

Effect of *Gocho*(苦椒) Extract Mesotherapy on Regional Fat Loss in Obese Korean Women.

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Objectives: The purpose of this study was to determine whether *gocho* (苦椒) extract mesotherapy can effectively reduce weight and abdominal fat in obese patients.

Methods: Forty obese participants were recruited and randomly assigned to two groups. Five participants dropped out voluntarily during the course of the study and four men were excluded from the analysis to avoid gender bias. Results are presented on a total of thirty-one women. Over an eight-week period, the treatment group (n=13) received *gocho* (苦椒) extract injections (100mcg/3cc) in the abdominal skin, twice per week; the control group (n=18) received normal saline injections (3cc). A mixed lidocaine and prilocaine cream (2.5%/2.5% EMLA cream) was applied before the injection.

At baseline and 8 weeks, body weight, body-mass index (BMI), waist circumference (WC), waist-hip ratio (WHR), abdominal fat, energy expenditure, and questionnaires (eating attitudes and physical activity) were evaluated in both groups.

Results: Reductions in body weight (p<0.005), BMI, and WC (p<0.05) were greater in the treatment group. WHR, total fat area, and visceral fat area decreased only in the treatment group (p<0.05). Resting metabolic rate (RMR) change was correlated with weight loss only in the control group (r=-0.498, p<0.05). Before and after the treatment, there were no significant differences between the two groups in questionnaire variables (p>0.05).

Conclusion: his study suggests that abdominal *gocho* (苦椒) extract mesotherapy might be an effective way to promote weight and abdominal fat loss in obese Korean women.

Key Words : *Gocho* (苦椒) extract mesotherapy, capsaicin, weight loss, abdominal fat, obesity

Introduction

Obesity is defined as an accumulation of excessive body fat¹. Obesity has become a major public health problem with high costs that affect both individuals and society at large². Well-organized weight-loss programs are continuously in demand.

In Korea, the intra-dermal injection of herbal medication using a mesogun is called herbal

mesotherapy. It includes injections of distilled herbal formulas with a syringe subcutaneously or intradermally at acupoints or areas of fat accumulation. Intradermal injection can compensate for defects of oral administration that are dependent on the dosage forms of medicine, gastric pH, difficulty of localization, and possibility of unsuspected systemic response from medication. Clinically, herbal mesotherapy is widely used to treat obesity in Korea, but only a few case-

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controlled clinical studies have been reported^{3,4}.

Natural substances derived from *gocho* (苦椒), have been shown to increase metabolism and reduce body fat in animal and human studies⁵⁻⁷. Injectable delivery using a mesogun might enhance *gocho* (苦椒)'s effects by bypassing the rapid metabolism of ingested *gocho* (苦椒).

The purpose of this study was to determine whether *gocho* (苦椒) extract mesotherapy can reduce weight and abdominal fat in obese patients.

Materials and Methods

1. Participants

Obese (BMI $\geq 25\text{kg/m}^2$) Korean participants between 18 and 65 years of age were enrolled in this randomized controlled, double-blinded study from 10th April to 20th October, 2009 after providing written informed consent. Forty participants were recruited; five dropped out voluntarily during the study, leaving 35 participants who completed the study. We excluded 4 men from the current analyses to avoid gender bias. Results from a total of 31 (13 in treatment group and 18 in control group) women are presented. Inclusion criteria required ambulatory participants from 18 to 65 years with a body-mass index (BMI) $\geq 25\text{g/m}^2$. Participants who either previously or currently had heart disease, diabetes mellitus, kidney disease, or malignant tumors were excluded from our study. Participants who had experienced weight changes over 3 kilograms within two months and who were or might be pregnant or who had given birth during the last six months were also excluded. Any participant with a compliance of less than 70% was removed from our analysis. This study was approved by the Institutional Review Board of Kyung Hee University Hospital at Gangdong. Recruitment was done through newspapers, advertisements and hospital websites.

