



White sweet potato

Anti-diabetic Supplement **CAIAPO**



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Diabetes

What is diabetes?

Diabetes is a disease that occurs when your blood glucose, also called blood sugar, is too high. Insulin, a hormone made by the pancreas, helps glucose from food get into your cells to be used for energy. Sometimes your body doesn't make enough—or any—insulin or doesn't use insulin well.

Over time, having too much glucose in your blood can cause health problems.

Countries with high diabetes prevalence

- 1.China: 114 million
- 2.India: 73 million
- 3.USA: 30 million

Reference: DIABETES ATLAS – 8TH EDITION 2017

Types of diabetes

Type 1: Around 5% of all cases. The pancreas doesn't make any insulin. Mostly hereditary.

Type 2: Around 95% of all cases. Insulin secretion is insufficient or sufficient insulin is produced, but its effectiveness is diminished (i.e. insulin resistance).

Complications

Nerve damage (neuropathy)

Kidney damage (nephropathy)

Eye damage (retinopathy)

CAIAPO supplement

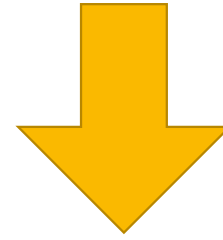
① CAIAPO is a **anti-diabetes supplement** using white sweet potato (peel part).

② We started to launch CAIAPO product from 1996 in Japan.

③ **For type 2 diabetes**



General diabetic medicines



Side effects

Low blood sugar • Body weight increase •
Swelling • Dehydration

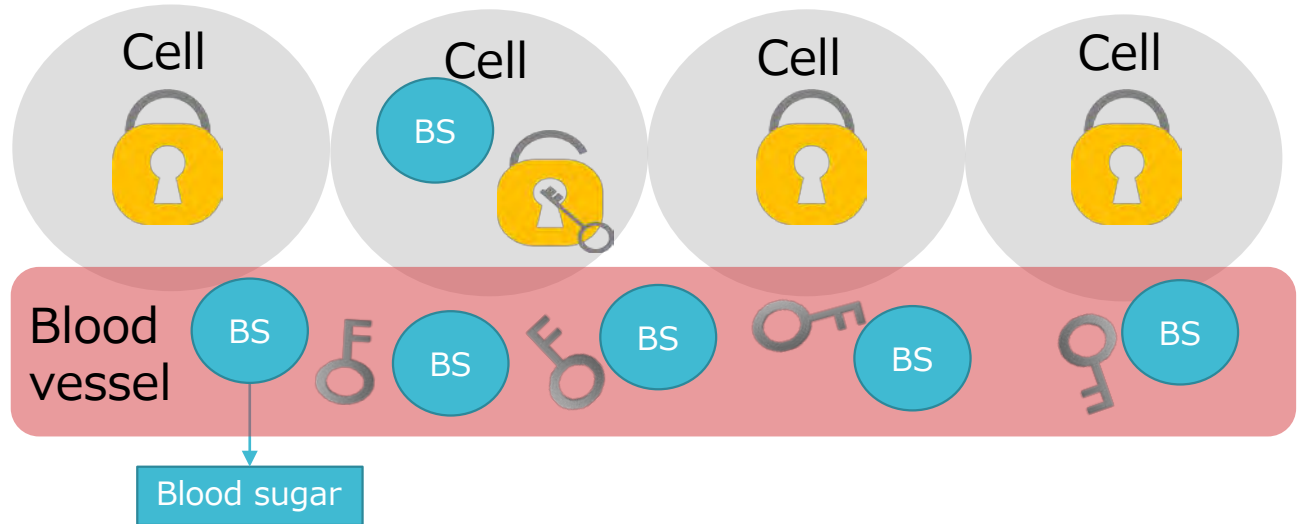
Feature 1

No side
effects

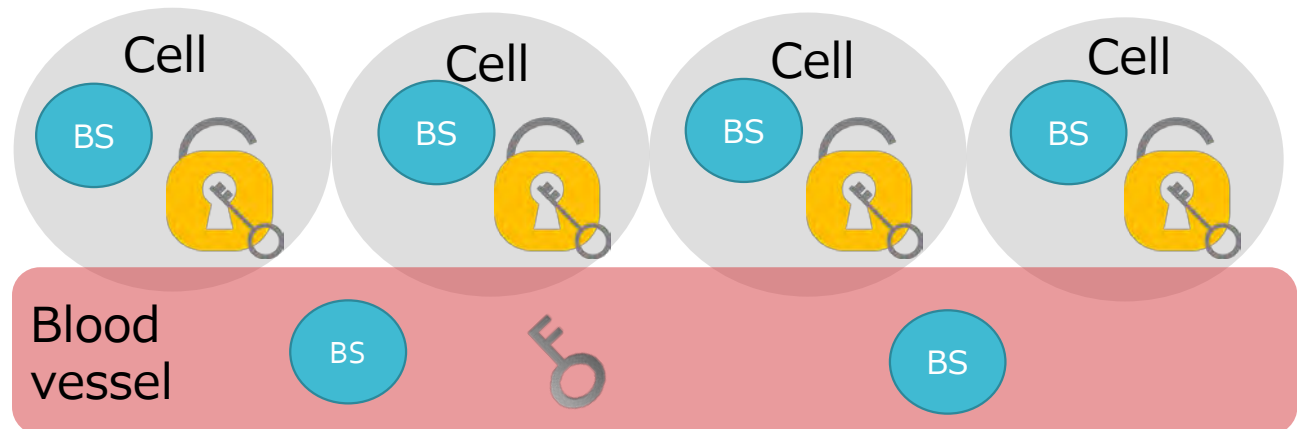
CAIAP0 will work to make insulin that has become ineffective to show its original effect. Since excessive insulin secretion does not occur, there are no side effects.

