activity was not decreased in cooking process. In these results mean that antioxidant activity of lignin as phytoestrogen in rice cake will not decrease. We introduce the potential of functional Korean rice cake that effective for ameliorating the symptoms of menopause.

Key words: Rice cakes, *Cicer arietinum*, antioxidant activity, menopause, phytoestrogen

INTRODUCTION

Menopause is caused by a dysfunction of the ovaries and involves a large number of physical and mental changes in middle-aged women (Nelson, 2008). Symptoms of menopause include night sweating, flushing, headache, joint pain, anxiety, vaginal dryness, mood swings, insomnia irritability, anxiety, depression, heart palpitations and memory decline (Bungay *et al.*, 1980); (Borrelli and Ernst, 2010). Also menopause is often the cause of obesity at middle aged women (Al-Safi and Polotsky, 2015) and extremely is often the cause of Alzheimer's disease (Henderson, 2014). As such, menopause will bring a lot of middle-aged disease in postmenopausal women (Blake, 2006). Studies have shown that decreasing ovarian function results in decreased production of estrogen (Kemper *et al.*, 2013). Lack of estrogen leads to bone turnover, activity of osteoclasts and absorption of bone material resulting in osteoporosis in postmenopausal women (Borjesson *et al.*, 2013). Moreover, decreased estrogen levels induce estrogen-dependent cancers, such as

breast and ovarian cancer (Strauss *et al.*, 2014). These diseases cause mental and physical distress in middle-aged women and may lead to suicide associated with depression (Kornstein *et al.*, 2010). Problems in postmenopausal women are no longer extended to social issues, not personal issues (Kornstein *et al.*, 2010). Classically, hormone replacement therapy for treatment of menopause has used a combination of estrogens with synthetic progesterone and recently phytoestrogens are a popular alternative estrogens/ progesterone therapy (Moreira *et al.*, 2014).

Historically, carbohydrates have been the primary energy source for humans (Song *et al.*, 2014). Carbohydrate intake is supplemented by rice in Eastern countries and wheat in Western countries (Painter and Burkitt, 1971). The discovery of carbonized rice in Stone Age ruins in South Korea (Kim, 2007) indicates that Koreans have a long history of rice supplementation and that Koreans have developed a culture of rice-oriented food (Kim and Choi, 2008). Koreans often make rice cakes out of steamed crushed rice and rough grains (Song and Park,

2003). Rice cakes were a food of the holidays and rituals, because rice was expensive and difficult to obtain. Since South Korea has become a developed country, the lifestyle and eating habits of Koreans have been changing rapidly. The westernization of food culture and the increase of instant food intake have led to an increased consumption of wheat and a decreased consumption of rice. The annual wheat consumption (2,000 years) has shown a trend to increase by 34 kg/year (Lee *et al.*, 2012), (Metcalf, 1984) and rice consumption has declined to below 70 kg/year in 2010 (Metcalf, 1984). Gluten, a structural protein of wheat, may contribute to conditions such as rhinitis, asthma and inflammation. In contrast, rice contains various essential nutrients and does not cause allergies (Bartlomiej *et al.*, 2012).

Recently, the interest of Koreans in a "healthy lifestyle" (or well-being) has increased and so has an interest in functional foods (Borneo and Leon, 2012). Functional foods are defined as foods supplemented with bioactive substances (Borneo and Leon, 2012). These foods are thought to protect against obesity, diabetes, cancer and etc. Functional foods containing raw materials are becoming increasingly popular (Ahmed *et al.*, 2011). These foods can be made and consumed at home. Noodles, rice wine, jam, cake and other products have been made of such functional raw materials (e.g., blueberries, purple sweet potatoes (Zeng *et al.*, 2013), cabbage, carrots (Abdel-Aal *et al.*, 2013) and chickpeas (Licznarska *et al.*, 2013). Functional rice cakes contain indole-3-carbinol from cabbage powder (Sunwoo *et al.*, 2013), ginsenosides from ginseng powder (Sunwoo *et al.*, 2013) and anthocyanin from purple sweet potatoes (Zeng *et al.*, 2013). These materials have been shown to have anti-cancer and anti-obesity effects and to protect against various diseases (Abdel-Aal *et al.*, 2013). Significant attention has been paid to the super-foods chickpeas (*Cicer arietinum*, also called Egyptian beans or chickpeas), lentils and quinoa (Hithamani and Srinivasan, 2014). *C. arietinum* is a low-calorie food and is high in protein, calcium and vitamin C and is low in fat content (Hithamani and Srinivasan, 2014). Above all, *C. arietinum* is known as a powerful antioxidant and contains high levels of flavonoids and polyphenol (Miquel *et al.*, 2006). Intake of food including antioxidants may help to protect menopausal woman against oxidative stress (Sierens *et al.*, 2001). As well, phytoestrogens are one of the important antioxidant in food (Sierens *et al.*, 2001).