2. Procedures

Before the treatment all participants had an intradermal allergy skin test to check for hypersensitivity reaction to the herbal solution. Volunteers were randomized into two groups. Each treated point was injected with 0.05cc, a total of 3cc per session. Injection of the solution was performed using a mesogun (MESO-PRI, Hyun-dae Meditech, Korea) in the skin overlying the abdomen, twice per week for eight weeks. The treatment group received a solution with 100mcg/3cc of *gocho* (苦椒) extract while the control group got 3cc of normal saline (Fig. 1.).

To minimize discomfort and maintain blinding, a mixed lidocaine and prilocaine cream (2.5%/2.5% EMLA cream) was applied before the injection. Participants were advised to follow a hypocaloric diet (<1200 Kcal per day) and to walk for at least 30 minutes three times a week.

Before and after the procedure, body weight, BMI, waist circumference (WC), waist-hip ratio (WHR), abdominal fat, energy expenditure, and questionnaires (eating attitudes and physical activity) were evaluated in both groups.

3. Materials

Herbal solution of *gocho* (苦椒) extract was supplied by Sigma Pharmaceuticals. To meet requirements of safety, sterility and endotoxin testing of herbal solution was performed by a microbiologist in ARL (ANALYTICAL RESEARCH LABORATORIES, Oklahoma, US). The sterility testing was regulated by test method USP (United States Pharmacopeia) 71, and the result was sterile. The endotoxin testing was regulated by test method USP 85 and the result was <1.0 EU/ml (limits based on a dose of 6 ml in 24 hours as specified by client: 1389 EU/ml). *Gocho* (苦椒) extract is derived from the dried fruit of *Capsicum frutescens* L., and it conforms to all applicable provisions of the Federal Food, Drug, and Cosmetic Act. The amount of specific major capsaicinoids in the product

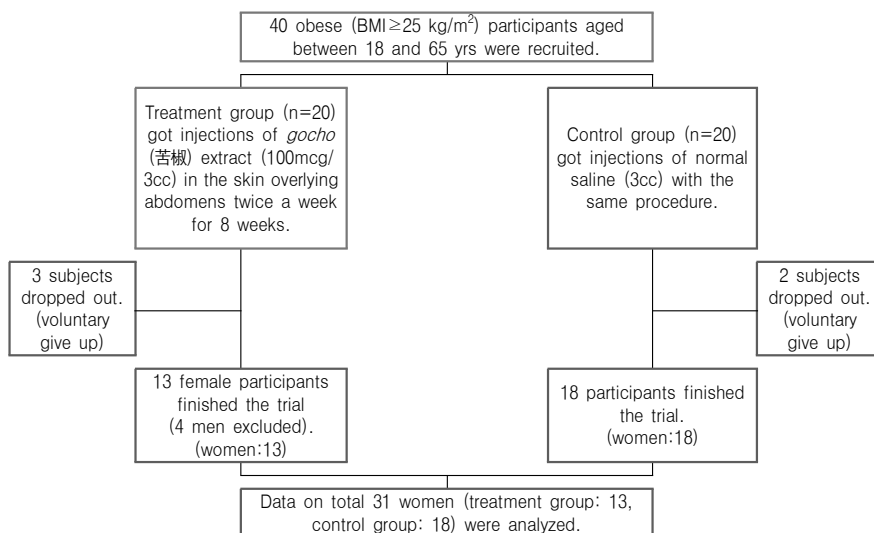


Fig. 1. Schematic diagram of study design. 40 participants were randomized into two groups.

During the study, 5 participants (3 in treatment group and 2 in control group) dropped out voluntarily and 4 men were subsequently excluded from the analysis to avoid gender bias. Results on a total of 31 (13 in treatment group and 18 in control group) women are presented.

reflects the natural balance found in *gocho* (苦椒). This balance will vary somewhat from lot to lot; it is approximately 36% capsaicin (CAS no. 404-86-4), 24% dihydrocapsaicin (CAS no.19408-84-5) and 10% nordihydrocapsaicin (CAS no. 28789-35-7). The balance of the product, approximately 30%, is the fatty acid fraction of the *gocho* (苦椒). The technical information is shown below (Table 1.).