Feature 2 Improves insulin resistance

Type 2 diabetes ... Since insulin (key) does not work well and the cell does not open, sugar is not absorbed into the cell.
(Insulin resistance)



After take CAIAPO... Insulin (key) works well and opens up the cell and sugar is absorbed. (Improves insulin resistance)



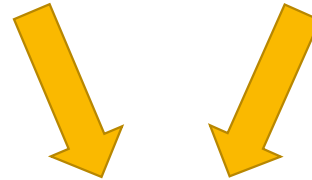
Feature 3 Treatment

General medicines
for diabetic

Temporary blood sugar control

General anti-diabetes
supplement

Moderate the absorption
of blood sugar




These aren't able to fundamentally treat diabetes.

CAIAPO

Improves insulin resistance



It leads to fundamentally treat diabetes.



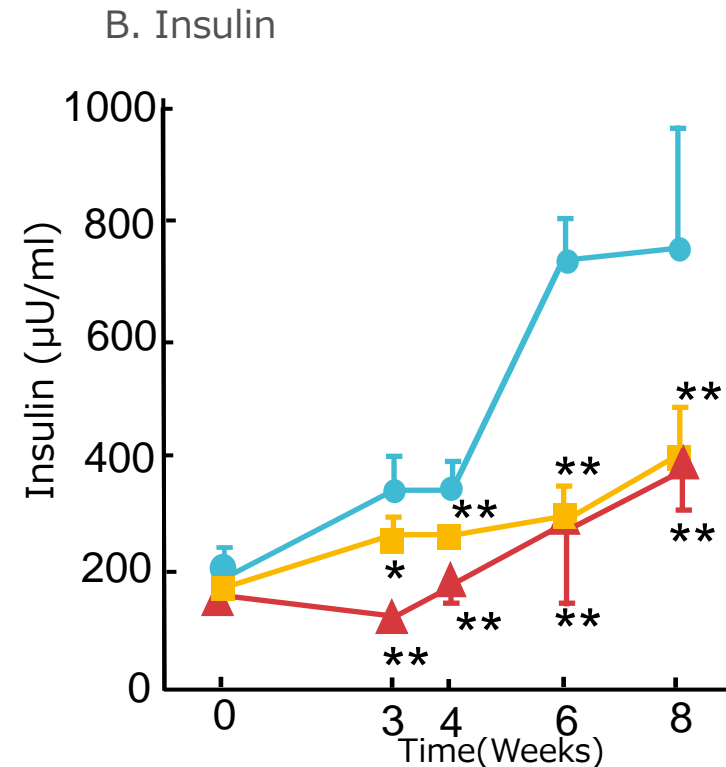
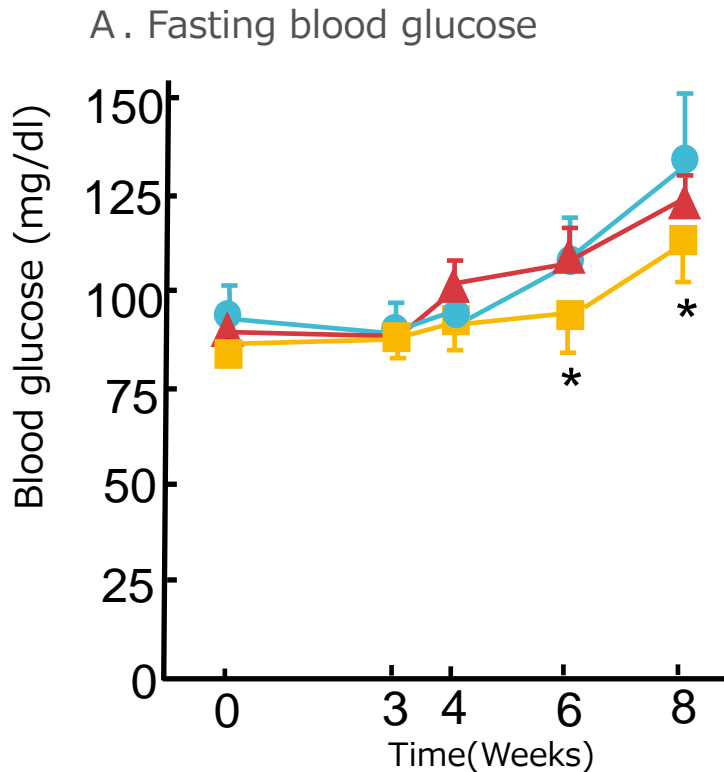
CAIAPO is an
innovative food
product with superior
anti-diabetic effect.

Animal test

Effects on Fasting Blood Glucose Levels①

An 8-weeks continuous administration test was performed on diabetic model Zucker *fa/fa* rats using an internal dialysis solution powder of Caiapo (100mg/kg/day).

