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Original article

Anti-obesity effects of Korean red ginseng extract in healthy beagles

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Abstract

The aim of this study was to evaluate the safety and anti-obesity effects of the Korean red ginseng extract in dogs. To this end, we fed healthy beagles a Korean red ginseng diet and/or snack for 8 weeks. The dogs were submitted to a thorough physical examination, complete blood count, serum biochemistry analysis, analysis of adipose tissue activity, and body fat-content analysis by computed tomography (CT). At the end of the study period, the dogs that were fed the ginseng extract-diet/snack showed a significant decrease in body weight, body condition score and leptin levels relative to the baseline value. The CT findings revealed a decrease in body fat content in dogs fed the ginseng extract diet but not in those fed the ginseng-extract snack. The results of blood analysis did not show any meaningful changes in any of the dogs. All dogs tolerated the diet/snack well, and there were no adverse events. Our results suggest that the Korean red ginseng extract diet can potentially serve as an anti-obesity diet for reducing fat mass in dogs.

Key words: anti-obesity, dog, ginseng

Introduction

In dogs, obesity is a common nutritional disorder affecting over 50% of the dogs in several countries (Courcier et al. 2010, Mao et al. 2013). Given that it is a risk factor for metabolic diseases, including insulin resistance and hypertension, obesity presents a serious health problem (German 2006). In addition, as this abnormal health status can cause discomfort and reduce the quality of life of both the affected dogs and their owners, its prevention and treatment are essential.

Ginseng (the root of *Panax ginseng Meyer*; family: Araliaceae) has been used in herbal medicine for 5000 years as a general tonic for promoting health in various Asian countries (Ao et al. 2011). When steamed at 98-100°C and dried, ginseng yields red ginseng, which can be preserved for a longer time than the former (Ao et al. 2011). Red ginseng is widely used in Oriental medicine as a remedy for various diseases, including diabetes mellitus, hepatitis and gastritis (Kim et al. 2007, Vuksan et al. 2008). The Korean red ginseng (KRG) marc is a fibrous and insoluble byproduct of the extraction process. Although the anti-obesity effects of ginseng are well reported in humans and rats, evidence of its effects in dogs is still lacking (Kim et al. 2005, Hasani-Ranjbar et al. 2009).

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The aim of this study was to investigate the anti-obesity effects of the KRG marc in dogs. To assess its efficacy and safety, we conducted physical examinations, blood tests, and computed tomography scans for measuring body fat mass and to estimate adipose tissue activity.

Materials and Methods

Animals and study design

This study included 21 healthy beagles (18 male; 3 female) with excess body weight relative to the ideal body condition. The mean age of the beagles was 6.3 years (range: 3-7 years). Each dog was housed in a separate cage at a relative humidity of 30-70% and a temperature of 23-28°C. All dogs were healthy, as judged by physical examination, and had no history of use of any drugs or biotics that could have affected their weight in the month prior to the study. Before the study, all dogs were fed the same diet for at least three months.

The dogs were randomly allocated to three groups, each group was comprised of one female and six male beagles. They were all fed their respective diets during the experiment, as follows.

Group A: diet without ginseng extract (300 g)
Group B: diet with ginseng extract (300 g)
Group C: diet without ginseng extract (275 g) + snack with ginseng extract (25 g)

Both the diet and snack with the ginseng extract were manufactured and supplied by Korea Medicine Biofermentation Co., Ltd. The test diet and snack contained 1% ginseng extract. The components of the diet, with the exception of the ginseng extract, were the same for all groups (crude protein; 27.0%, crude fat; 14.0%, crude fiber; 3.0%, crude ash; 9.0%, calcium 1.0%, phosphorous; 0.6%, moisture 12.0%), and the total calorie intake from both the diet and snack was the same for all dogs. Each dog was fed approximately 300 g of the food product once per day, and the food intake was confirmed by a veterinarian. Dogs allocated to group C were given the snack once a day after being fed the diet.