4. Evaluations

1) Anthropometry

Body weight (BSM330, BIOSPACE, Korea) and height (BSM330, BIOSPACE, Korea) were measured

to the nearest 0.1kg and 0.5cm, respectively, while participants wore a hospital gown. Waist circumference (WC) and hip circumference (HC) were measured using flexible measuring tape by the same observer three times according to the World Health Organization (WHO) method, mid-point between the lower end of the rib cage and top of the iliac crest in a standing position, which is usually 3cm above the anterior superior iliac spine.

2) Abdominal Fat Computed Tomography (CT) Scanning

Abdominal fat area was measured by CT scanning (GEMINI 16 Power CT, Philips Medical systems,

Table 1. Technical Information of Herbal Solution of *Gocho* (苦椒) Extract

Major Capsaicinoids	60% to 80% (Official Monographs of the USP 25)
Color intensity	Not applicable
Appearance	A light brown viscous oil to a crystalline solid
Aroma and Flavor	Not applicable
Dispersibility	Dispersible in vegetable oil and other nonpolar carriers when warmed to 50°C and agitated. Dispersible in cetyl alcohol and ethyl alcohol when warmed to 50°C and agitated.
Storage conditions	Dry warehousing in full, tightly sealed containers at temperatures not to exceed 75°F. Shelf life under these conditions is one year.
GMO status	Does not contain ingredients from genetically modified source materials; where appropriate, ingredients are traceable back to their origin with an Identity Preserved system.

Cleveland, US) at the level between the L4 and L5 vertebrae. Cross-sectional total fat area (TFA) and visceral fat area (VFA) were estimated by delineating the regions and calculating at an attenuation range of 190 to 30 Hounsfield units (HUs)⁴⁾.

3) Energy expenditure

Oxygen consumption (VO₂, ml/min) was measured by indirect calorimetry (MedGem, Health Tech, US). At baseline and 8 weeks, each individual participant was evaluated at a pre-scheduled time. Participants were told not to engage in physical activity for 24h before testing. Measurements were performed after participants rested for 30minutes in a supine position. In our laboratory, the daily variability in RMR is 4~5%. Participants were told to breath through the mouth with a mouthpiece inserted for about 20~30minutes^{8,9)}. Resting metabolic rate (RMR, kcal/day) was calculated using the Weir's equation:

$$\text{Resting metabolic rate} = [(3.941)(\text{VO}_2) + (1.106)(\text{VCO}_2)(\text{RQ})]^{10)}$$

4) Questionnaires

At baseline and 8weeks, all subjects completed questionnaires on eating attitudes and physical activities. The three-factor eating questionnaire R18 (TFEQ)¹¹⁾ to estimate eating attitudes and international physical activity questionnaire (IPAQ)¹²⁾ to estimate physical activities were used. The TFEQ-R18 consists of 18 items and item scores are summated into scale scores for cognitive restraint, uncontrolled eating, and emotional

eating^{13,14)}. The IPAQ consists of 7 items; six questions are about the number of days and the number of minutes per day of their participation in all kinds of vigorous, moderate and walking physical activities during the last seven days. The seventh question is about the time that participants spend sitting during an average weekday¹⁵⁾.

5. Data analysis

All values are mean ± SD. Correlation between changes in body weight loss and changes in RMR were performed by Pearson's correlation. Between both groups, weight reduction, BMI, WC, WHR, abdominal fat, energy expenditure and questionnaires were compared by independent t-test using the Statistical Package for the Social Sciences (SPSS) 12.0 program for Windows. A p-value less than 0.05 was considered statistically significant.

Results

1. Demographic Characteristics of Participants

Data from 31 women from 22 to 61 years of age with a BMI from 25.0kg/m² to 31.0kg/m² were analyzed. Participants' demographic and anthropometric characteristics are summarized in Table 2. There were no significant differences between the two groups in baseline demographics.