● Control
■ Caiapo 100mg/kg^{*}
▲ Troglitazone 50mg/kg



Effects of Caiapo on Fasting Blood Glucose Levels and Insulin Levels

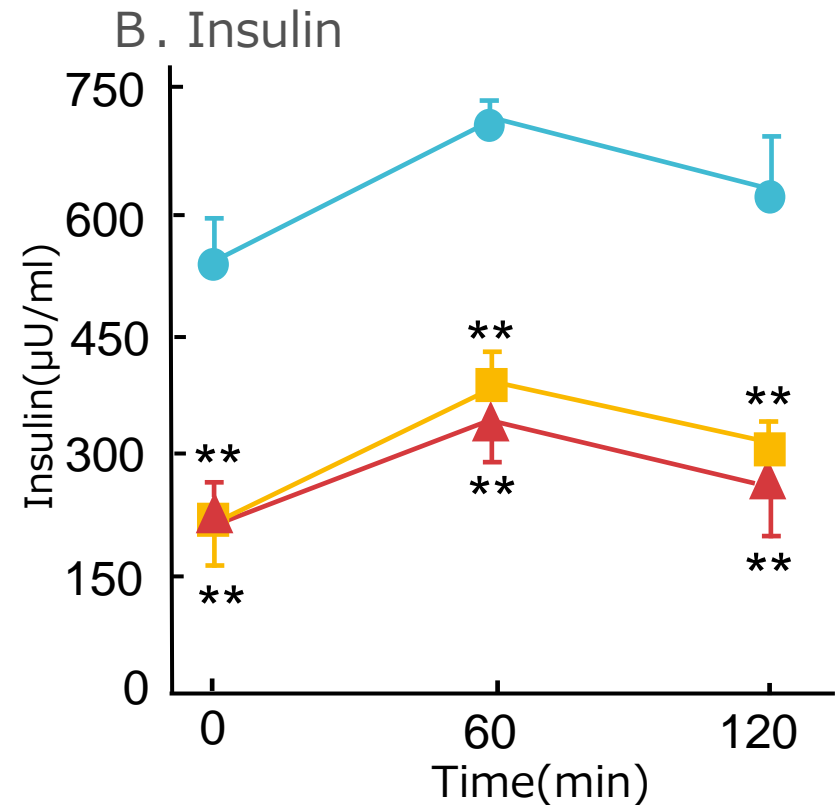
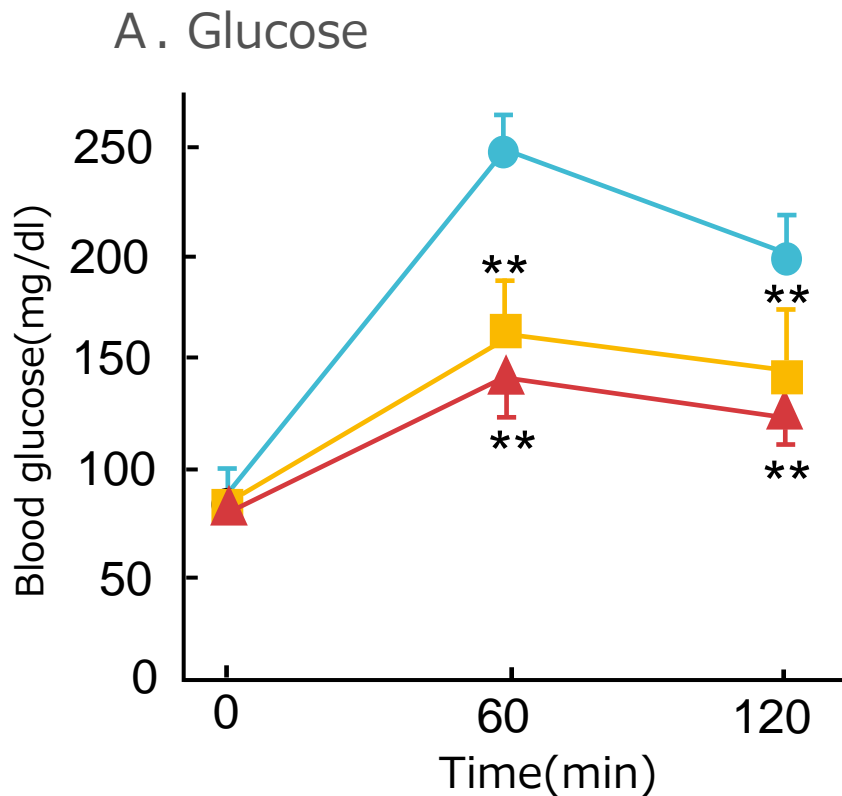
Mean±SD (n =7):* $p < 0.05$, ** $p < 0.01$ VS. Control group
★Caiapo skin peel powder approx.3.46g/kg/day

Animal test

Effects on Fasting Blood Glucose Levels ②

The results of an oral glucose tolerance test (amount of glucose load: 2g/kg) performed at 7-Weeks demonstrated that, in comparison with the control group, the increase in blood glucose and insulin secretion after loading were significantly suppressed in the Caiapo group.

