



ORYZA OIL & FAT CHEMICAL CO., LTD

MOUNTAIN CAVIAR EXTRACT

Control of postprandial blood glucose
(Suppression of glucose absorption)

- **Mountain Caviar Extract-P**
(Water-soluble powder, for foods)



Aerial parts of mountain caviar

ORYZA OIL & FAT CHEMICAL CO., LTD

Ver. 1.0 HS

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1. Introduction

Processed "Mountain caviar" is locally called "Tonburi" in Odate City, Akita Prefecture and is popular for topping ingredients on Japanese foods. Because it has a caviar or sermon low texture and looks, it is known overseas as "Mountain caviar".

Also, in China, it is called "Jifushi", and in the Later Han dynasty's "Shen Nong Herbal Medicine", it is said that it can reduce heat in the bladder, improve urination, replenish the "qi" of the kidneys when taken for a long time. Moreover, it is said that it makes one's ears and eyes brighter, more agile, and suppresses aging. Mountain caviar has a history of being used as a crude drug for more than 2,000 years. It is said to have been brought to Japan from China during the Heian period, and there are records of the cultivation of mountain caviar in the literature of the Edo period, "Nogyo Zensho" and "Kayo". It is said that the fruit was eaten on special occasions such as vegetarian meals.

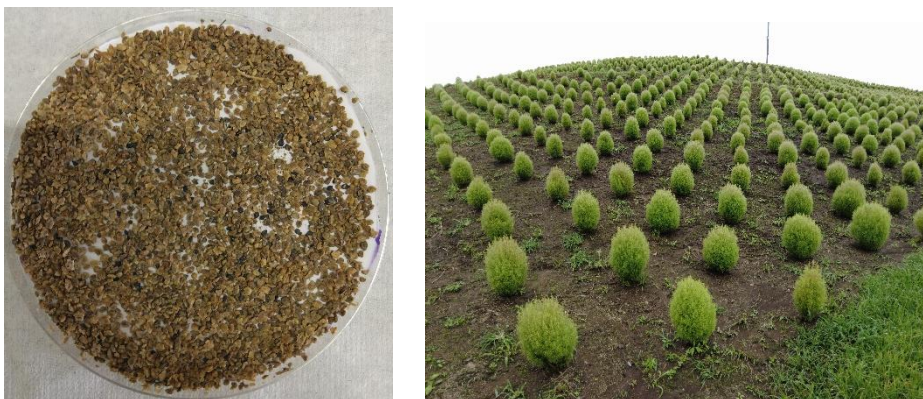


Fig. 1. Fruits (left) and aerial parts (right) of mountain caviar

In the Heisei era, a group of Professors Yoshikawa and Matsuda in Kyoto Pharmaceutical University, who are authorities on saponin research in Japan, vigorously studied the components and physiological activities of mountain caviar, and as a result, saponin momordin Ic was discovered. It has been reported that the active substance

suppresses the increase in blood glucose level in a glucose tolerance test in rats.¹⁾ The mechanism of action is based on the suppression of glucose transfer from the stomach to the small intestine^{2,3)} and the suppression of glucose absorption⁴⁾ by inhibiting the sodium-dependent glucose transporter 1 (SGLT1) in the small intestinal mucosa. Therefore, unlike blood sugar control foods (Salacia, mulberry leaf extract, etc.) that inhibit α -glucosidase, mountain caviar is characterized by suppressing the absorption of glucose, a "monosaccharide" used in soft drinks. In other words, by suppressing the absorption of carbohydrates such as glucose and fructose, which have lower molecular weights than oligosaccharides and maltose, it promotes a wide range of carbohydrate absorption suppression.

Focusing on this paper published a quarter of a century ago, Oryza Oil & Chemical conducted a glucose tolerance test on in-house volunteers and found that it exhibited an excellent suppressive (delaying) effect on the rise of blood sugar levels. Based on these results, we have developed Mountain Caviar Extract-P with a standardized content of the active ingredient "momordin Ic" of 2% or more. The recommended dosage are 200 to 400 mg, and it is effective to take it before the meal of the day with the highest carbohydrate intake timing (usually before dinner).