Table 2. Characteristics of the Participants (n=31)

Variables	Treatment group (n=13)	Control group (n=18)	p-value
Age	44.46±10.39	39.39±10.35	0.189
Weight (kg)	66.83±6.93	71.92±9.03	0.100
BMI (kg/m ²)	27.55±2.24	28.01±2.35	0.186
WC (cm)	91.14±6.10	92.71±7.33	0.532
WHR	0.910±0.036	0.896±0.045	0.392
TFA (cm ²)	288.86±65.07	316.69±68.82	0.265

Values represent the mean ± SD
BMI: Body-mass index

WC: Waist circumference

WHR: Waist-hip ratio

TFA: Total fat area

2. Reduction of weight, BMI, WC, WHR, and TFA

Weight loss occurred in both treatment (-2.71kg; $p=0.001$) and control (-0.92kg; $p=0.009$) groups with a greater reduction in the treatment group ($p=0.003$). The changes in BMI, WC, WHR, and TFA were also greater in the treatment group (Table 3).

3. The Change of VFA

Baseline values for VFA (treatment group: $70.18 \pm 28.86 \text{cm}^2$ vs. control group: $75.76 \pm 24.10 \text{cm}^2$; $p=0.563$) were not different. After eight weeks of treatment, VFA reduced significantly in the treatment group ($10.42 \pm 13.65 \text{cm}^2$; $p=0.017$) but not in the control group ($2.70 \pm 9.24 \text{cm}^2$; $p=0.232$) (Fig. 2.).

4. Energy expenditure

Due to a technical issue with the indirect calorimeter

(the display screen on the indirect calorimeter was cracked), the RMR of two participants (control group) could not be measured. Therefore, data for 29 participants (treatment group: 13, control group: 16) are presented. There were no significant between-group differences in baseline RMR (treatment group: $1470.77 \pm 169.72 \text{kcal/day}$ vs. control group: $1638.75 \pm 271.95 \text{kcal/day}$; $p=0.083$). The change in RMR was significantly correlated with change in weight ($r=0.498$, $p<0.05$) (Fig. 3.) in the control group but not in the treatment group ($r=0.313$, $p>0.05$).

5. Questionnaires

There were no significant differences at baseline or 8 weeks for eating attitudes and physical activity ($p>0.05$) questionnaires. The scale score for cognitive restraint of TFEQ-R18 questionnaire significantly increased in the control group ($p=0.009$) only.

Table 3. Reduction of Weight, BMI, WC, WHR, and TFA

Variables	Before	After	Decrease	p-value [†]	p-value [‡]
Weight					
Treatment group	66.83±6.93	64.12±6.50	2.71±1.71	0.000**	0.003**
Control group	71.92±9.03	71.00±9.27	0.92±1.31	0.009**	
BMI					
Treatment group	27.55±2.24	25.87±2.01	1.04±0.69	0.000**	0.011*
Control group	28.01±2.35	27.58±2.46	0.42±0.58	0.007**	
WC					
Treatment group	91.14±6.10	84.78±6.14	6.35±2.51	0.000**	0.012*
Control group	92.71±7.33	89.97±7.13	2.74±4.37	0.016*	
WHR					
Treatment group	0.910±0.036	0.863±0.046	0.042±0.027	0.000**	0.005**
Control group	0.896±0.045	0.891±0.044	0.004±0.043	0.633	
TFA					
Treatment group	288.86±65.07	256.36±64.25	32.50±33.47	0.004**	0.005**
Control group	316.69±68.82	316.09±77.91	0.60±25.57	0.921	

Values represent the mean ± SD

BMI: Body-mass index

WC: Waist circumference

WHR: Waist-hip ratio

TFA: Total fat area

† : Difference of values before and after treatment in each group

‡ : Difference of values between the two groups

*: Decrease is significant at the 0.05 level

** : Decrease is significant at the 0.01 level

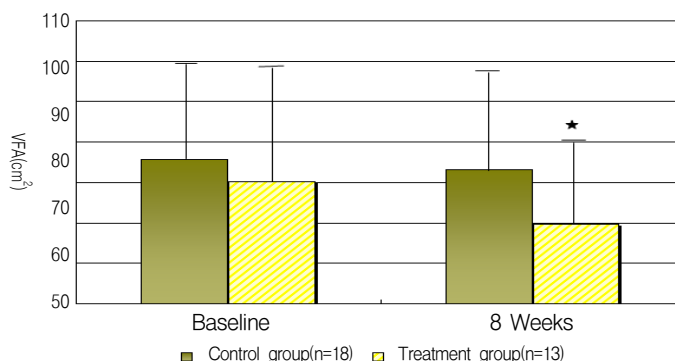


Fig. 2. Changes in VFA after eight weeks of treatment. Values represent the mean \pm SD. \star :Significantly different from baseline. $p < 0.05$.

