8-Week Clinical Study of Green Coffee Bean Extract on Women with Mild Obesity

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1. Objectives

Green coffee bean extract is extracted from raw coffee bean using ethanol (H_2O/EtOH) followed by pulverization. Green coffee bean extract is rich in caffeine and chlorogenic acids. Caffeine has been reported to promote metabolism and improve bowel motion while chlorogenic acids are effective in the inhibition of gluconeogenesis and stabilization of blood sugar level. Experiments on mice and rats revealed that coffee bean extract inhibits fat absorption, fat combustion and sugar absorption. Coffee bean extract also assist in the promotion of lipolysis and fat combustion. Meanwhile, in a 4-week study on normal healthy males, coffee bean extract demonstrated reduction in body weight, body fat, hip size and blood sugar level respectively. Evaluations on green coffee bean extract has been carried out by the authors.

In this study, coffee bean extract was given to 24 women with mild obesity, BMI range 22-30 for 8 weeks. Physical assessment and biochemical analysis was conducted to measure changes on body weight, body fat, hip size and biochemical markers after 8 weeks administration of coffee bean extract.

2. Materials

Green coffee bean extract (Lot.Q321) was produced from extraction of raw coffee beans using hot aqueous ethanol (H_2O/EtOH) followed by solvent removal and spray-drying. The extract contains chlorogenic acid 25.6%, chlorogenic acids related compounds 46.6% and caffeine 13.6% as confirmed by HPLC quantitative assays. Subjects were given oral coffee bean extract in a hard capsule formulation containing coffee bean extract 100mg and dextrin 210ml. Placebo capsules contains only dextrin 310mg in identical hard capsules were produced for placebo group.

3. Subjects

Inclusion Criteria

24 female aged between 20 – 65 with 22 BMI 30 were selected. Individuals with body fat more than 24% having either one of the following conditions will be excluded.

Exclusion Criteria

i.   On medications or nutrient supplements to improve fat & sugar metabolism
ii.   On medications containing green coffee bean extract or caffeine
iii. Regular user of coffee, green tea and black tea and total volume consumed exceeds 1 liter.

iv.	History of allergy to certain foods
v.	Patients of diabetes mellitus, hepatic diseases, renal diseases or cardiac diseases.
vi.	Participating other clinical studies
vii.	Pregnant or planning to conceive
viii.	Physically / mentally unwell as certified by physician-in-charge

The average age of subjects is 46.1. All individuals received an explanatory document and consent letter approved by IRB. Q&A session was conducted during orientation to ensure thorough understanding of the clinical studies. All subjects have to sign the consent letter before participation in clinical studies.

4. Methods

The subjects were randomly divided into 2 groups. One group was on coffee bean extract capsules while the other was on placebo. The dosage was 1 capsule twice daily before lunch and dinner respectively. The duration of study was 8-week. Assessment of the following parameters was performed prior to, 4-week & 8-week after the administration of coffee bean extract.

Analytical items:

i.	Obesity indexes: height (initial reading only), weight (to determine BMI), body fat percentage (impedance method), circumferences (abdomen, hip, neck, upper wrist)
ii.	Blood profile: white blood cell (WBC) count, red blood cell count (RBC), haemoglobin (Hb), hematocrit, platelet, triglyceride (TG), total cholesterol, free fatty acid, blood sugar, AST (GOT), ALT (GPT), ALP, LDH, -GTP, total protein, albumin, bilirubin, blood urea nitrogen, creatinine, uric acid, Na, K and Cl.
iii.	Diagnosis statistic: blood pressure and pulse
iv.	CT scan: one subject was randomly selected for abdominal spot imaging for internal fat calculation.