Phytoestrogens are plant-derived hormone analogues that their structural is similar to mammalian estrogens and they play both estrogen effects and anti-estrogen effects (Borrelli and Ernst, 2010). Phytoestrogen are classified with isoflavones, coumestans and lignans (Sierens *et al.*, 2001). Isoflavones present a lot of soybeans, soybean product and red clover (Soni *et al.*,

2014). Lignans are found in flaxseed which present at considerable concentrations in fibre-rich foods (Fritz *et al.*, 2013) and coumestans are existed clover and soybean sprouts that have a large number of coumestans (coumestrol and 4-methoxycoumestrol) predominantly coumestrol and 4-methoxycoumestrol (Landete, 2012). Isoflavones are a class of phytoestrogens (which are a type of polyphenols) that stimulate estrogen receptors and hence mimic physiological estrogen in women (Cornwell *et al.*, 2004). Isoflavone-rich foods are thought to help overcome menopause (HaiRong *et al.*, 2013). Complementary and alternative medicine (CAM) to alleviate menopausal symptoms used many prescription include phytoestrogen (Borrelli and Ernst, 2010). Phytoestrogen had the function of scavenging harmful free radicals (Sierens *et al.*, 2001). The daidzein (one of phytoestrogen) had function of decreased ROS-induced toxicity by antioxidant and estrogenic action (Brandao *et al.*, 2009) and isoflavones prevent various diseases caused by oxidative stress (Liu *et al.*, 2006). For this reason, the confirm of antioxidative effect will be an index to determine the content of the phytoestrogen.

In this study, we report the intake frequency of legumes containing isoflavones (in the form of rice cakes) in middle-aged South Korean women with the aim to alleviate symptoms of menopause through phytoestrogen intake and we suggest alleviating menopause through rice cake that have antioxidant in *C. arietinum*.

MATERIALS AND METHODS

Study participants: Of the 25,534 individuals that participated in the 5th Korean National Health and Nutrition Examination Survey (KNHANES, 2011), 1,992 middle-aged women (> 40 years old) were enrolled in this study. KNHANES data collection was approved by the Korea Centers for Disease Control Institutional Review Board (2011-02CON-06-C).

Materials: Commercially available rice was purchased and *C. arietinum* was harvested in Australia. We purchased 1,1-diphenyl-2-picrylhydrazyl (DPPH) from Sigma Chemical Co. (St. Louis, MO).

Survey: The dietary intake frequencies of 1,992 middle-aged women (> 40 years old) were derived from the 5th KNHANES (2011). We conducted a cross-sectional analysis of the intake frequency of rice, beans, tofu and bean sprouts in these women. It was confirmed ratio in the comparison rice is the staple food of Korea.

Preparation of *C. arietinum* flour: *C. arietinum* was washed with running water and then immersed in water for 24 h. The soaked *C. arietinum* was boiled for 50 minutes and subsequently dried. The dried *C. arietinum* was grinded with a mixer (Hanil electricity Co. Ltd., South

Korea) and a thin powder was produced by sieving multiple times with a 30-mesh sieve (Joungwoo Industry, South Korea).

Preparation Rice Cake added *C. arietinum* flour:

Prepared rice flour (500 g) and *C. arietinum* flour (50 g) was immersed in water (150 ml) for 5 h. After adding an appropriate amount of salt and to the flour, the rice and *C. arietinum* powder and all supplements (salt; 5 g, sugar; 50 g) were mixed well. The mixture was turned into a thin powder mix using a sieve. The rice flour was steamed in a bamboo steamer for 25 min and the boiled rice was allowed to settle for 5 min.