References:

- 1) Yoshikawa M., Shimada H., Morikawa T., Yoshizumi S., Matsumura N., Murakami T., Matsuda H., Hori K., Yamahara J. Medicinal foodstuffs. VII. On the saponin constituents with glucose and alcohol absorption-inhibitory activity from a food garnish "Tonburi", the fruit of Japanese *Kochia scoparia* (L.) Schrad.: Structures of scopariosides A, B, and C. *Chem. Pharm. Bull.*, **45**, 1300–1305 (1997).
- 2) Matsuda H., Li Y., Yamahara J., Yoshikawa M. Inhibition of gastric emptying by triterpene saponin, momordin Ic, in mice: roles of blood glucose, capsaicin-sensitive sensory nerves, and central nervous system. *J. Pharmacol. Exp. Ther.*, **289**, 729–734 (1999).
- 3) Matsuda H., Li Y., Murakami T., Yamahara J., Yoshikawa M. Structure-related inhibitory activity of oleanolic acid glycosides on gastric emptying in mice. *Bioorg. Med. Chem.*, **7**, 323–327 (1999).
- 4) Matsuda H., Li Y., Murakami T., Matsumura N., Yamahara J., Yoshikawa M. Antidiabetic principles of natural medicines. III. Structure-related inhibitory activity and action mode of oleanolic acid glycosides on hypoglycemic activity. *Chem. Pharm. Bull.*, **46**, 1399–1403 (1998).

2. Mountain Caviar Saponins

Mountain caviar saponins are oleanane-type triterpene saponins shown in Figure 2. In addition, it contains kochianosides⁵⁾ and scoparianosides¹⁾ as minor saponins.

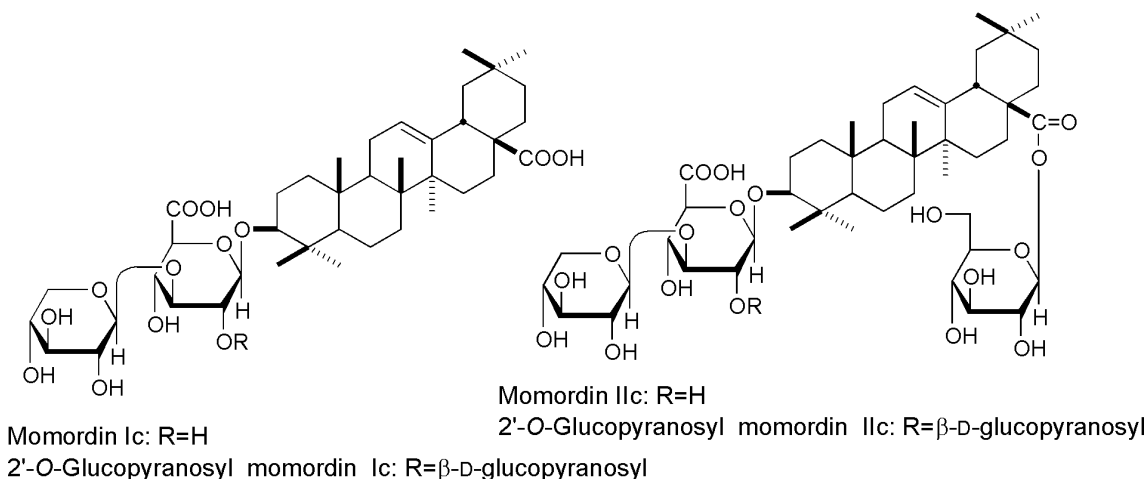


Figure 2. Saponins of Mountain Caviar Extract

Reference:

- 5) Yoshikawa M., Dai Y., Shimada H., Morikawa T., Matsumura N., Yoshizumi S., Matsuda H., Matsuda H., Kubo M. Studies on Kochiae Fructus. II. On the saponin constituents from the fruit of Chinese *Kochia scoparia* (Chenopodiaceae): chemical structures of kochianosides I, II, III, and IV. *Chem. Pharm. Bull.*, **45**, 1052–1055 (1997).