Meanwhile, the subjects were requested to record and document the amount of consumption, subjective symptoms and medication (if any) throughout the study. The following requirements were adhered to ensure accuracy of study:

| i. | Excessive vigorous exercise, overeating and diet are forbidden throughout the study period. |

ii.   Avoidance of medication or food containing caffeine. Consumption of not more than 2 cups of coffee per day

iii.   Fasting for 8 hours prior to physical and biochemical assessment

iv.   Avoidance of alcohol for 2 days prior to physical and biomedical assessment

v.   Documentation of medication history that affects fat & sugar metabolism. Documentation of other medication if any

5. Adverse Reactions & Side Effects

Adverse reactions and side effects are defined as follows:

i.   Definition of adverse reactions

Any reaction that occur to the subject throughout the period of extract consumption and produces undersirable medical responses. Determination of adverse reaction is not implicated in a cause-effect relationship of the extract.

ii.   Records of adverse reactions

Series of steps need to be taken in the event of adverse reaction. A full report on the symptoms complaint, diagnosis, the extent of adverse reaction, severity, relevance with the extract, onset of reaction, discontinuation of reaction, measures taken, outcome etc is documented.

Extent

Mild: Almost no interference with daily life
Moderate: Interfere with daily life
Severe: Significantly interfere and affect daily life

Severity

The following definitions are defined as severe adverse reactions:

- Death
- Symptoms that may lead to death
- Admission into hospital / Extension of stay in hospital
- Disability (hindrance to daily life due to functional incompetence)
- Symptoms that may lead to diability
- Any severe illness which may apply to the above definitions
- Congenital illness or abnormality in descendant generations

iii. Side effects

An adverse reaction arises that is suspected to be caused by or likely caused by the extract.

6. Statistical Analysis

1. Efficacy

Efficacy is determined by comparing the difference of major indexes between week 0 and week 4 and between week 0 and week 8. The differences were compared between and within the 2 groups. (paired t-test, $P<0.05$)

2. Safety

Safety of study is conducted by monitoring on changes of all indexes and clinical findings throughout the study period. Medical doctors in-charge of the study are responsible for the safety.

7. Results

i. Changes in obesity index

No adverse reaction and side effects were reported throughout the study period. Subjects with protein, infiltrating blood in the urea and high γ-GTP level were excluded from the analysis. Changes on the obesity index are shown in Table 1.

In the coffee bean extract consumption group, there was a decline on body weight and BMI value after 8 weeks; 0.5kg (p=0.05) and 0.3 (p=0.06). 7 out of 10 subjects have successfully lost weight; the maximum weight loss is 1.8kg while the minimum weight lost is 0.4kg (as illustrated in Fig. 1). Meanwhile, 8 out of 10 subjects have a significant decline in BMI value with maximum reduction of 0.8 and minimum of 0.2 (as illustrated in Fig. 2). Almost no significant changes observed in placebo group.

There were no changes in measurements of body fat, abdomen circumference and neck circumference in group consuming coffee bean extract as shown in Table 1. However, there was a significant decrease of 0.4cm in hip circumference within 4 weeks and only a decrease of 0.5cm in 8 weeks (p<0.05) as shown in Table 1. 90% of subjects demonstrated significant decline in week 8 with maximum reduction of 1.5cm and minimum reduction of 0.2 cm.

As for upper wrist circumference, there was a significant decline of 0.4cm within 4 weeks and 0.5cm within 8 weeks (p<0.01). 90% of the subjects shown reduction in upper wrist circumference. The maximum reduction was 1.4cm while the minimum reduction was 0.2cm (as illustrated in Fig. 2).

CT scan of abdominal spot of a randomly selected subject is shown in Fig. 3. The cross section area of internal fat was 155.8cm^2 at week 0 and reduced to 145.9cm^2 at week 8. Hence, a total reduction of 10cm^2.

Fat reduction in the intestine adjoining part (upper part) is clearly illustrated in Fig. 3.

ii. Changes in blood profile

Changes on blood profile are as shown in Table 2. There was no significant changes observed in total cholesterol, free fatty acids and creatinine. However, there was a significant decline in triglyceride level in both groups. TG level is reduced from 247mg/dL at week 0 to 110mg/dL at week 4. No changes observed in blood sugar level in placebo group while decline in group consuming coffee bean extract.

iii. Safety indexes

Other safety indexes such as blood pressure, pulse and blood urea are shown in Table 3. No significant changes on the safety indexes observed in both groups. No abnormal fluctuations due to coffee bean extract consumption was observed.

