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Research Article

Ob-X: An Anti-Angiogenic Dietary Supplement's Effect on Body Composition and Visceral fat in Overweight Adults

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Abstract

Purpose: This study aimed to evaluate the efficacy of Ob-X, a mixture of standardized herbal extracts, on body weight, body composition, and abdominal fat in overweight or abdominally obese individuals, without the necessity of a calorie-restricted diet and exercise. **Participants and Methods:** A total of 30 participants with abdominal obesity or a Percent of Ideal Body Weight exceeding 110% were recruited, with 25 completing the 12-week study. The study used a before-and-after intervention design without a control group. Participants maintained their usual diet and physical activity, taking 250 mg of Ob-X six times daily. Anthropometric measurements, CT scans, blood tests, and antioxidant system tests were conducted at baseline and after 12 weeks. **Results:** Participants experienced an average reduction in body fat of 2.1 kg after 12 weeks. There was an average increase in lean body mass of 0.9 kg, contributing to a significant average weight loss of 1.2 kg. The body fat percentage decreased by 1.6%, and the lean body mass significantly increased by 2%, indicating significant improvements in body composition. Both mean PIBW and BMI showed statistically significant decreases. The mean hip circumference significantly reduced. The visceral fat area significantly decreased by 7.5%, and the ratio of visceral fat to subcutaneous fat also significantly decreased. There was a considerable reduction in apolipoprotein B, and in the ratio of total cholesterol to HDL cholesterol and the ratio of LDL cholesterol to HDL cholesterol, demonstrating a significant improvement in the atherogenic index. **Conclusion:** The anti-angiogenic dietary supplement Ob-X reduces body weight, PIBW, BMI, body fat, and hip circumference while increasing lean body mass in individuals with overweight or abdominal obesity. CT scans revealed a significant decrease in visceral fat in the lower abdomen and a significant reduction in the ratio of visceral fat to subcutaneous fat. Additionally, there was a notable reduction in the ratio of total cholesterol to HDL cholesterol and the ratio of LDL cholesterol to HDL cholesterol, indicating a significant improvement in the atherogenic index. These results suggest that Ob-X is a practical and effective supplement for obesity management.

Keywords: Anti-Angiogenesis; Herbal Extracts; Body Weight; Visceral Fat; Atherogenic Index

Introduction

Obesity is characterized by an excess of adipose tissue, with the volume of adipose tissue determined by the number of fat cells and the amount of stored fat. Adipose tissue is composed primarily of fat cells and endothelial cells, with a highly developed vascular network surrounding each fat cell and very few other cell types. The development of adipose tissue is closely related to angiogenesis and even in adulthood, fat cells can enlarge and shrink [1,2].

Abdominal obesity, in particular, is closely linked to the pathogenesis of metabolic syndrome and cardiovascular disease [3-6], and visceral adiposity is more strongly associated with all obesity-related complications than total adiposity [7-10].

It is well-established that adipose tissue growth is angiogenesis-dependent, and the mass of adipose tissue can be regulated by its vasculature [11]. Angiogenesis inhibitors such as TNP-470, angiostatin, and endostatin have been shown to reduce body fat

and weight by inhibiting the formation of blood vessels in adipose tissue, as demonstrated in ob/ob mice [12].

Mature adipocytes and cultured fat cells secrete an enzyme known as matrix metalloproteinase (MMP), which is particularly active during adipocyte differentiation. Specifically, the secretion of MMP-2 and MMP-9 is induced during this process [13,14].

Matrix metalloproteinase (MMP) enzymes play a crucial role in breaking down the basement membrane during angiogenesis and metastasis, and they are involved in the formation of obese tissues by contributing to the necessary matrix remodeling. In obese mice, the expression of MMP-2 increases, and the application of synthetic MMP inhibitors or antibodies neutralizing MMP to preadipocytes results in decreased differentiation into adipocytes, indicating that MMPs are essential for adipose tissue formation [14]. Additionally, studies have shown that inhibiting MMP enzymes in mice fed a high-fat diet can suppress the development of adipose tissue [15].

Therefore, inhibiting angiogenesis, particularly through targeting MMP enzymes, can suppress the development and growth of adipose tissue, reduce body fat, and serve as a novel approach for anti-obesity and therapeutic agents. These agents have the potential to be developed into orally administrable formulations with fewer side effects.