3. Suppression of Carbohydrates Absorption

1) Effects on postprandial blood sugar in carbohydrates-loaded mice

We investigated the effect of saponin fraction of mountain caviar extract on elevation of blood glucose level when various carbohydrates were orally administered in mice. As a result, it was found that saponins in mountain caviar have the delaying effect and moderating the rapid rise in blood sugar levels, especially when glucose or starch is ingested (Figure 3). In addition, although no significant difference was observed during sucrose loading, a tendency to suppress blood glucose levels was seen in the early stages.

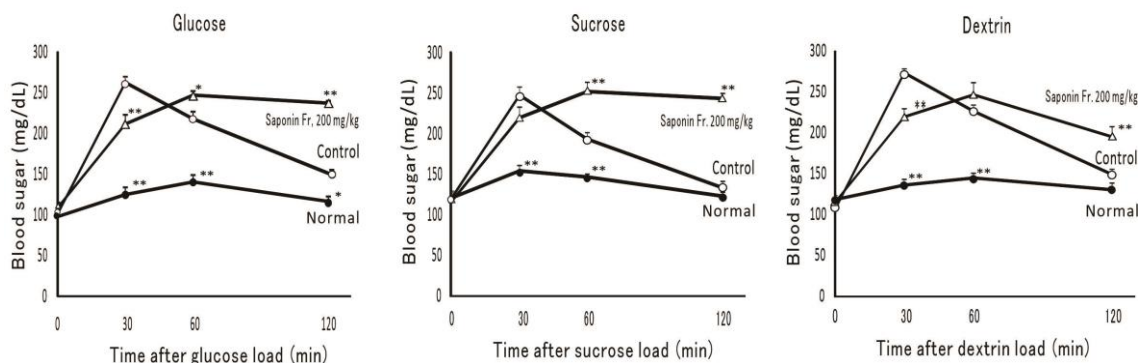


Figure 3. Effect of Mountain Caviar Saponin Fraction in Carbohydrates-loaded Mice
 Mean±SE (n=5-7), **: $p < 0.01$, *: $p < 0.05$.

Similar effects were confirmed in rats,⁵⁾ and momordin Ic and 2'-O-glucopyranosyl momordin Ic were involved in the effect.

Table 1. Suppressive Effects of Mountain Caviar Saponins on Blood Glucose in Glucose-loaded Mice

	Dose (mg/kg)	Blood Glucose (mg/dL)		
		30 min	60 min	120 min
Normal	-	87.1±4.6**	101.6±7.7**	94.8±9.3*
Control	-	149.7±5.2	137.2±4.8	115.0±3.1
Momordin Ic	100	98.9±2.0**	131.7±3.0	125.3±4.0
2'-O-Glucopyranosyl momordin Ic	100	108.8±7.0**	119.7±6.7	110.6±4.0
Momordin IIc	100	147.6±6.9	145.9±4.4	108.9±6.1
2'-O-Glucopyranosyl momordin IIc	100	137.4±8.2	142.5±4.1	113.1±4.4

Mean±SE, *: $p < 0.05$, **: $p < 0.01$

2) Comparison of Mountain Caviar Extract with the other Materials Possessing Blood Sugar Control Activity (Glucose-loaded Mice)

We compared the effects of Mountain Caviar Extract and other materials (excluding α-glucosidase inhibitors) on blood glucose elevation in glucose-laded mice. The dosage were decided according to the literatures.^{6, 7)} As a result, high dose of inulin and indigestible dextrin showed no inhibitory effect in glucose-loaded mice (Figure. 4).