Analysis of the antioxidant activity of rice cakes supplemented with *C. arietinum*:

To analyze the antioxidant activity of rice cakes, 1 g of the rice cake and 9 mL methanol were mixed and shaken at room temperature for 16 h. The supernatant was centrifuged for 1 min at 13,000 rpm and mixed with methanol to achieve various concentrations (0, 20, 40, 60, 80 and 100 mg/ml). We added 1 mL DPPH (0.2 mM) to the supernatant and the mixture was incubated at room temperature for 30 min. Absorbance was analyzed at 517 nm.

Statistical analysis: Data of at least three different experiments were collected and are presented as mean±standard deviation. All data were analyzed using SPSS (version 12.0, Raleigh, NC, USA). The statistical significance of differences was evaluated by one-way analysis of variance and a least significant difference test at a 95% confidence level (p<0.05).

RESULTS

Intake frequency of bean-derived products: A total of 1,992 middle-aged women (>45 years; 23.39% of the total respondents in the 5th KNHANES (2011) answered the questionnaire. Response options included 'no intake', 'once/week' and 'three times/day'. Among the women reporting an intake of bean-derived products of 3 times/day, 1,327 (66.62%) and 457 (22.94%) reported rice and bean intake, respectively and no women reported tofu or bean sprout intake. Among those reporting an intake of 'once/week', 6 (0.30%), 465 (23.34%), 116 (5.82%) and 539 (27.06%) reported rice, tofu, bean and bean sprout intake, respectively. Finally, 1 (0.05%), 156 (7.83%), 263 (13.20%) and 114 (5.72%) women who answered 'no intake' reported rice, tofu, bean and bean sprout intake, respectively (Table 1).

Antioxidant activity of normal rice cake and rice cake supplemented with *C. arietinum*:

Normal rice cake and rice cake supplemented with *C. arietinum* had IC₅₀ values of 510.57 and 41.51 mg/ml, respectively. Rice cake supplemented with *C. arietinum* thus had an antioxidant activity that was 10 times higher than that of normal rice cake.

Table 1: Consumption⁽¹⁾ of bean-derived products in middle-aged women in South Korea

No	consumption ⁽¹⁾	6-11		2-3		Once/month		times/month		Once/week		times/week		2-3		4-6		times/week		Once/day		Twice/day		Three times/day		Total		
		F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	F (%)	
Rice	1	0.1	1	0.1	0	0.0	0	0.0	0	0.1	0	0.0	4	0.2	58	2.9	575	28.9	575	28.9	575	28.9	575	28.9	575	28.9	1,992	100.00
Tofu	21	1.1	21	1.1	65	3.3	181	9.1	294	14.8	443	22.2	112	5.6	45	2.3	10	0.5	1	0.1	1,992	100.00	1,992	100.00	1,992	100.00		
Beans	131	6.6	62	3.1	107	5.4	180	9.0	212	10.6	233	11.7	68	3.4	114	5.7	65	3.3	21	1.1	1,992	100.00	1,992	100.00	1,992	100.00		
Bean sprouts	24	1.2	19	1.0	89	4.5	202	10.1	360	18.1	400	20.1	74	3.7	19	1.0	5	0.3	1	0.1	1,992	100.00	1,992	100.00	1,992	100.00		

⁽¹⁾Cross-sectional data of KNHANES (2011) (South Korea). F: Frequency

DISCUSSION

Menopausal women suffer from melancholia associated with the loss of femininity and hormone-related diseases caused by decreasing hormone levels (Dixit *et al.*, 2012). Recently, there is an attempt to treat menopause by CAM (Borrelli and Ernst, 2010). The Complementary and alternative therapies for the menopause have many treatment that are acupuncture (Freeman *et al.*, 2014), calcium (Lee *et al.*, 2009), homeopathy (Lanham-New, 2008), phytoestrogens (Ernst, 2002) and vitamins (Jacobs *et al.*, 2009). In addition, many herbal plants were used to treat menopause of CAM. Black cohosh (*Cimicifuga racemosa* L.) (Papadimitropoulos *et al.*, 2002), Dong quai (*Angelica sinensis* Oliv.) (Heyerick *et al.*, 2006), Hops (*Humulus lupulus* L.) (Papadimitropoulos *et al.*, 2002), Wild yam (*Dioscorea villosa* L.) (Hirata *et al.*, 1997), Ginseng (*Panax ginseng* C.A. Mey) (Komesaroff *et al.*, 2001) are mainly herbals of CAM.