Ob-X, a mixture of standardized herbal extracts from *Melissa officinalis* L. (Labiatae; lemon balm), *Morus alba* L. (Moraceae; white mulberry), and *Artemisia capillaris* Thunb. (Compositae; Yin Chen wormwood), has demonstrated anti-angiogenic and MMP-inhibitory activities [16,17]. Ob in Ob-X stands for obesity, and X means to be absent.

The anti-angiogenic dietary supplement Ob-X reduced adipose tissue in high-fat diet-induced obese mice, providing evidence that adipose tissue growth and development may be prevented by inhibiting angiogenesis [17]. Additionally, the study demonstrated that regulating adipose tissue growth by inhibiting angiogenesis may alter the expression of genes involved in angiogenesis and the MMP system [17].

A study on nutritionally induced obese mice demonstrated that Ob-X can prevent obesity and lipid disorders caused by a high-fat diet [18]. In vivo and in vitro treatments with Ob-X were found to regulate serum lipid profiles, adipose tissue mass, and body weight by inducing the mRNA expression of PPARα target genes responsible for fatty acid β-oxidation in high-fat diet-fed obese mice [18].

In genetically obese ob/ob mice, Ob-X also reduced body weight gain and visceral fat mass, demonstrating that Ob-X specifically targets adipose tissue [19]. Since Ob-X inhibits angiogenesis and MMP activity, it suppresses adipogenesis in 3T3-L1 adipocytes by inhibiting the differentiation of pre-adipocytes into adipocytes [20].

In a 12-week randomized, double-blind, placebo-controlled human study, the Ob-X group showed a significant reduction in visceral fat by 20.5% with a calorie-restricted diet and exercise compared to baseline, as measured by computed tomography [21].

In the present study, the effect of Ob-X was evaluated on body weight, body composition, and abdominal fat in humans with overweight or abdominal obesity before and after the intervention, without a calorie-restricted diet and exercise.

Materials and Methods

Subjects

Human subjects aged 19 to 60 years were recruited from volunteers whose Percent of Ideal Body Weight (PIBW) exceeded 110% or who had abdominal obesity, defined as a waist circumference greater than 90 cm for men and 80 cm for women. The efficacy of the intervention was assessed exclusively in the test group, which did not adhere to a calorie-restricted diet or engage in exercise, utilizing a simple before-and-after intervention study design.

Exclusion criteria included a history of serious diseases or current treatment for a disease, uncontrolled medium/high blood pressure, thyroid disease, pregnancy, planned pregnancy, lactation, diagnosis of diabetes and treatment with drug therapy, or the use of medications that could affect body weight (e.g., Xenical, diuretics, antidepressants, appetite suppressants). Additionally, employees of AngioLab, Inc., acquaintances of the researchers, and students supervised by the principal investigator were excluded from the study.

Informed consent was obtained from all subjects, and ethical approval for the study was granted by the Institutional Review Board at Yonsei University, in accordance with the Helsinki II Declaration.

Preparation of Ob-X

Ob-X was prepared using food-grade aqueous extracts of *Melissa officinalis* L. (lemon balm), *Morus alba* L. (white mulberry), and *Artemisia capillaris* Thunb. (Injin or Yin Chen Hao). The quality of each herbal extract contained in Ob-X was controlled through standardization with reference compounds using high-performance liquid chromatography (HPLC). The corresponding reference compounds used for standardization were rosmarinic acid for *Melissa officinalis* L., 1-deoxynojirimycin for *Morus alba* L., and 6,7-dimethylesculetin for *Artemisia capillaris* Thunb. For the human study, 250 mg of Ob-X was encapsulated in a Good Manufacturing Practice (GMP) facility.

Study design

This human study was conducted to evaluate the efficacy of Ob-X over a 12-week period without a calorie-restricted diet and exercise. A simple before-and-after intervention method without a control group was employed. Subjects who voluntarily signed the study consent form and met the inclusion and exclusion criteria were enrolled and took Ob-X for 12 weeks.

Prior to the study's commencement, a nutritionist instructed all subjects to maintain their usual diet and activities throughout the study period without altering their lifestyle. Calorie intake and expenditure for each subject were monitored. To assess the calories consumed and expended during the study period, subjects were required to maintain a dietary diary and activity log. The daily nutrient intake, including total calorie intake (TCI) and the intake of each nutrient, was analyzed using CAN Pro 2.0 (Korean Nutrition Society).