All assessments for evaluating the effects of the ginseng extract were conducted in weeks 0 (day 0) and 8 (day 56). The study protocol was reviewed and approved by the Institutional Animal Care and Use committee (approval number, 20180088).

Physical examination

Obesity was assessed by measuring the body weight and the 9 point Body Condition Score (BCS: ranging from 1 [underweight] to 9 [obese]). All physical examinations were conducted by the same investigator before feeding. All dogs were evaluated for adverse events including vomiting, diarrhea, lethargy, and fever throughout the study.

Blood sampling and analysis

Blood samples were collected during fasting, before (at week 0) and after (after week 8) the study period. Approximately 5 mL of blood was obtained by jugular venipuncture and collected in both ethylenediaminetetraacetic acid and heparin tubes. Complete blood count and serum biochemistry analysis were performed to evaluate the general condition of the dogs. The serum biochemistry parameters included alkaline phosphatase, alanine transaminase, aspartate aminotransferase, gamma glutamyl transferase, total bilirubin, total protein, glucose, cholesterol, triglycerides (TG), blood urea nitrogen (BUN), creatinine, C-reactive protein, and electrolytes.

For evaluating adipose tissue activity, serum was separated immediately after blood clotting on days 0 and 56, and stored at -20°C until analysis. The serum adiponectin, leptin, tumor necrosis factor alpha (TNF-α), and insulin-like growth factor (IFG)-1 levels were then measured by using commercially available assay kits in accordance with the manufacturers' protocols.

Body fat content

For evaluating the changes in body fat content, computed tomography (CT) was performed for all dogs before and after the study period. The dogs were made to fast for 12 hours before imaging. The CT images were obtained under anesthesia, which was induced by intramuscular injection of ketamine (7 mg/kg) and medetomidine (40 μg/kg). Imaging was performed with a 32-row multisided CT device (Alexion; Toshiba, Tokyo, Japan) under the following conditions: tube voltage: 120 kV; tube current: 200 mA; image slice thickness: 3 mm. All dogs were kept in the prone position during imaging.

Body fat content was calculated from the measurements by using the following formula, based on a previous study (Witzel et al. 2014):

Fat mass (g) = 229.04 × body weight – hind-limb length + 157.78 × (thoracic circumference – head circumference) + 908.79.

Statistical analysis

Statistical analysis was performed using commercially available software (SigmaPlot® 12.0; Systat Software Inc., San Jose, CA, USA). All values are

Table 1. Mean body weight of beagles prior to and following the study.

	Group A	Group B	Group C
Day 0	11.16 ± 0.42	11.31 ± 0.21	11.16 ± 0.42
Day 56	10.61 ± 0.26	9.56 ± 0.21**	10.42 ± 0.35*

* p<0.05, ** p<0.01 vs before

Table 2. Mean body condition score of beagles prior to and following the study.

	Group A	Group B	Group C
Day 0	6.00 ± 0.53	6.14 ± 0.59	6.28 ± 0.42
Day 56	6.71 ± 0.42	4.71 ± 0.52**	5.71 ± 0.60

** p<0.01 vs before

Table 3. Changes in blood chemistry from day 0 to day 56.

		Group A	Group B	Group C
BUN (RI:9.2-29.2)	Day 0	12.40 ± 1.16	12.30 ± 0.78	12.49 ± 1.46
	Day 56	18.14 ± 1.69 **	18.69 ± 1.46 *	19.61 ± 1.25 *
Cholesterol (RI: 111-312)	Day 0	279.86 ± 13.61	257.00 ± 19.54	290.86 ± 19.73
	Day 56	266.14 ± 21.19	226.43 ± 16.26 *	267.43 ± 25.60
Triglyceride (RI: 30-133)	Day 0	54.71 ± 1.96	60.14 ± 2.14	62.29 ± 1.57
	Day 56	51.86 ± 5.82	49.43 ± 2.95 *	63.57 ± 3.12
Total bilirubin (RI: 0.1-0.5)	Day 0	0.24 ± 0.03	0.21 ± 0.03	0.24 ± 0.02
	Day 56	0.34 ± 0.04 *	0.33 ± 0.03 **	0.31 ± 0.03

BUN; blood urea nitrogen, RI; reference index, * p<0.05, ** p<0.01 vs before

expressed as mean ± standard error of the mean. The differences in each parameter between before and after the study were examined by Student's t-test. *P* values ≤ 0.05 were considered significant.