- Control
- Caiapo 100mg/kg^{*}
- ▲ Troglitazone 50mg/kg



Oral Glucose Tolerance Test after Continuous Administration of Caiapo

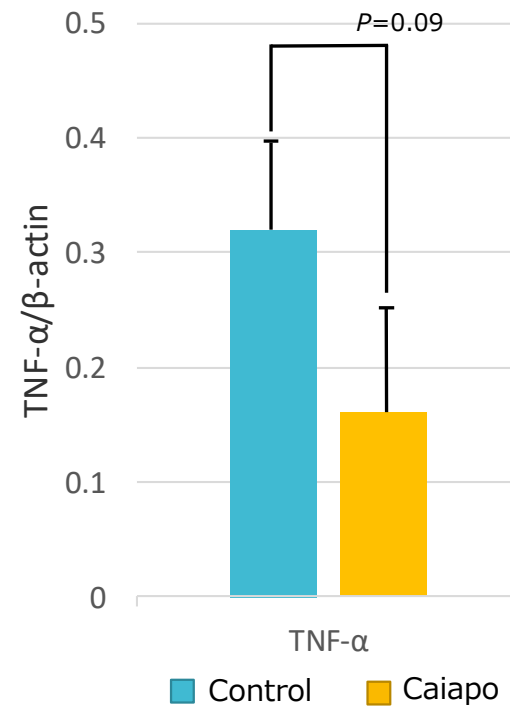
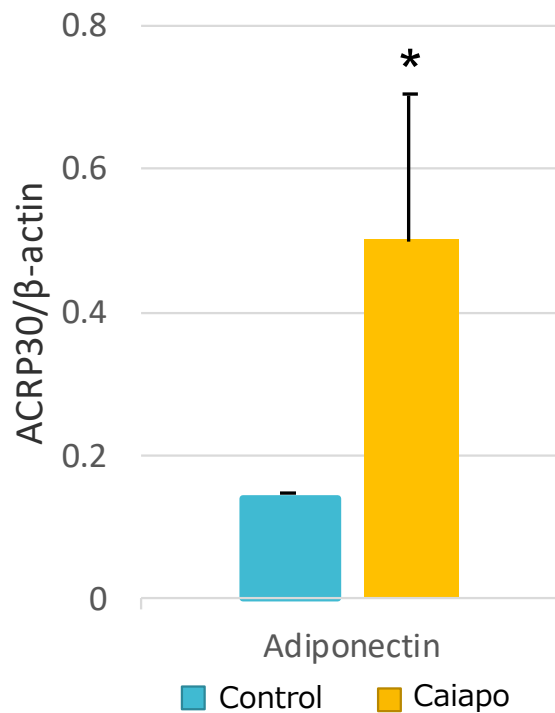
Mean±SD(n=7);**p<0.01VS.Control
★Caiapo skin peel powder approx.3.46g/kg/day

Mechanism of Action

Measurement of the Expression in Adipose Tissue

To examine the mechanism of hypoglycemic action of Caiapo, a continuous administration test was performed in *KKA* mice. After completing the administration, adipose tissue was extracted to examine the effects of administration on the expression level of adipocytokine.

Test method : PCR



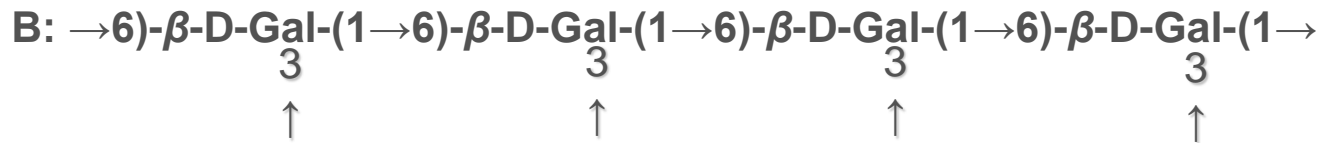
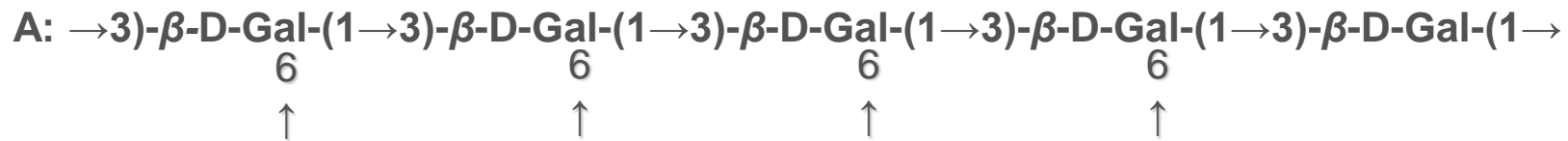
ACRP30: Mouse-derived adiponectin, which has a structure / function very similar to human adiponectin

TNF-α: Tumor necrosis factor, inhibition of uptake of glucose into cells, decrease insulin sensitivity

Mean±SE (n=3): *p<0.05 vs. Control

Active components

Structure of AGP from Caiapo (Arabinogalactan-protein)



© Protein 5~10%

17 amino-acids : hydroxyproline (24.5mol%)

alanine (18.2mol%) , serine (13.7mol%)