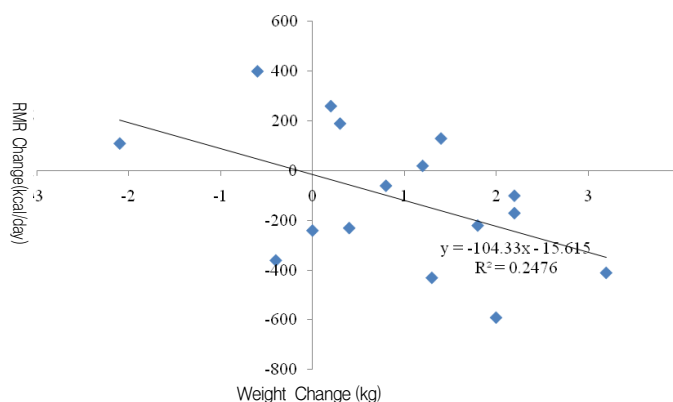


Fig. 3. The relationship between change in body weight and change in resting metabolic rate (RMR) in control group. RMR decrease in control group was significantly correlated with weight loss ($r = -0.498$, $p < 0.05$).

6. Adverse events

Ten moderate adverse events possibly related to treatment were reported by 6 participants, 4 in the treatment group and 2 in the control (Table 4.). Multiple answers were chosen by each participant. Almost all of them were symptoms related to anesthesia cream or injection of solutions, and disappeared in a day. No serious adverse events were reported.

In previous studies, capsaicin injections were associated with typical burning pain which diminished during the first few minutes and lasted for about 10 or 15 minutes¹⁶. Therefore, we did not calculate typical pain as an adverse event.

Discussion

Gocho (苦椒) is the fruit of plants from the genus *Capsicum*, members of the nightshade family *Solanaceae*¹⁷. Its traditional herbal name is *ralcho* (辣椒) or *beoncho* (番椒). *Gocho* (苦椒) is hot and spicy, so it warms the inside, keeps out the cold, unblocks the stomach, and increases body temperature¹⁸. *Gocho* (苦椒) spread from Japan to Korea about 400 years ago, and was widely cultivated in the 1700's. Now it is an important dietary seasoning in Korea¹⁹.

Capsaicin is the active component from which a hot taste derives in *gocho* (苦椒). It was first isolated in pure form by Thresh, who gave it the name capsaicin.

Table 4. Adverse Events

	Treatment group	Control group
Pain	1 (over 2 hours)	1 (not burning, but severe)
Nausea after anesthesia with EMLA cream	1	0
Continued dull sensation after anesthesia with EMLA cream	3 (for 5~7 hours)	0
Itching	1	0
Tingling when breathing in	1	0
Fatigue	1	0
Easily overheated with a slight movement	0	1
Sum	8	2

Number of the report cases, the subjects could give multiple answers.

Micho revealed its molecular formula ($C_{18}H_{27}NO_3$), Nelson elucidated its structure by chemical synthesis¹⁹.

The ingredients of *gocho* (苦椒) differ due to drying temperature, processing method, storage condition, kinds of *gocho* (苦椒), growing condition, ripening period, and parts of *gocho* (苦椒) used^{17,19-26}. Therefore, to maintain the reproducibility of expected effects, we made a herbal solution not with whole plants, but with major capsaicinoids including capsaicin, because they are the main ingredients which have anti-obesity effects of *gocho* (苦椒), and the injectable dosage into the human body without harmful side effects has been shown in previous studies^{16,27-8}.