Glucose-loaded mice

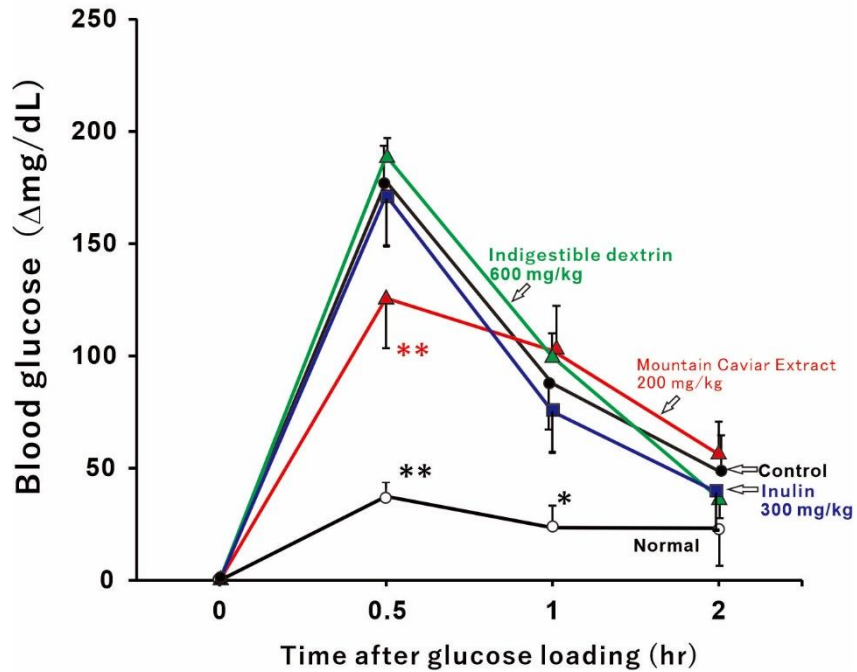


Figure 4. Effects of Mountain Caviar Extract and Other Blood Glucose Controlling Materials. Mean with the SE., *: $p < 0.05$, **: $p < 0.01$

References:

- 6) Wakabayashi S. The Effects of Indigestible Dextrin on Sugar Tolerance: I. Studies on Digestion-Absorption and Sugar Tolerance. *Folia Endocrinol.*, **68**, 623-635 (1992).
- 7) Gao T, Jiao Y., Liu Y., Li T., Wang Z., Wang D. Protective Effects of Konjac and Inulin Extracts on Type 1 and Type 2 Diabetes. *J. Diabetes Res.*, 2019 Oct 7;2019:3872182. doi: 10.1155/2019/3872182 (2019).

3) Inhibition of Mechanism on Glucose Absorption

The glucose absorption inhibitory mechanism of mountain caviar extract is based on the suppression of the transition of sugar from the stomach to the small intestine (1) and the inhibition of glucose from the mucosa of the small intestine (2).⁴⁾

The former action is that momordin Ic acts on the gastric mucosa and inhibits the transfer of stomach contents to the small intestine, which slows down the time when sugar moves to the small intestine, which is the site of decomposition and absorption. This makes glucose absorption mild (Figure 5).