© Carbohydrate 90~95%

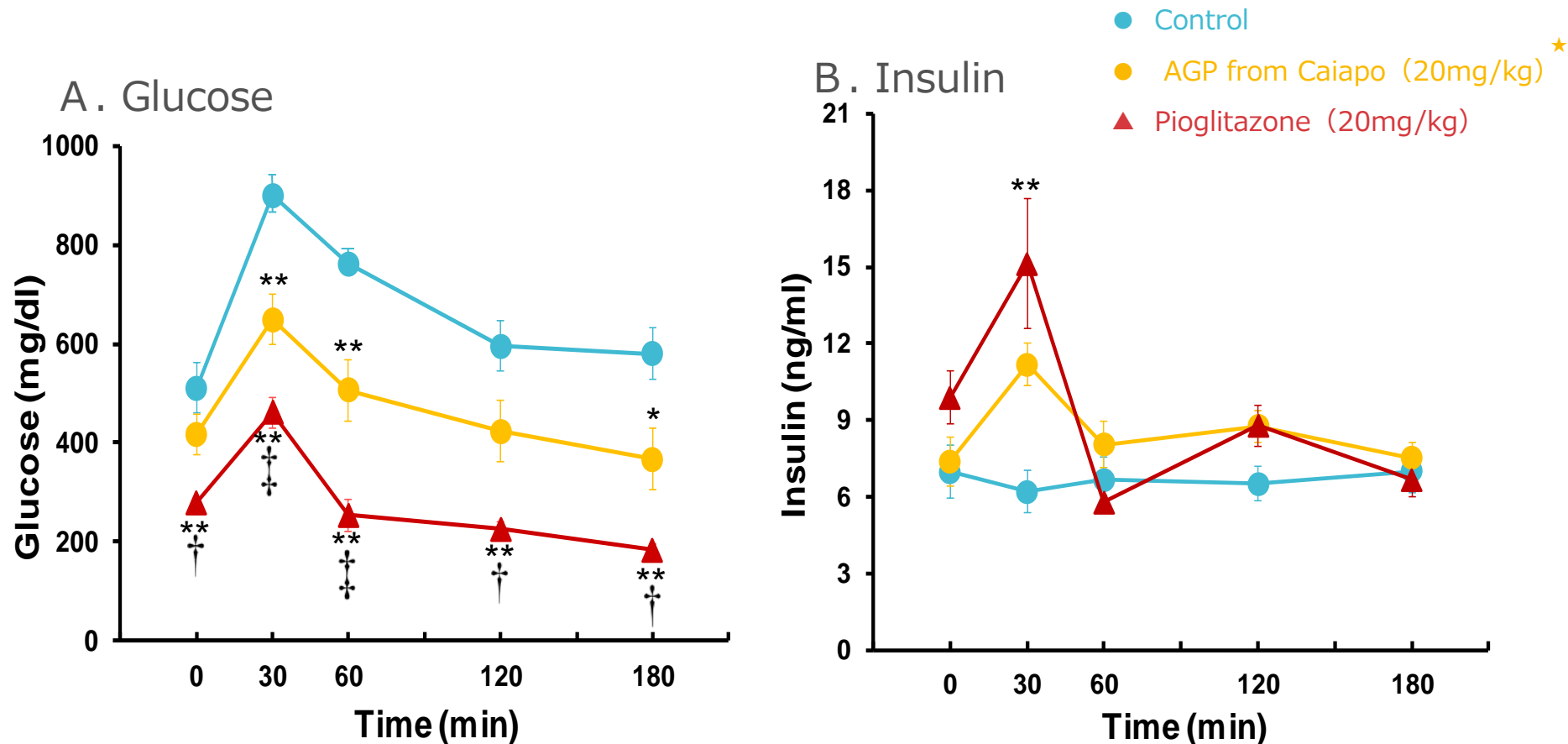
© Molecular weight of approximately 130,000

Effects of the Active Components①

Oral Glucose Tolerance Test after Administration of AGP from Caiapo

A continuous administration test was conducted using gavage administration to spontaneously diabetic animal models (*db/db* mice), to examine the antidiabetic effect of AGP from Caiapo.

Specifically, an OGTT (glucose: 1g/kg) was carried out at Week 6 in the control group(purified water), AGP from Caiapo group(20mg/kg), and pioglitazone group(20mg/kg) as a positive control.