8. Discussion

The study demonstrated a significant reduction in body weight, BMI value, hip and upper wrist circumferences after 8-week oral treatment with green coffee extract (200mg/day). Statistical analysis confirmed the effect of green coffee extract on hip and upper wrist circumferences. There was no diet restriction and exercise tolerance during the study period. Findings revealed positive anti-obesity effect demonstrated by green coffee extract. Previous study shown that consumption of coffee bean extract (200mg/day) for 4 weeks on normal healthy males demonstrated significant positive effects on reducing body weight, body fat, abdomen circumference, hip circumference and abdominal subcutaneous fat. Again, similar improvement on obesity indexes were observed. In addition, remarkable reduction in abdominal fat was observed as shown in CT scan illustration on abdominal fat of female subject.

Moreover, triglycerides and blood sugar level of test subjects has shown significant improvement. Changes in creatinine level were not significant either. Previous study on

healthy males shown significant improvement on blood profile. It is suggested that the difference may be due to amount of exercise and sex-induced lypolysis among subjects in the 2 studies.

No side effects reported throughout the study period, hence concern of negative effects is insignificant. This study concludes that green coffee bean extract may be beneficial in reducing body weight, BMI, hip and upper wrist circumference. There is no undesirable effect documented.

Abstract

A significant effect is demonstrated by green coffee extract, a 8-week consumption at concentration 200mg/kg, on the reduction of body weight, BMI, abdomen and upper wrist circumference in women with BMI value between 22-30 and more than 24% body fat.

Table. 1: Changes in Obesity Indexes

|		Week 0	Week 4	Week 8
Weight（kg）	E	61.3±1.9	61.0±1.9	60.8±2.0 p=0.08
	P	62.1±2.6	62.0±2.8	61.9±2.9
BMI	E	25.6±0.7	25.4±0.7	25.3±0.7 p=0.06
	P	25.1±0.6	25.1±0.7	25.0±0.7
Body Fat（%）	E	36.2±1.3	35.5±1.2	36.0±1.4
	P	36.0±1.2	35.4±1.1	36.2±1.2
Abdomen Circumference(cm)	E	90.0±1.9	90.0±1.7	90.1±1.7
	P	89.6±2.4	89.8±7.5	89.5±2.3
Hip Circumference(cm)	E	95.5±1.1	95.1±1.0	95.0±1.1 p<0.05
	P	96.4±1.8	96.6±1.8	96.5±1.8
Abdomen / Hip Ratio	E	0.94±0.02	0.95±0.01	0.95±0.01
	P	0.93±0.02	0.93±0.02	0.93±0.02
Neck Circumference(cm)	E	33.3±0.7	33.2±0.7	33.4±0.7
	P	33.3±0.7	33.3±0.6	33.6±0.6
Upper Wrist circumference（cm）	E	30.1±0.7	29.7±0.6 p=0.06	29.6±0.6 p<0.01
	P	30.8±0.7	30.4±0.7 p=0.07	30.4±0.7

E: Extract group; P: Placebo group

The results are shown in mean ± SE (n=10); p: rate of risk calculated based on data at week 0 and t-test