Results

Physical examination

The effects of the ginseng extract on body weight (Table 1) and BCS (Table 2) are shown. After eight weeks, both body weight and BCS had decreased in groups B and C. In contrast, the body weight of the dogs in group A had decreased, whereas their BCS had increased by day 56. No side effects were observed during the study.

Blood analysis

Relative to the baseline (day 0) condition, there were no significant changes in serum biochemistry parameters after the study period, except in BUN, cholesterol, total bilirubin, and TG levels. Although BUN levels had increased after eight weeks in all three groups, they included the reference ranges. The cholesterol and TG levels had decreased significantly in group B (p<0.05). Although the total bilirubin levels had increased in groups A and B (p<0.05), the values were within the reference range. The changes in blood biochemistry parameters throughout the study period are shown in Table 3.

The changes in adipose tissue activity are shown in Table 4. Among the cytokines, only leptin showed a significant change in concentration in groups B and C after the study (p<0.05).

Body fat content

The changes in body fat content are shown in Table 5. The fat mass increased after the study period in groups A and C; however, the mean fat mass decreased significantly in group B (p<0.05).

Discussion

Obesity has become one of the more common abnormalities in companion animals, often leading to several complications such as diabetes and arthritis

Table 4. Changes in cytokine levels from day 0 to day 56.

		Group A	Group B	Group C
IGF-1 (μg/mL)	Day 0	0.08 ± 0.01	0.07 ± 0.01	0.08 ± 0.01
	Day 56	0.07 ± 0.01	0.07 ± 0.01	0.07 ± 0.01
Leptin (ng/mL)	Day 0	4.18 ± 0.68	7.90 ± 0.69*	4.40 ± 0.81*
	Day 56	3.93 ± 0.24	1.98 ± 0.54*	1.60 ± 0.53*
Adiponectin (μg/mL)	Day 0	1.12 ± 0.08	1.16 ± 0.14	1.23 ± 0.14
	Day 56	1.04 ± 0.09	1.15 ± 0.08	1.11 ± 0.08
TNF-alpha (ng/mL)	Day 0	0.069 ± 0.006	0.070 ± 0.005	0.066 ± 0.005
	Day 56	0.071± 0.011	0.068 ± 0.003	0.068 ± 0.006

IGF; insulin-like growth factor, TNF; tumor necrosis factor, * $p<0.05$ vs before

Table 5. Mean fat mass estimated by computed tomography imaging of beagles prior to and following the study.

	Group A	Group B	Group C
Day 0	2538 ± 523.79	2388.94 ± 568.18*	2311.06 ± 298.09
Day 56	3156.43 ± 667.80	1944.64 ± 531.31*	2780.61 ± 378.89

* $p<0.05$

(German 2006). In the current study, we fed healthy dogs a diet or snack containing ginseng extract to confirm its anti-obesity effects.

First, for assessing obesity, we measured the body weight and BCS, and estimated the body fat content by CT analysis. The BCS system is commonly used in clinics for measuring obesity; it is assessed by tracing a thorough body outline including fat coverage, and by the ability to palpate the ribs, and then categorized on the basis of the results. An adequate body weight loss entails reduction of fat mass with lean mass retention. However, BCS is a subjective estimate. Additionally, neither the body weight nor BCS has the ability to reveal body composition. Therefore, to assess the body fat mass more accurately, we performed a CT analysis and calculated the body fat content. As expected, although body weight and BCS had decreased in groups B and C, the body fat content (determined by CT analysis) decreased significantly only in group B. Thus, it could be concluded that successful body weight loss was obtained in dogs that were fed ginseng extract diet.