Subjects were instructed to take two capsules (250 mg per capsule) three times a day, for a total of six capsules per day (1.5 g). The daily dose of Ob-X was estimated based on results from animal studies. The 1.5 g daily dose of Ob-X comprised 0.9 g of active ingredients and 0.6 g of dextrin as an excipient. All subjects were instructed to maintain their lifestyle and were scheduled for hospital visits at baseline (week 0) and week 12.

Compliance was monitored by counting the returned unused capsules and comparing this with the number of capsules that should have been consumed after 12 weeks of treatment. Each subject was considered compliant if they took at least 70% of the provided supplement.

The study initially enrolled 30 subjects. After excluding 5 subjects due to dropouts and loss of contact, a total of 25 subjects completed the study. A final efficacy evaluation was conducted with 24 subjects who met the Per Protocol (PP) criteria. Assessments included measurements of body weight, body composition, fat and muscle areas at four different levels of the body via CT, lipid and lipoprotein concentrations, glucose, insulin, and antioxidant system test results at baseline and at week 12 following the start of Ob-X supplementation.

Measurements and assessment

Anthropometric Measurement

Upon entry into the study, baseline characteristics and demographic data were recorded by medical staff to evaluate the eligibility of the subjects. Measurements of body weight, height, waist and hip circumferences, BMI, and vital signs such as systolic and diastolic blood pressure and heart rate were taken. Body composition was analyzed using a body fat analyzer (InBody, Korea). These measurements were used to establish baseline values and to monitor changes throughout the intervention period.

Computed Tomography (CT)

Cross-sectional abdominal visceral and subcutaneous fat areas were measured using a High-Speed Advantage 9800 Scanner (General Electric, Milwaukee, WI). CT scans were performed during the first visit (week 0) and the second visit (at the end of the 12-week period). Measurements were taken at the upper abdomen (L1), lower abdomen (L4), thigh, and calf.

For the abdomen, the total abdominal fat area was calculated by measuring the area at the lumbar spine positions L1 for the upper abdomen and L4 for the lower abdomen. The area inside the boundary of the abdominal and back membranes was defined as the visceral fat area, while the area outside this boundary was defined as the subcutaneous fat area. For the thigh, the fat area was calculated by measuring the midpoint between the anterior superior iliac spine (ASIS) and the patella. The thigh muscle area was divided by body weight to obtain the muscle area per unit of body weight.

Laboratory Measurement

Blood samples were drawn after an overnight fast of at least 12 hours. The following parameters were determined using routine biochemical methods: triglycerides, total cholesterol, Low-Density Lipoprotein (LDL) cholesterol, High-Density Lipoprotein (HDL) cholesterol, apolipoprotein A1, apolipoprotein B, glucose, insulin, free fatty acids, Glutamate Oxaloacetate Transaminase (GOT), Glutamate Pyruvate Transaminase (GPT), Blood Urea Nitrogen (BUN), creatinine, white blood cells, red blood cells, hemoglobin, hematocrit, and thrombocytes. Oxidized LDL, Malondialdehyde (MDA), and Prostaglandin (PGF) F2α were measured as indices of the antioxidant system.

Serum lipid and lipoprotein concentrations were measured during the first visit (week 0) and the second visit (week 12). Total cholesterol, HDL cholesterol, and triglycerides were measured using an Auto Chemistry Analyzer (Bayer Model Express Plus). HDL cholesterol was measured using a precipitation method, and free fatty acids were measured using a Hitachi 7150 Autoanalyzer (Hitachi Ltd., Tokyo). Apolipoprotein A1 and apolipoprotein B were measured using a turbidity method at 340 nm with a Cobas Integra (Roche, Switzerland). Blood glucose and insulin tests were conducted during the first visit (week 0) and the second visit (week 12). Blood glucose was measured using an enzymatic method, and insulin concentration was measured using a radioimmunoassay kit from INC (Immuno Nucleo Cooperation, Stillwater, USA).