Inhibitory mechanism on glucose absorption 1

Suppression of sugar transport from stomach to intestine

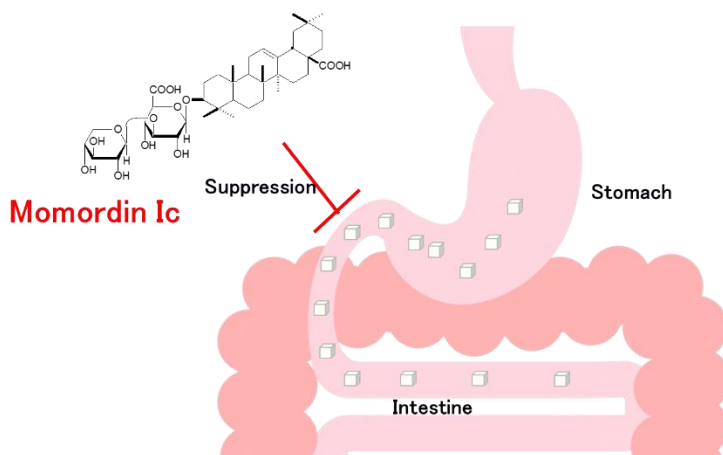


Figure 5. Suppression of Gastric Emptying by Momordin Ic

The second mechanism of momordin Ic is inhibition of glucose uptake from the mucosa of the small intestine. This is due to inhibition of sodium-dependent glucose transporter (SGLT1) by momordin Ic (Figure 6).

Inhibitory mechanism on glucose absorption²

Inhibition of Na⁺-dependent glucose transporter 1 (SGLT1)

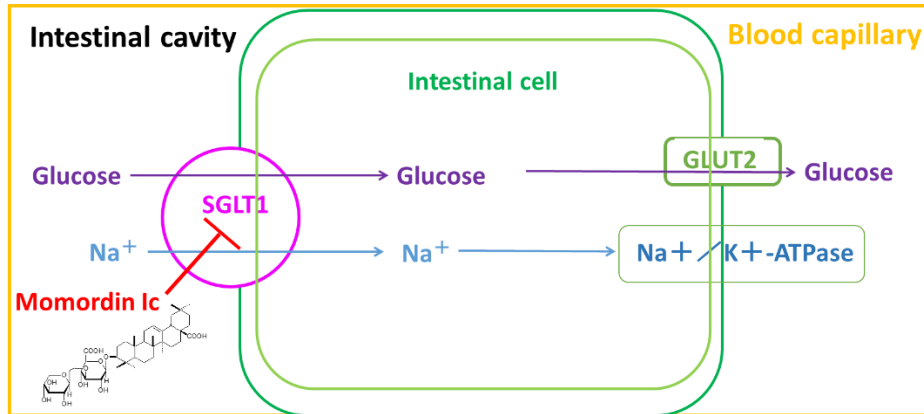


Figure 6. Suppression of Glucose Absorption by Momordin Ic: SGLT1 Inhibition

The digestive enzymes, α -amylase and α -glucosidase are responsible for the digestion of starch and disaccharides (such as sucrose), respectively. When these enzymes work together, carbohydrates are broken down into glucose. Primrose seed extract, Salacia, and mulberry leaves are known as materials that inhibit the activity of these enzymes.

On the other hand, Mountain Caviar Extract delays the speed of oligosaccharides and maltose which are decomposed by α -amylase and maltose move from the stomach to the small intestine by contracting the pylorus region of the stomach. Furthermore, during the absorption stage of glucose generated by α -glucosidase in the small intestine, the function of SGLT1 is suppressed, thereby suppressing its absorption by momordin Ic (Figure 7).