In this study, body weight, BMI, and WC of both groups significantly reduced after treatment. The drop of body weight, BMI, and WC in the control group was slight but statistically significant, which may result from advised co-intervention to follow a hypocaloric diet and to walk for at least 30 minutes three times a week.

Gocho (苦椒) extract mesotherapy might be attributed regional fat loss. Although weight loss was observed in both groups, abdominal fat loss was significant only in the treatment group. This fat loss in the targeted region contributed to the drop of WHR and VFA.

Effects of capsaicin on fat loss have been already reported in previous studies. Snitker *et al.* reported that oral ingestion of capsaicinoids (6mg/d) for 12

weeks appeared to be safe and was associated with abdominal fat loss²⁹. Kawada *et al.* reported that capsaicin stimulates lipid mobilization from adipose tissue and lowers serum triglyceride concentration in rats³⁰.

Kang *et al.* studied roles of capsaicin in the adipose tissues of obese mice. Adipokines are associated with obesity-induced chronic inflammatory response which plays major roles in the development of obesity-related complications. The study demonstrated that capsaicin can suppress the expressions of IL-6 and MCP-1 genes and protein release from the adipose tissues and adipocytes of obese mice³¹.

According to these studies, using *gocho* (苦椒) extract mesotherapy for obesity treatment might be useful by regulating obesity-induced chronic inflammatory molecules as well as reducing regional fat.

Clinical research on capsaicin showed that consumption of a breakfast with capsaicin caused an increase in diet-induced energy expenditure (23%) immediately after the meal ingestion in Japanese males³². In 13 female subjects addition of red pepper to the experimental meals increased postprandial energy expenditure and lipid oxidation as well³³. These increases were assumed to be caused by enhanced catecholamine secretion from adrenal medulla, mainly through activation of the central nervous system³⁴⁻³⁶ and by β -adrenergic stimulation³⁷.

Our study suggests that *gocho* (苦椒) extract

mesotherapy might be effective to maintain energy expenditure without RMR decrease following weight loss and useful on weight loss. The most commonly reported metabolic consequence of weight loss is a reduction in energy requirement expected from the loss of body mass³⁸. In our study, we could not find a reduction of RMR following weight loss in the treatment group, whereas the reduction of RMR in the control group was significantly correlated with weight loss. Although there were no significant differences in questionnaires on eating attitudes and physical activities between two groups before and after treatment, the weight loss of the treatment group was significantly larger than that of the control. This result might be derived from *gocho* (苦椒) extract maintaining energy expenditure during weight loss.

There are conflicting studies about association between capsaicin and appetite. In previous study, oral exposure to capsaicin increased satiety and reduced energy and fat intake³⁹. Yoshioka *et al.* also reported that the ingestion of red pepper decreases appetite and subsequent protein and fat intakes in Japanese females and energy intake in Caucasian males⁴⁰.

However, Astrid *et al.* reported that capsaicin supplementation of one meal in a postprandial state has no effects on appetite feelings⁴¹. Before and after treatment in our study, we could not find a significant difference between the two groups in the questionnaire about eating attitudes except the scale score for cognitive restraint of the TFEQ-R18 questionnaire, which significantly increased only in the control group.

According to these results, significant weight loss in the treatment group compared to the control might be derived not from appetite but from energy expenditure.

This study had several limitations. First, our sample size was too small to generalize the results. Second, our study did not have a broad racial/ethnic con-

sideration since we included only Korean participants. Therefore, additional studies are necessary that include more diverse ethnic groups. Third, since the mechanism of weight and abdominal fat loss is not clear, further studies are required to identify the detailed mechanism of *gocho* (苦椒) extract mesotherapy on fat loss in human participants. Fourth, we had difficulty keeping our study double-blinded because of the typical burning pain participants experienced following *gocho* (苦椒) extract mesotherapy. To make clinical applications of *gocho* (苦椒) extract mesotherapy possible in practice, development of a new form that could diminish discomfort is needed.

In conclusion, this study suggests that abdominal *gocho* (苦椒) extract mesotherapy might be an effective way to promote weight and abdominal fat loss. Further evaluations using more participants to isolate the mechanism are necessary.

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