On blood chemistry tests, the group fed with the ginseng-extract diet without the snack showed a significant decrease in cholesterol and TG levels after the study period. Both cholesterol and TG are risk factors for hyperlipidemia, and are usually considered as obesity markers during the analysis of anti-obesity effects (Yamka et al. 2007). There is a lack of studies demonstrating the anti-obesity effect of ginseng on pets. However, some studies showed that ginseng improved hyperlipidemia in experimental animals and humans (Joo 1980, Kim et al. 2002, Kim et al. 2011). Ginseng decreased blood cholesterol levels by increasing cholesterol excretion through the stimulation of bile acid formation (Joo 1980). In addition, ginseng also reduced serum TG concentration and inhibited the accumulation of TG in adipose tissue through the inhibition of pancreatic lipase (Kim et al. 2011).

Obesity is mainly characterized by the expansion of adipose tissue. In adipose tissue, adipocytes are the common cell type, and they secrete several cytokines such as leptin, adiponectin and TNF-α, the substances we measured in this study to evaluate adipocyte activities (Wang et al. 2008, Laflamme 2012). Leptin and adiponectin regulate energy metabolism and body fat mass (Wynne et al. 2005). Generally, relating to obesity, leptin has a positive correlation with obesity, although adiponectin has a negative correlation (Wang et al. 2008, Laflamme 2012). The TNF-α is a proinflammatory cytokine produced from fat mass (Wang et al. 2008, Laflamme 2012). Thus, TNF-α concentration is increased in obese subjects. However, the concentration of these cytokines varies according to the subject's environment, and the correlation with obesity is not consistent (Laflamme 2012). In this study, only leptin showed a significant change in concentration after the intake of the ginseng extract diet. Leptin was the first adipokine to be identified, and the presence of elevated plasma leptin levels in obese dogs regardless of their breed, age and sex, could be a useful marker for the quantitative assessment of obesity in small animals (Wynne et al. 2005). Previous studies showed that the positive relationship between body fat content in dogs and plasma leptin concentration is more pronounced

than association with other variables such as cholesterol, TG, and other adipocytes. Thus, a significant decrease in leptin concentration in group B was a very significant finding with real fat mass reduction visualized on the CT scan.

In addition, we also measured IGF-1, a hormone similar to insulin. It is secreted from the liver and plays an important role in anabolism (Smith 1996). In humans, IGF-1 secretion increases with an increase in the body fat mass (Smith 1996); however, such changes were found to be sex-dependent in dogs. In a previous study, IGF-1 increased when body weight increased in castrated male beagles but remained within the normal range in intact male dogs (Martin et al. 2006). In the current study, the level of IGF-1did not show significant changes in all groups. We thought the IGF-1 value was stable in our study, because almost all of the beagles were intact male dogs.

Ginseng is a widely used herb in Asia, and many studies have demonstrated its benefits in several abnormal states (Kim et al. 2007, Vuksan et al. 2008). Moreover, ginseng also exerts anti-obesity effects through the suppression of lipid absorption and regulation of peroxisome proliferator-activated receptor (PPAR)-γ (Hwang et al. 2009). The PPAR is an important transcription factor for lipid and glucose homeostasis. Three isotypes of PPAR have been identified, and among these isotypes PPAR-γ is expressed in the adipose tissue. By expressing PPAR-γ, adipogenesis is induced. Therefore, the inhibition of PPAR-γ activation can induce anti-obesity effectively (Hwang et al. 2009). In this study, we could not conduct histopathologic examination for assessing the difference in PPAR-γ before and after feeding the dogs with a ginseng extract diet. However, we assumed that the anti-obesity effect of ginseng in dogs is similar to that in other species.

In conclusion, the overall results of this study showed that canine food rich in ginseng marc has a beneficial anti-obesity effect and can be used for weight loss in companion animals. However, to achieve loss of real fat mass and successful diet effects, a snack of ginseng extract is not enough. Further studies are needed to evaluate the exact mechanism through which ginseng marc inhibits fat accumulation. Additionally, a similar study should be conducted among female and intact male dogs prior to the commercialization of this food.

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