Many plant extracts are known to exert beneficial effects on postmenopausal women as they contain phytoestrogens (also referred to as natural estrogen-mimicking compounds) (Wiklund *et al.*, 1998). Phytoestrogens are found in many plant-derived human foods (e.g., soy beans and legumes) (Landete, 2012) and have been reported to prevent cancer (Jungbauer and Medjakovic, 2014). Considering this point, intake of soybean with middle-aged women are respected (Soni *et al.*, 2014).

We analyzed the legume intake frequency in middle-aged women using data from the 5th National Health and Nutrition Examination Survey (KNHANES, 2011). Legume consumption of middle-aged women (>40 years) was analyzed to low level compared to the consumption of rice. A total of 13% women reported no legume intake. Based on these findings, opportunities were able to compensate for female hormone decreased by low consumption of legumes. Some women can afford to replenish their hormone levels through the intake of functional foods or hormone injections; however, the majority of homemakers are not able to do so due to financial constraints. Therefore, the replenishment of hormone substitutes through food intake should be recommended. However, middle-aged women often prioritize their families first and not themselves. This leads to a loss in confidence and susceptibility to depression in these women. To overcome menopausal symptoms, the activity for only themselves needed for them.

Functional food and drugs must be demonstrated to have a pharmacological effect. This procedure is very costly and preclinical and clinical tests are time-consuming and expensive. In reality, functional foods are able to prevent the disease that can be easily accessed. The goal of this study was to provide information on the intake of functional rice cakes in middle-aged women with the aim of disease prevention.

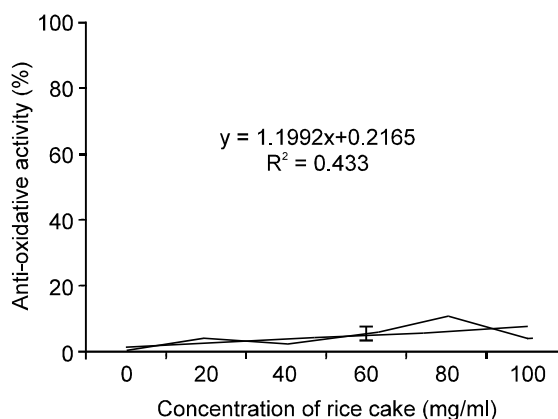


Fig. 1: Antioxidant Effect of Rice cake without *Cicer arietinum*. Antioxidant activities were analyzed by DPPH radical scavenging activity. The IC₅₀ calculated by the trend line was 510.57 mg/ml. Values are shown as means±standard deviation and data are from three independent experiments. DPPH, 1,1-diphenyl-2-picrylhydrazyl

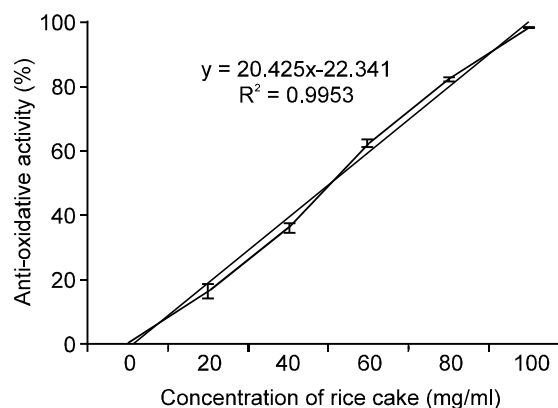


Fig. 2: Antioxidant Effects of Rice cake Supplemented with *Cicer arietinum*. Antioxidant activities were analyzed by DPPH radical scavenging activity. The IC₅₀ calculated by the trend line was 41.51 mg/ml. Values are shown as means±standard deviation and data are from three independent experiments. DPPH, 1,1-diphenyl-2-picrylhydrazyl