A) Weight

Extract Group

Placebo Group

B) BMI

Extract Group
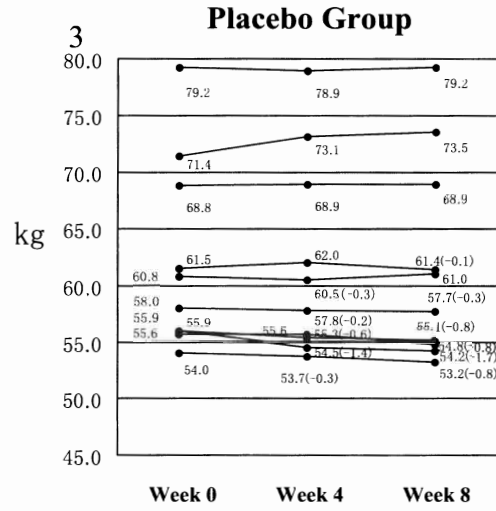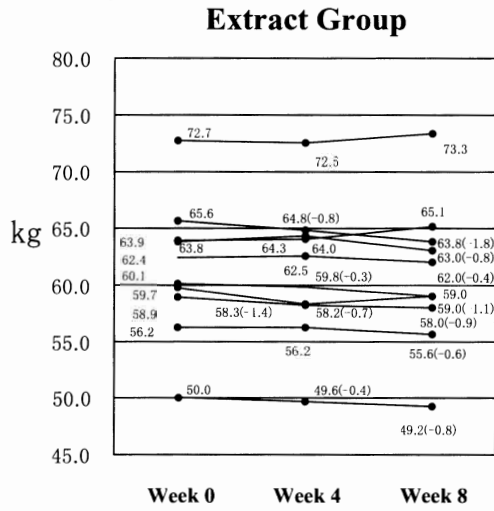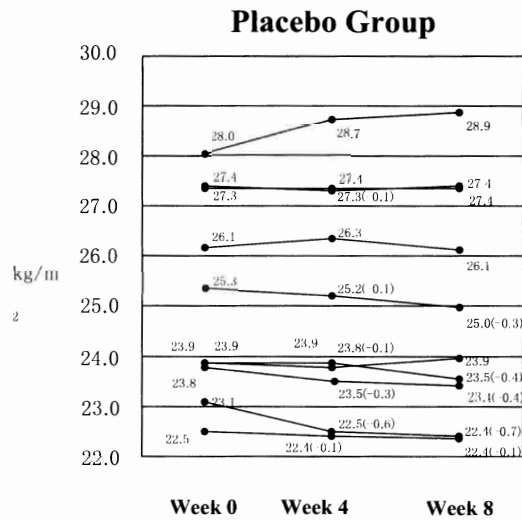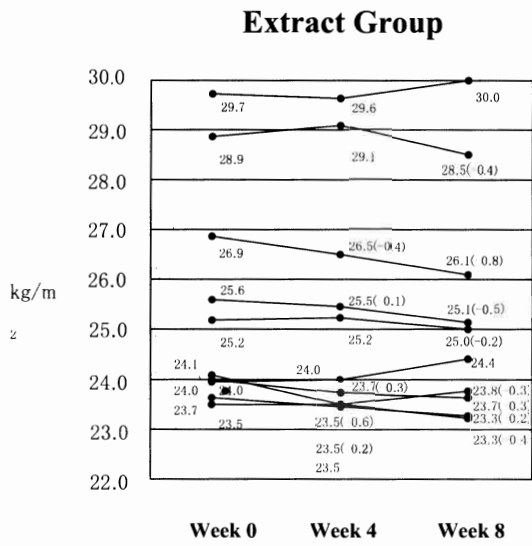
Placebo Group

C) Hip Circumference
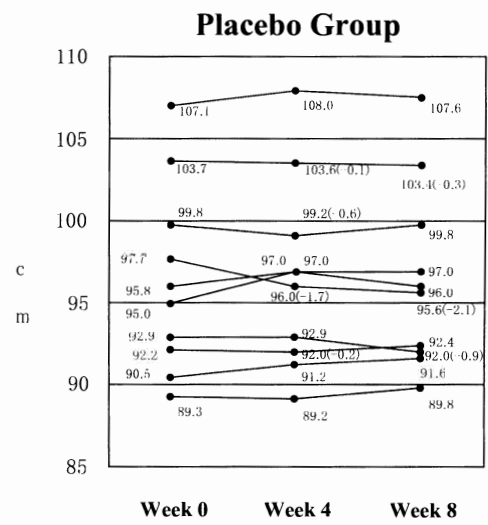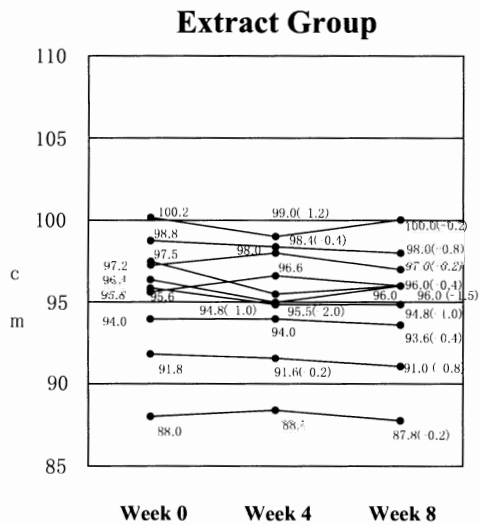
Extract Group