Antioxidant System Tests

As part of the antioxidant system test, plasma oxidized LDL (ox-LDL), malondialdehyde (MDA), and urinary 8-epi-prostaglandin

F2α (8-epi-PGF2α) concentrations were measured at the first visit (week 0) and the second visit (week 12). Plasma ox-LDL concentration was measured using the Mercodia Oxidized LDL ELISA Kit (Mercodia, Uppsala, Sweden) and detected at a wavelength of 450 nm with Perkin Elmer's Wallac Victor2. Urinary 8-epi-PGF2α concentration was measured using the Bioxytech Urinary 8-Isoprostane Assay Kit (OXIS International, Inc.) and detected at a wavelength of 450 nm with Perkin Elmer's Wallac Victor2. Urinary creatinine concentration was measured using the Express Plus autoanalyzer (Chiron Diagnostics Co., MA, USA) through an alkaline picrate reaction. The final urinary 8-epi-PGF2α concentration was expressed as pg 8-epi-PGF2α per mg creatinine. Plasma lipid peroxides, specifically MDA, were measured using Buckingham's method with a luminescence spectrophotometer (Amico Bowman Series). The fluorescence intensity was measured at excitation 500 nm and emission 553 nm, and quantified by comparison with a standard solution.

Statistical Analysis

The effect of Ob-X was assessed by analyzing data collected at week 12 in comparison to baseline (week 0). Results are presented as mean and standard error (S.E.). Data were analyzed using the SPSS statistical program, and the significance of the differences in mean values between week 0 and week 12 was tested using a paired t-test. A p-value of less than 0.05 was considered statistically significant.

Results

Changes in Anthropometric Parameters and Blood Pressure

A total of 30 participants were initially recruited; however, 5 individuals discontinued participation due to either cessation of intake or loss of contact, resulting in a final 25 participants who completed the 12-week study. Statistical analysis was conducted on the data from these 25 participants.

As shown in Table 1, the intake of Ob-X resulted in significant changes in various anthropometric parameters over a 12-week period compared to the start of the study. Participants experienced an average reduction in body fat of 2.1 kg (p=0.003). There was an average increase in lean body mass of 0.9 kg (p=0.049), contributing to a significant average weight loss of 1.2 kg (p=0.014). The body fat percentage decreased by 5.6%, from 39.4 ± 1.46% to 37.2 ± 1.38% after 12 weeks, and the lean body mass significantly increased by 2%, from 45.3 ± 1.40 kg to 46.2 ± 1.40 kg, indicating significant improvements in body composition (Table 1 and Figure 1).

	Subject(n=25)	
	week 0	week12
male / female	3 / 22	
age (year)	31.8±1.51	
height (cm)	162.8±1.31	
body weight (kg)	75.2±2.11	74.0±2.18*
PIBW (%)	133.3±3.17	131.2±3.40*
BMI (kg/m^2)	28.4±0.67	27.9±0.72*
body fat (%)	39.4±1.46	37.2±1.38**
lean body mass (kg)	45.3±1.40	46.2±1.40*
waist circumference (cm)	91.4±1.73	90.0±1.78
hip circumference (cm)	104.9±1.44	103.6±1.47**
waist / hip ratio	0.87±0.01	0.86±0.01
tricep skinfold thickness (mm)	26.1±1.32	26.2±0.91
systolic blood pressure (mmHg)	125.3±3.38	124.2±2.64
diastolic blood pressure (mmHg)	77.5±2.09	82.2±2.46**
current smoker (n(%))	5(20)	
tabacco (cigarettes/day)	7.70±3.03	
current drinker (n(%))	18 (72)	
alcohol intake (g/day)	8.82±2.72	
mean ± S.E. *p<0.05, **p<0.01 compared with 0-week value		

Table 1: Changes in anthropometric parameters before and after intervention with Ob-X.

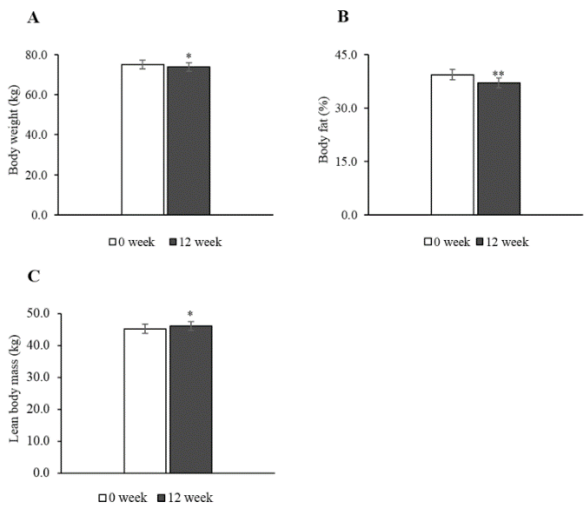

Figure 1: Impact of Ob-X supplementation on body weight and composition before and after intervention. This figure illustrates the changes in body weight(A), body fat percentage(B), and lean body mass(C) over a 12-week period of Ob-X supplementation. *p<0.05, **p<0.01 compared with 0-week value.