Phytoestrogens (isoflavones, coumestans and lignans) are found in soybeans and other legumes (Soni *et al.*, 2014). Isoflavones in soybeans include daidzein, genistein and glycitein (Dodge *et al.*, 1996), (Csaky and Fekete, 2004). High contents of isoflavones are found in beans, rosaceae (Csaky and Fekete, 2004) and iridaceae (Daruhazi *et al.*, 2013). Isoflavones are well known for their anti-oxidative (Lee *et al.*, 2011), anti-bacterial (Xiao *et al.*, 2011), cholesterol-lowering (Weber *et al.*, 2013) and blood pressure-lowering effects (Lee *et al.*, 2013). These phytoestrogen are effected lack of

hormones related dyspnea, flushing etc. (Lee *et al.*, 2013). Moreover, phytoestrogens stimulate osteoblasts and inhibit osteophages to being densely density of bone cells (Borjesson *et al.*, 2013). It has also been shown that lignin supplementation results in a reduction of oxidized low-density lipoprotein levels, decreases the incidence of cardiovascular disease (Liu *et al.*, 2012) and is effective for the prevention of breast cancer and osteoporosis d4 (Borjesson *et al.*, 2013; Strauss *et al.*, 2014) Hydnocarpin (a lignin) is thought to be effective for colon cancer prevention (Hillman *et al.*, 1985). The anti-oxidative and anti-cancer effects of coumestans have also been demonstrated (Brandao *et al.*, 2009).

HaiRong (HaiRong *et al.*, 2013) reported high level of isoflavones in *C. arietinum*. The administration of isoflavone extracted from *C. arietinum* in mice with removed ovaries increased bone mineral density and bone and tissue volume and positively affected intrabecular thickness and trabecular separation. Isoflavones extracted from *C. arietinum* have also been reported to affect breast and prostate cancer. *C. arietinum* has been reported to contain 2.17 ± 0.654 g/100 g lignin in its raw form, 0.59 ± 0.756 g/100 g when immersed in water and 2.50 ± 0.721 g/100 g when cooked. Lignin is a precursor of lignan, which is a phytoestrogen. *C. arietinum*, which contains phytoestrogens, has a high antioxidant effect. The hormonal alterations of menopause in middle-aged women is vulnerable to prevent oxidative stress (Cameron *et al.*, 1997) and diet supplementation with antioxidants help to overcome menopause against oxidant stress in the female hormone deficiency (Sierens *et al.*, 2001). In additionally, the anti-cancer and other pharmacological effects of phytoestrogens have been shown to be associated with their antioxidant activity. Hence, functional rice cakes made of *C. arietinum* are thought to be beneficial for menopausal women. Our findings confirmed the antioxidant activity of rice cake supplemented with *C. arietinum*. Normal rice cake had antioxidant effects with an IC_{50} of 510.57 mg/ml and rice cake supplemented with *C. arietinum* had antioxidant effects with an IC_{50} of 41.51 mg/ml. The antioxidant effect of *C. arietinum* extract was not analyzed in this study because functional cuisine is made of raw foods. Moreover, it has been shown that the antioxidant effect of *C. arietinum* is not reduced by the cooking process.

The lignan content of *C. arietinum* in meals was similar to that in raw *C. arietinum* and *C. arietinum* immersed in water. Lignan is a major factor of the antioxidant effect of rice cake supplemented with *C. arietinum*. Unchanged antioxidant effect during making rice cake supplemented with *C. arietinum* enables speculation that in no change in phytoestrogen levels. Premenopausal middle-aged women have decreased hormone levels. Phytoestrogens can compensate for these reduced levels.

Our study introduced a potential of rice cake supplemented with *C. arietinum* as a hormone replacement strategy for middle-aged women. These rice cakes can easily be made at home. The purpose of the female hormone replacement is clear as functional foods that will be helped recovery of menopausal by giving satisfaction.

Conclusions: Rice cakes can easily be made at home and *C. arietinum*, which has a significant antioxidant effect, can be added to rice cake. The antioxidant effect of *C. arietinum* is not reduced by cooking. Importantly, this attribute of *C. arietinum* can help ameliorate menopausal symptoms. Thus, the intake of functional foods should be recommended for middle-aged women.

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