Placebo Group

Fig.1. Changes in body weight, BMI, and hip size between Extract and Placebo Group
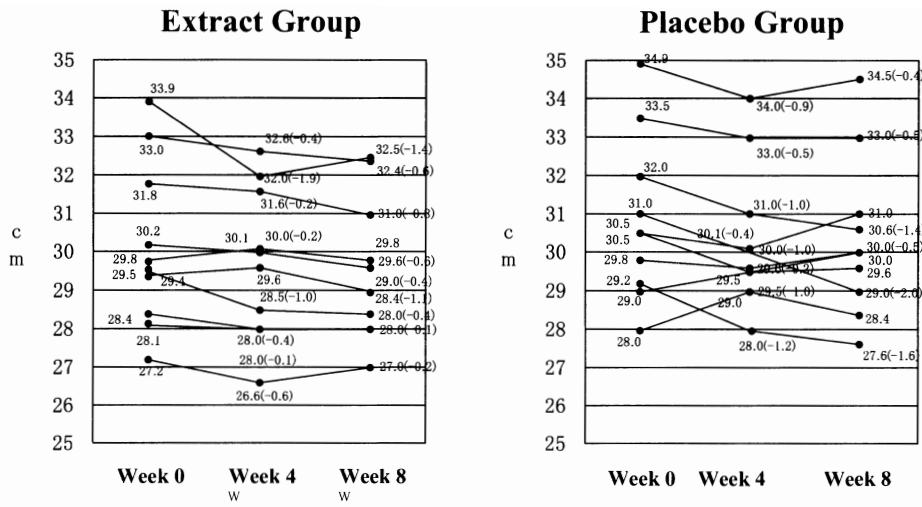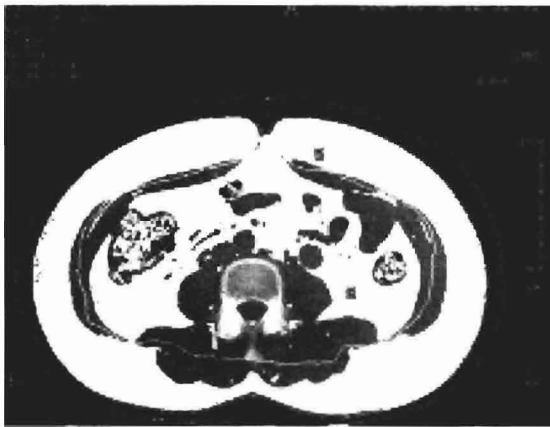
Fig. 2. Changes in the upper wrist circumference between Extract and placebo group

Week 0 (internal fat area 155.8cm²)   Week 8 (internal fat area 145.9cm²)

Fig. 3. CT Scan of abdominal (internal fat) of 32- year old female subject of the study

Table 2. Changes in blood profile of subjects under study

		Week 0	Week 4	Week 8
Total cholesterol	E	201.9±6.0	204.4±5.5	199.4 6.2
(mg/dL)	P	219.2±14.7	218.6±17.9	216.8±17.0
Nuetral Fat	E	110.0±18.9	92.7±11.4	101.7±9.2
(mg/dL)	P	121.8±14.9	103.9±13.5	111.5±12.9
Free Fatty Acid	E	0.49±0.05	0.55±0.06	0.56±0.08
(mEq/L)	P	0.58±0.05	0.58±0.05	0.61±0.05
Creatinine	E	0.75±0.03	0.77±0.03	0.73±0.03
(mg/dL)	P	0.77±0.03	0.80±0.03	0.77±0.02
Blood sugar	E	91.5±1.8	92.5±1.5	88.7±1.9
(mg/dL)	P	93.4±1.6	96.5±2.3	96.1±2.2