Both mean Percent Ideal Body Weight (PIBW) and mean Body Mass Index (BMI) showed statistically significant decreases (p=0.018 and p=0.02, respectively). The mean waist circumference decreased to some extent, and the hip circumference significantly reduced (p=0.006). Additionally, mean diastolic blood pressure increased within the normal range after 12 weeks.

Changes in Fat and Muscle Areas Analyzed by CT Scanner

The changes in fat and muscle areas at four different levels of the body before and after administration of Ob-X were analyzed by CT. As shown in Table 2, the fat in the upper abdomen scanned at the first lumbar vertebra (L1) did not show any significant change, but the fat in the lower abdomen scanned at the fourth lumbar vertebra (L4) decreased. The visceral fat area significantly decreased by 9.5% (p=0.007), and the ratio of visceral fat to subcutaneous fat also significantly decreased (p=0.001) (Table 2 and Figure 2).

	Subject(n=25)	
	week 0	week 12
1st lumbar vertebra (upper abdomen)		
total fat (cm^2)	260.9±13.1	256.6±12.2
visceral fat (cm^2)	99.4±6.54	98.7±5.59
subcutaneous fat (cm^2)	161.5±9.66	157.9±9.43
visceral fat/subcutaneous fat (ratio)	0.65±0.05	0.67±0.05
4th lumbar vertebra (lower abdomen)		
total fat (cm^2)	313.0±11.7	301.6±13.4
visceral fat (cm^2)	81.5±4.40	73.8±4.72**
subcutaneous fat (cm^2)	231.5±11.4	227.8±11.5
visceral fat/subcutaneous fat (ratio)	0.38±0.03	0.33±0.02**
Mid-thigh		
fat (cm^2)	87.7±4.83	85.2±4.64
muscle (cm^2)	113.8±3.36	115.5±3.81
Calf		
fat (cm^2)	29.8±1.84	30.1±2.00
muscle (cm^2)	73.4±2.84	72.9±3.31
mean ± S.E. **p<0.01 compared with 0-week value		

Table 2: Changes in fat and muscle areas at four different levels of the body.

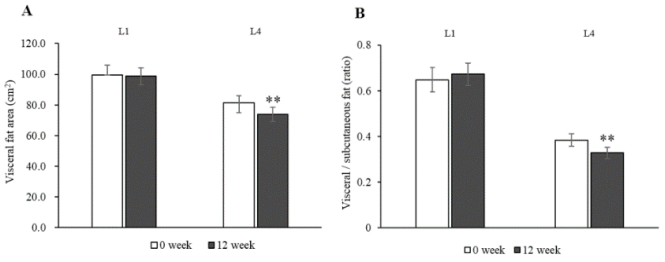

Figure 2: Reduction in visceral fat area and visceral to subcutaneous fat ratio before and after intervention. This figure shows the changes in abdominal fat areas, specifically visceral fat (A) and the ratio of visceral fat to subcutaneous fat (B), measured at the first lumbar vertebra (L1) and fourth lumbar vertebra (L4) levels. **p<0.01 compared with 0-week value.

Changes in Serum Concentrations of Lipid, Lipoprotein, Fasting Glucose, and Insulin

As shown in Table 3, there were no significant changes in the concentrations of triglycerides, total cholesterol, LDL cholesterol, and HDL cholesterol. However, apolipoprotein B decreased considerably (p=0.020). Fasting blood glucose, insulin, and free fatty acid concentrations did not change significantly.

There was a considerable reduction in the ratio of total cholesterol to HDL cholesterol (p=0.029) and the ratio of LDL cholesterol to HDL cholesterol (p=0.025) (Table 3 and Figure 3), demonstrating a significant improvement in the atherogenic index (p=0.029).