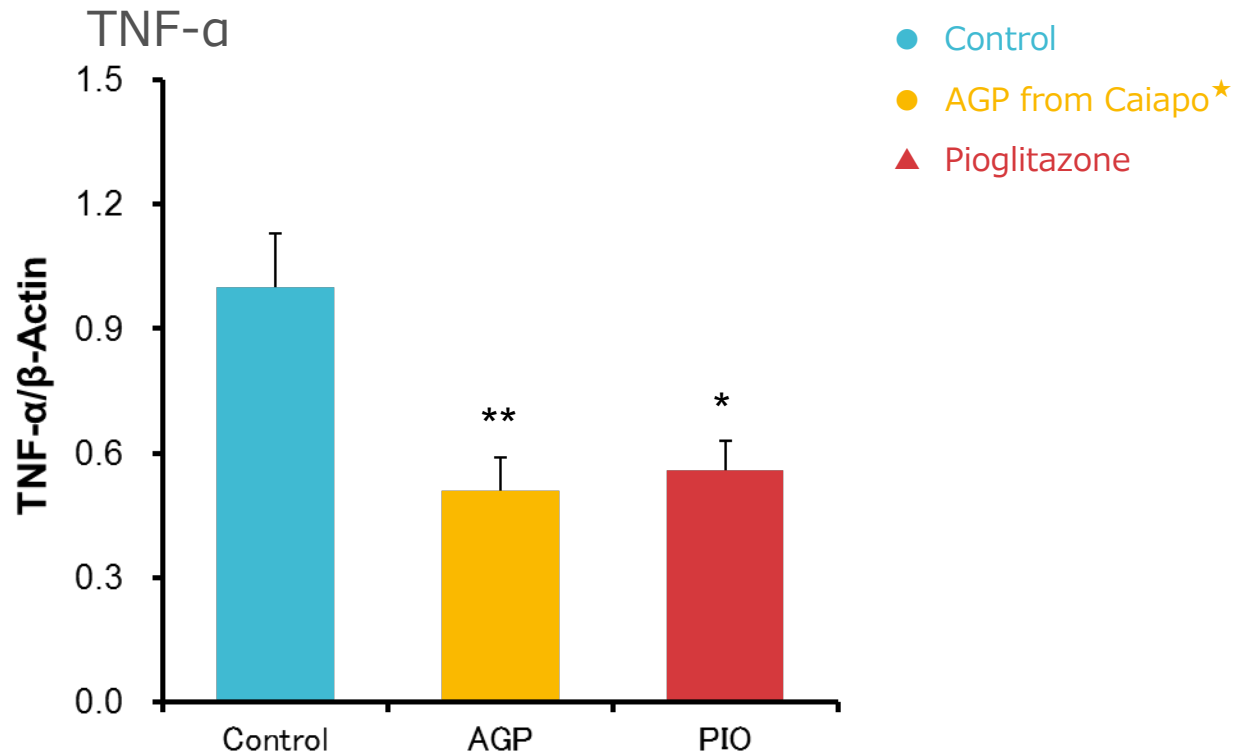


Mean±SE(n=6) : * $p < 0.05$, ** $p < 0.01$ vs. Control Group, † $p < 0.05$, ‡ $p < 0.01$ vs. AGP from Caiapo Group
★Caiapo peel powder approx. 3~4g/kg/day

Effects of the Active Components②

Effects on Inflammatory Cytokines

A gene expression analysis was performed on the mesenteric fat extracted to investigate the effects on inflammatory cytokines.



Expression Analysis of Inflammatory Cytokines in Adipose tissue

Mean±SE(n=6) : * $p < 0.05$, ** $p < 0.01$ vs Control

★Caiapo peel powder approx.3~4g/kg/日

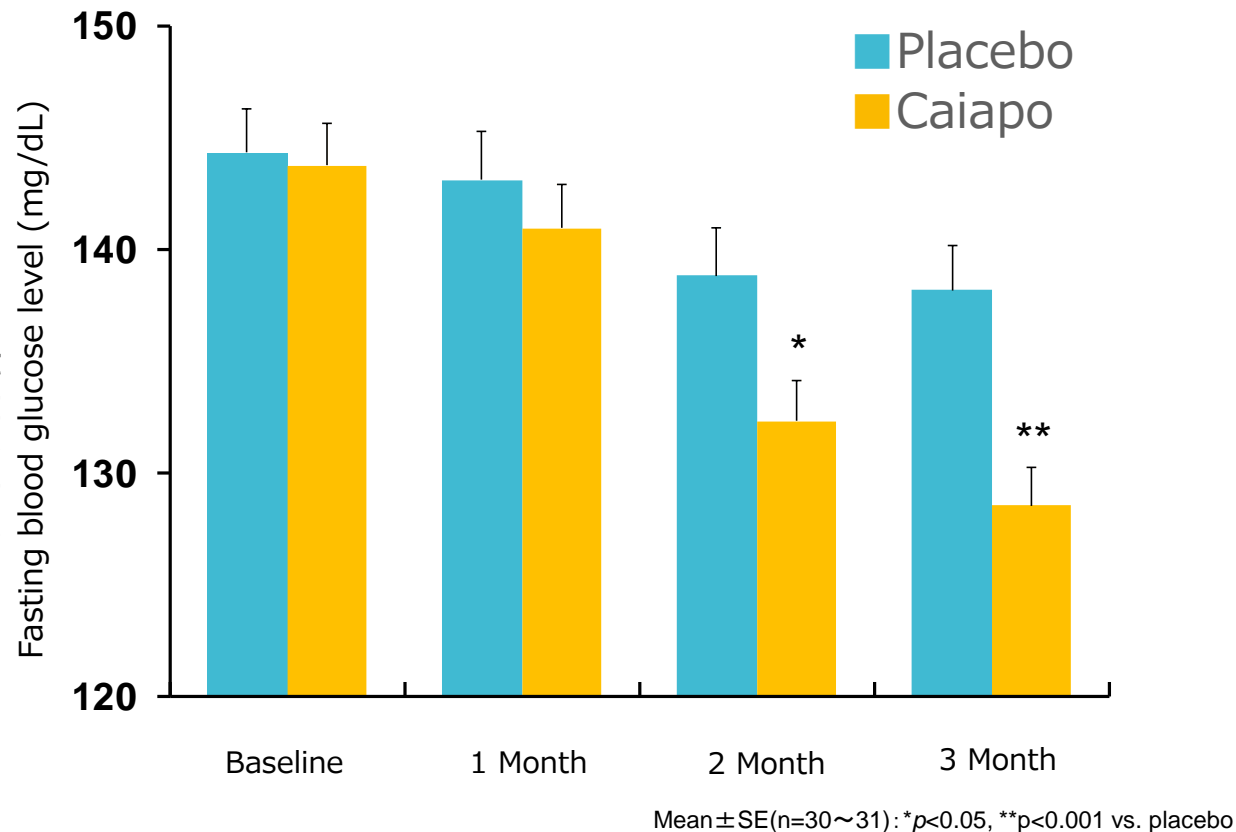
Examination in Human Clinical Trials①

Effect of Caiapo Intake on Fasting Blood Glucose Level

Reference : Ludvik, B., Neuffer, B., et al., *Diabetes Care*, **27**, 436-440(2004)

A 12-week intake study using a double-blind method was conducted in 61 obese patients with type 2 diabetes. Efficacy was evaluated by comparing the fasting blood glucose levels at baseline, 1 Month, 2 Month, and 3 Month after intake, blood glucose level at 2 hours after loading in the glucose tolerance test(glucose load amount: 75g), and HbA_{1c}.