E: extract group; P: placebo group
The result are shown in mean ± SE (n=10)

Table 3. Changes in BP, Pulse & other biochemical markers in throughout the study

		Week 0	Week 4	Week 8
Systolic BP	E	118.7±3.5	118.4±3.5	116.1±5.0
(mmHg)	P	127.6±4.3	124.4±3.7	125.3±4.5
Diastolic BP	E	72.2±3.4	73.5±2.2	72.9±3.5
(mmHg)	P	80.6±2.9	77.1±3.1	79.2±3.3
Pulse	E	73.6±2.9	77.3±2.5	71.9±3.6
(strokes/min)	P	80.0±3.4	74.1±3.7	74.7±2.5
Total bilirubin	E	0.5±0.1	0.5±0.1	0.5±0.1
(mg/dL)	P	0.6±0.1	0.7±0.1	0.6±0.1
ALP	E	208.4±24.4	202.9±26.5	203.4±26.0
(IU/L)	P	205.8±14.2	202.2±13.0	203.0±14.7
LDH	E	225.0±19.6	200.7±5.7	195.8±4.4
(IU/L)	P	200.1±7.6	209.2±10.8	196.0±8.9
γ-GTP	E	21.4±2.3	20.0±1.5	19.4±1.4
(IU/L)	P	24.3±5.1	22.7±3.1	25.1±5.3
AST	E	18.4±1.2	17.7±1.1	19.1±1.2
(IU/L)	P	19.8±2.8	22.1±4.9	22.2±46
ALT	E	15.0±1.1	15.6±1.5	17.3±2.1
(IU/L)	P	21.9±6.6	28.3±12.4	24.6±8.8
Total protein	E	7.5±0.1	7.4±0.1	7.4±0.1
(g/dL)	P	7.6±0.1	7.5±0.1	7.6±0.1
Albumin	E	4.8±0.1	4.8±0.1	4.7±0.1
(g/dL)	P	4.7±0.1	4.7±0.1	4.6±0.1
BUN	E	16.3±1.5	18.9±0.9	15.5±1.1
(mg/dL)	P	15.3±1.4	18.8±1.5	16.2±1.7
Uric acid	E	4.5±0.3	4.4±0.2	4.4±0.2
(mg/dL)	P	5.4±0.2	5.3±0.2	5.3±0.3
Na	E	143.9±0.7	142.6±0.6	141.5±0.8
(mEq/L)	P	144.1±0.5	144.2±0.7	143.3±0.8
K	E	4.0±0.2	3.9±0.1	3.9±0.1
(mEq/L)	P	4.0±0.1	4.0±0.1	3.9±0.1
Cl	E	104.7±0.5	103.8±0.5	103.3±0.5
(mEq/L)	P	105.1±0.4	105.5±0.4	104.2±0.4
Red Blood Cells	E	442.4±7.5	437.7±6.9	437.9±9.0
(10^4 cells/mL)	P	438.0±8.4	427.7±9.5	426.3±9.0
White Blood Cells	E	6200±695	5980±332	6020±419
(cells/mL)	P	5910±310	5960±223	6060±355
Haemoglobin	E	13.4±0.4	13.2±0.4	13.2±0.5
(g/dL)	P	13.3±0.3	12.9±0.4	13.0±0.3
Haematocrit	E	43.2±1.1	42.8±1.0	41.7±1.1
(%)	P	42.1±0.7	41.1±0.9	41.0±0.8
Platelet	E	27.1±1.8	26.5±1.8	26.5±2.3
(10^4/mL)	P	24.9±1.4	24.0±1.1	24.7±1.3
Urine Protein	E	-	-	-
	P	-	-	-
Urine Sugar	E	-	-	-
	P	-	-	-
Urobilinogen	E	-	-	-
	P	-	-	-

Infiltrating blood	E	-	-	-
	P	-	-	-

E: extract group; P: Placebo group
The results are shown in mean ± SE (n=10)