	Subject (n=25)	
	week 0	week 12
triglyceride (mg/dl)	124.9±11.0	119.2±10.7
total cholesterol (mg/dl)	203.3±6.97	197.1±6.36
LDL cholesterol (mg/dl)	126.7±6.29	119.7±5.99
HDL cholesterol (mg/dl)	51.6±2.21	53.6±2.38
atherogenic index[1]	3.10±0.21	2.82±0.18*
total cholesterol / HDL cholesterol	4.10±0.21	3.82±0.18*
LDL cholesterol / HDL cholesterol	2.57±0.16	2.33±0.15*
apolipoprotein A1(mg/dl)	146.7±4.24	142.1±3.93
apolipoprotein B(mg/dl)	81.6±3.80	75.4±3.23*
blood sugar (mg/dl)	91.6±3.33	92.5±3.96
insulin (μIU/ml)	12.4±1.10	11.7±1.30
free fatty acid (μEq/L)	499.7±27.8	431.6±42.2
atherogenic index [1] = (total cholesterol - HDL cholesterol) / HDL cholesterol		
mean ± S.E. *p<0.05 compared with 0-week value		

Table 3: Changes in serum concentrations of lipids, apolipoproteins and fasting glucose level before and after intervention.

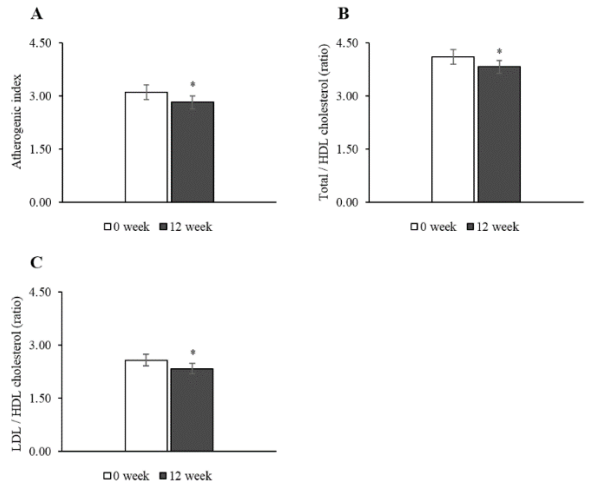

Figure 3: Changes in the atherogenic index (A) and composition of lipids (B and C) before and after intervention. Atherogenic index = (total cholesterol - HDL cholesterol) / HDL cholesterol. *p<0.05 compared with 0-week value.

Changes in Biochemical Values

As shown in Table 4, the concentrations of GOT and GTP, which are liver function indexes, and the concentrations of BUN and creatinine, which are kidney function indexes, were within the normal range and showed no changes after taking Ob-X. However, the levels of red blood cells (p=0.034) and white blood cells (p<0.001) increased within the normal range after 12 weeks. There were no changes observed in the concentrations of hemoglobin, hematocrit, and the number of thrombocytes.

	Subject (n=25)	
	week 0	week12
GOT (U/L)	19.3±0.99	21.5±1.34
GPT (U/L)	18.4±2.44	20.7±2.57
BUN (mg/dl)	12.6±01.52	11.7±0.49
creatinine (mg/dl)	0.52±0.03	0.52±0.03
white blood cells (×10³/□)	4.92±0.29	6.38±0.26***
red blood cells (×10⁶/□)	4.48±0.14	4.73±0.11*
hemoglobin (g/dl)	13.2±0.47	13.7±0.38
hematocrit (%)	38.7±1.38	40.0±1.11
thrombocyte (×10³/□)	306.0±17.3	310.0±13.5
mean ± S.E. *p<0.05, ***p<0.001 compared with 0-week value		

Table 4: Changes in biochemical values before and after intervention.

Analysis of Daily Calorie Intake and Energy Expenditure

As shown in Table 5, there were no significant differences in total calorie intake and total energy expenditure between week 0 and week 12.

	subject(n=25)	
	0 week	12 weeks
TEE[1]	2029.8±36.6	2012.9±38.2
TCI[2]	2352.3±43.9	2325.0±45.4
TEE / TCI	0.86±0.11	0.87±0.12
carbohydrates (% of TCI)	62.5±0.43	62.1±0.26
proteins (% of TCI)	17.2±0.33	16.9±0.27
fats (% of TCI)	20.6±0.38	21.1±0.44
cholesterol (mg)	425.8±41.7	435.8±33.3
TEE[1] = total energy expenditure		
TCI[2] = total calorie intake		
mean ± S.E. No particular changes between week 0 and week12 values.		

Table 5: Daily calorie intake and total energy expenditure.

Changes in the Concentration of Oxidized LDL and Lipid Peroxides

As shown in Table 6, there was no changes in the concentration of oxidized LDL, MDA (a lipid peroxide in blood), and 8-epi-PGF2α (a lipid peroxide in urine) after taking Ob-X.