Dosage : Caiapo peel powder 4g/day



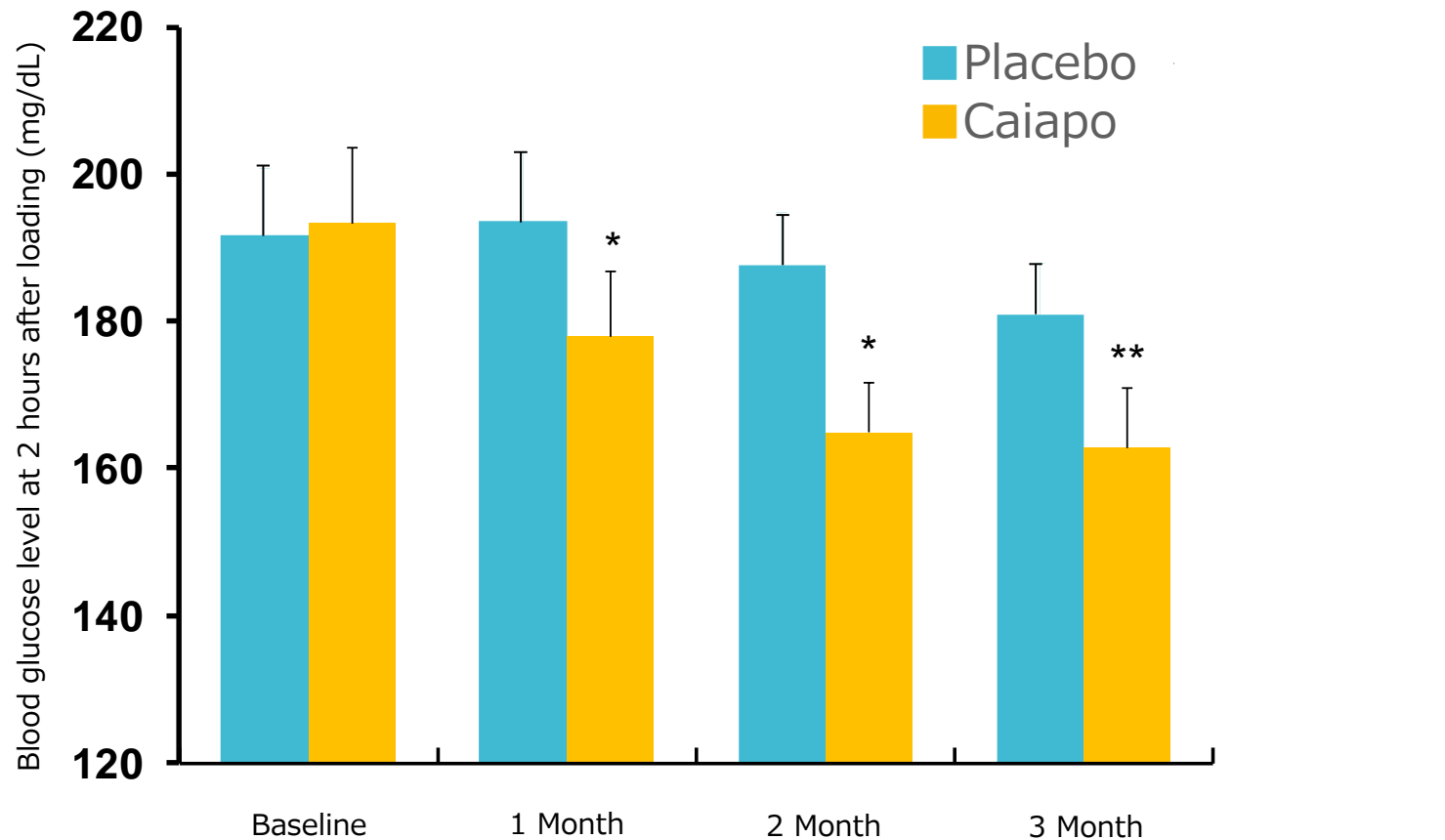
Examination in Human Clinical Trials②

Effect of Caiapo Intake on 2-h Glucose Levels

Reference : Ludvik, B., Neuffer, B., et al., *Diabetes Care*, **27**, 436-440(2004)

A 12-week intake study using a double-blind method was conducted in 61 obese patients with type 2 diabetes. Efficacy was evaluated by comparing the fasting blood glucose levels at baseline, 1 Month, 2 Month, and 3 Month after intake, blood glucose level at 2 hours after loading in the glucose tolerance test (glucose load amount: 75g), and HbA_{1c}.