	Subject (n=25)	
	0 week	12 weeks
LDL oxidation		
Oxidized LDL (U/L)	37.2±1.99	36.5±2.17
Lipid peroxidation		
MDA (nmol/mml)	3.15±0.29	2.92±0.17
PGF2α (pg/mg creatinine)	1391.2±145.8	1125.2±180.9
mean ± S.E. No particular changes between week 0 and week12 values		

Table 6: Changes in the concentrations of oxidized LDL and lipid peroxides.

Adverse Reactions

No adverse reactions due to the consumption of Ob-X were observed among 30 participants who took part in this human study.

Discussion

Obesity is characterized by an excessive and imbalanced energy supply, leading to the over-differentiation of adipocytes, which results in an increase in both the number of fat cells and the amount of stored fat. Adipose tissue is primarily composed of adipocytes and vascular endothelial cells, making it a highly vascularized tissue. Adipose tissue can expand and regress throughout life, and its growth is dependent on angiogenesis, similar to the growth of cancer cells [11]. Therefore, regulating angiogenesis could potentially reduce the size of growing adipose tissue, and the use of angiogenesis inhibitors presents a novel approach for the suppression and treatment of obesity.

AngioLab has reported that Ob-X, composed of three herbal extracts from *Melissa officinalis*, *Morus alba*, and *Artemisia capillaris*, possesses MMP-inhibiting and anti-angiogenic properties, as demonstrated through in vitro and in vivo tests [16,17]. These studies identified a reduction in body weight and white adipose tissue in both high-fat diet-induced obese mice [17,18] and ob/ob mice [19].

This human study was conducted using a before-and-after intervention method without a control group. It aimed to objectively determine the effects and safety of 12 weeks of Ob-X administration on body weight, body composition, and abdominal fat in thirty overweight or abdominally obese adults without requiring any changes to their lifestyle.

Subjects in this study had a mean BMI of 28.4 kg/m² and a body fat percentage of 39.4%, indicating a high level of abdominal obesity. After 12 weeks of Ob-X intake, compared to the start of the study, the mean body fat mass decreased by 2.1 kg (p=0.003), and mean lean body mass increased by 0.9 kg (p=0.049), resulting in a significant mean body weight reduction of 1.2 kg (p=0.014). Both mean PIBW and mean BMI also showed statistically significant decreases (p= 0.018 and p=0.02, respectively). The mean waist circumference decreased slightly, and the hip circumference significantly reduced (p=0.006). These results demonstrate that Ob-X intake leads to significant improvements in body composition and reductions in key anthropometric measures, contributing to better overall health.

CT scans of abdominal fat showed a significant reduction in visceral fat area by 9.5% in the lower abdomen (L4) (p=0.007). Consequently, the ratio of visceral fat to subcutaneous fat area also decreased significantly (p=0.001). In terms of blood lipid levels, there were no significant changes in triglyceride and cholesterol levels. However, there was a significant reduction in apolipoprotein B concentration (p=0.020), as well as improvements in the atherogenic index (p=0.029), the total cholesterol to HDL cholesterol ratio (p=0.029), and the LDL cholesterol to HDL cholesterol ratio (p=0.025).

Rupnick, et al. [11] reported that the administration of TNP-470, an angiogenesis inhibitor, reduced body weight and body fat in a concentration-dependent manner in ob/ob mice lacking the leptin gene. This suggests that the development of adipose tissue is closely related to angiogenesis and that the amount of adipose tissue is sensitive to angiogenesis inhibitors, which inhibit vascular endothelial cell proliferation. These findings indicate the potential use of angiogenesis inhibitors in the treatment of obesity.

Through this human trial, it was demonstrated that Ob-X, by inhibiting angiogenesis and MMP enzymes, can reduce body weight and decrease body fat, particularly rapidly growing visceral fat by 9.5%, without calorie-restricted diets and exercise.

In a randomized, placebo-controlled, double-blind human study, Ob-X led to a statistically significant reduction in visceral fat by 20.5% compared to baseline, alongside a calorie-restricted diet and exercise. All subjects were instructed to restrict their total energy intake to a 500-kcal deficit of the recommended daily calorie intake and were advised to exercise, corresponding to an energy expenditure of 250 kcal per day, three times a week [21]. The selective effect of Ob-X in reducing visceral fat may be attributed to the properties of visceral fat, where angiogenesis actively occurs, making it more sensitive to angiogenesis inhibitors.

Kim SK, et al. [22] showed that as visceral fat thickness (VFT) increases, HDL-cholesterol levels decrease, triacylglycerol levels increase, and the risk of cardiovascular disease rises. Jeong SK et al. [23] revealed that increased visceral fat content and reduced

physical activity could be therapeutic targets in the treatment of metabolic syndrome. Therefore, it can be inferred that reducing visceral adipose tissue (VAT) can lower the risk of metabolic diseases.

The results of two human studies demonstrated that Ob-X significantly reduces visceral fat both with and without a calorie-restricted diet and exercise, indicating that Ob-X has the potential to improve metabolic syndrome.

Bolkent, et al. [24] observed that supplementation with Melissa leaf extract, which possesses antioxidant properties due to its flavonoid and phenolic compounds, improved blood cholesterol concentrations, increased liver and blood glutathione (GSH) concentrations, and decreased levels of Malondialdehyde (MDA), a lipid peroxide, in hyperlipidemic rats. However, in the present human study, 12 weeks of Ob-X supplementation did not affect blood cholesterol and oxidized LDL concentrations, plasma MDA concentrations (a marker of lipid peroxides), and urinary 8-epi-PGF2α levels. This is likely due to the fact that more than half of the subjects in this study had blood cholesterol concentrations within the normal range, and the intervention period was too short to show significant improvements in lipid patterns and antioxidant activity.

Treatment with Ob-X for 12 weeks resulted in a significant increase in red blood cell count ($p=0.034$) and white blood cell count ($p<0.001$), both within the normal range. Although increased immune responses due to Melissa extract have been reported in animal studies [25,26], this study did not evaluate endpoints to confirm such responses. Therefore, the increase in white blood cell count may suggest a potential immune response, but the results of this study cannot conclusively determine that Ob-X had a positive effect on immune responses.

Throughout the 12-week intervention period, no adverse reactions were observed among the participants. This indicates that Ob-X is a safe supplement for consumption, further supporting its potential for widespread clinical use.

This human study evaluated the effects of Ob-X without requiring calorie restriction or increased physical activity, allowing for the assessment of the supplement's pure effects.

Ob-X reduced body weight and body fat, particularly visceral fat, and improved the atherogenic index through the inhibition of angiogenesis and MMP activity without necessitating substantial lifestyle changes. This suggests that Ob-X could be easily integrated into the daily routines of individuals, thereby enhancing its practical clinical applicability for obesity management.

Limitations of this study include the lack of a control group, the relatively short duration of the study, and the small sample size, which may limit the generalizability of the findings. Future studies should explore the supplement's impact on various populations and investigate other potential health benefits, such as its effects on metabolic syndrome and cardiovascular health by reducing visceral fat.

Conclusion

The present study investigates the effects of the anti-angiogenic dietary supplement Ob-X on body weight, body composition, and abdominal fat in overweight and abdominally obese adults. The findings indicate that Ob-X, composed of standardized herbal extracts, effectively reduces body weight, PIBW, BMI, body fat, and hip circumference while increasing lean body mass. Notably, the visceral fat area in the lower abdomen decreased significantly, highlighting the supplement's potential to target harmful visceral adipose tissue. Additionally, the study observed significant improvements in lipid profiles. Serum apolipoprotein B levels decreased, and the atherogenic index, along with the ratios of total cholesterol to HDL cholesterol and LDL cholesterol to HDL cholesterol, showed marked improvements. By inhibiting angiogenesis, Ob-X limits the vascularization necessary for adipose tissue growth, thereby reducing the formation and accumulation of fat. This novel approach to obesity management offers a promising alternative to traditional methods.

In conclusion, Ob-X demonstrates significant potential as a practical and effective supplement for obesity management. Its ability to reduce body weight and body fat, and improve lipid profiles without requiring lifestyle changes, makes it an attractive option for individuals seeking alternative weight loss strategies.

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Ethical Guidelines

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Ethical approval for the study was obtained from the Institutional Review Board (IRB) at Yonsei University (approval number: 2005-015).

All participants provided written informed consent prior to their inclusion in the study. The consent process ensured that participants were fully informed about the nature, purpose, and potential risks of the study. Participants were assured of their right to withdraw from the study at any time without any consequences.

Conflicts of Interest

The authors declare that they have no conflicts of interest regarding this work

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