Dosage : Caiapo peel powder 4g/day



Mean \pm SE (n=30~31); *p<0.005, **p<0.001 vs. Placebo

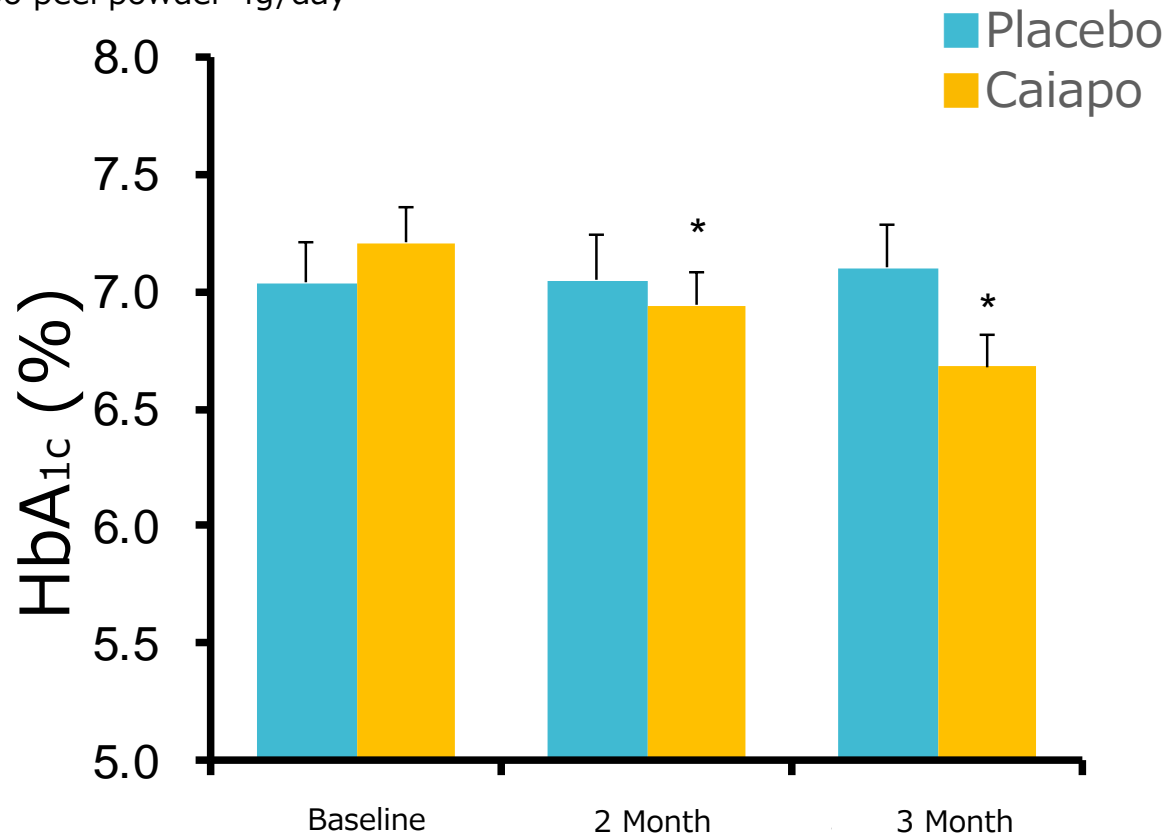
Examination in Human Clinical Trials③

Effect of Caiapo Intake on HbA_{1c}

Reference : Ludvik, B., Neuffer, B., et al., *Diabetes Care*, **27**, 436-440(2004)

A 12-week intake study using a double-blind method was conducted in 61 obese patients with type 2 diabetes. Efficacy was evaluated by comparing the fasting blood glucose levels at baseline, 1 Month, 2 Month, and 3 Month after intake, blood glucose level at 2hours after loading in the glucose tolerance test(glucose load amount: 75g), and HbA_{1c}.

Dosage : Caiapo peel powder 4g/day



Mean ± SE (n=30~31); *p < 0.001 vs. Placebo

List of Safety Tests and Results

Tests	Test Methods	Results
Ames Test	Test bacteria: <i>Salmonella typhimurium</i> TA1535, TA1537, TA98, TA100, <i>Escherichia coli</i> WP2uvrA ⁻ Test substance : Caiapo Test concentrations : 312.5, 625, 1,250, 2,500, 5,000µg/plate	Negative
Chromosomal Aberration Test	Cells : Fibroblasts of the lung of Chinese hamster (CHL/IU) Test substance : Caiapo Test concentrations : 0, 625, 1,250, 2,500, 5,000µg/mL	Negative
Acute Toxicity Test	Animal : SD rats (male and female, 5 in each group) Test substance : Caiapo	NOAEL Male/Female: $\geq 2\text{g/kg}$
Subchronic test (13-week)	Animal : SD rats (male and female, 10 in each group) Test substance : Caiapo Dosages: 0.2%, 1.0%, and 5.0% (in the diet)	NOAEL Male: $\geq 3.4\text{g/kg}$ Female: $\geq 3.8\text{g/kg}$
Long-term intake Test (12-week)	Subject: Patients with borderline/ mild type 2 diabetes (n=66) Intake amount: Caiapo 6.24g/day	No abnormal finding
(13-week)	Subject: Patients with borderline/ mild type 2 diabetes (n=31) Intake amount: Caiapo 6.24g/day	No abnormal finding
(6-month)	Subject: Healthy volunteers and patients with type 2 diabetes (n=23) Intake amount: Caiapo 6.24g/day	No abnormal finding
Overdose test (30 days)	Subject: Healthy volunteers (n=19) Intake amount: Caiapo 18.72g/day (3 times the recommended amount)	No abnormal finding

Stability test (30-month long-term study)

Test	Test method	Result
Long term study	<p>Test term: 30-month</p> <p>Caiapo was sealed in aluminum packages and store at room temperature (19-26°C) for 30 month for the following 8 test items</p> <ul style="list-style-type: none">DescriptionIdentification (coloration reactions)Purity (heavy metals, arsenic)Loss on dryingTotal ashActive ingredient contentTotal viable count<i>Escherichia coli</i> count	<p>Caiapo has a quality preservation period of 24 month, calculated on the basis of safety factor 0.8</p>