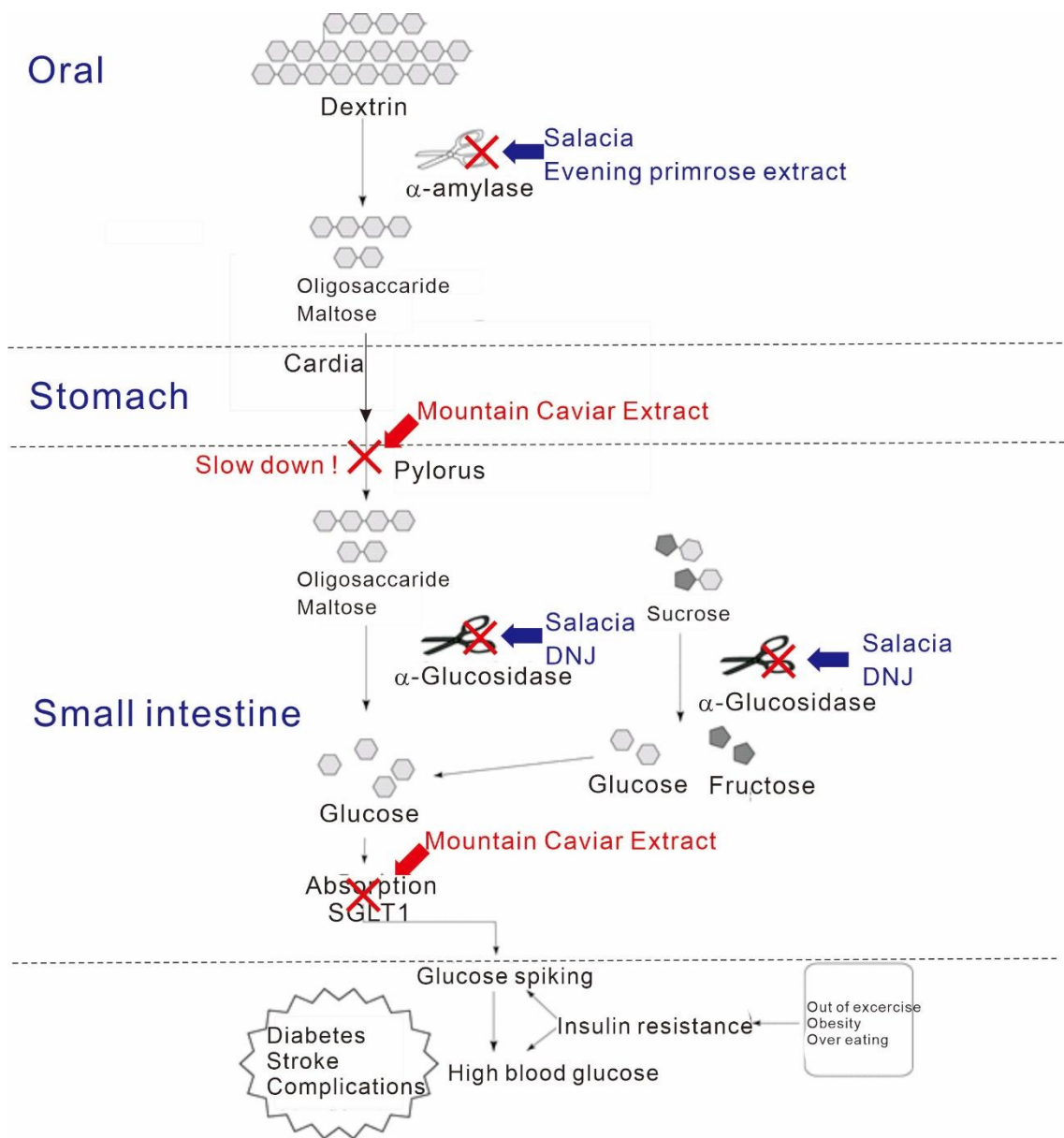


Figure 7. Relationship of Blood Sugar Controlling Materials and Carbohydrates Digestion and Absorption

4. Effect on Human Postprandial Blood Glucose Elevation

1) Oral Glucose Tolerance Test

The inhibitory effect of Mountain Caviar Extract on blood glucose elevation was investigated by a glucose (50 g) tolerance test (OGTT). In the test, 30 minutes after ingestion of Mountain Caviar Extract-P (200 mg or 400 mg), glucose (50 g) was ingested. Then blood was collected to measure changes in blood sugar levels. As a result, ingestion of Mountain Caviar Extract (200 mg) significantly decreased the blood glucose level. It

also decreased area of blood concentration curve (AUC). Furthermore, at intake of 400 mg Mountain Caviar Extract, a significant decrease in blood glucose change and AUC were observed. Based on these results, we recommend 200 to 400 mg of Mountain Caviar Extract-P for daily use.

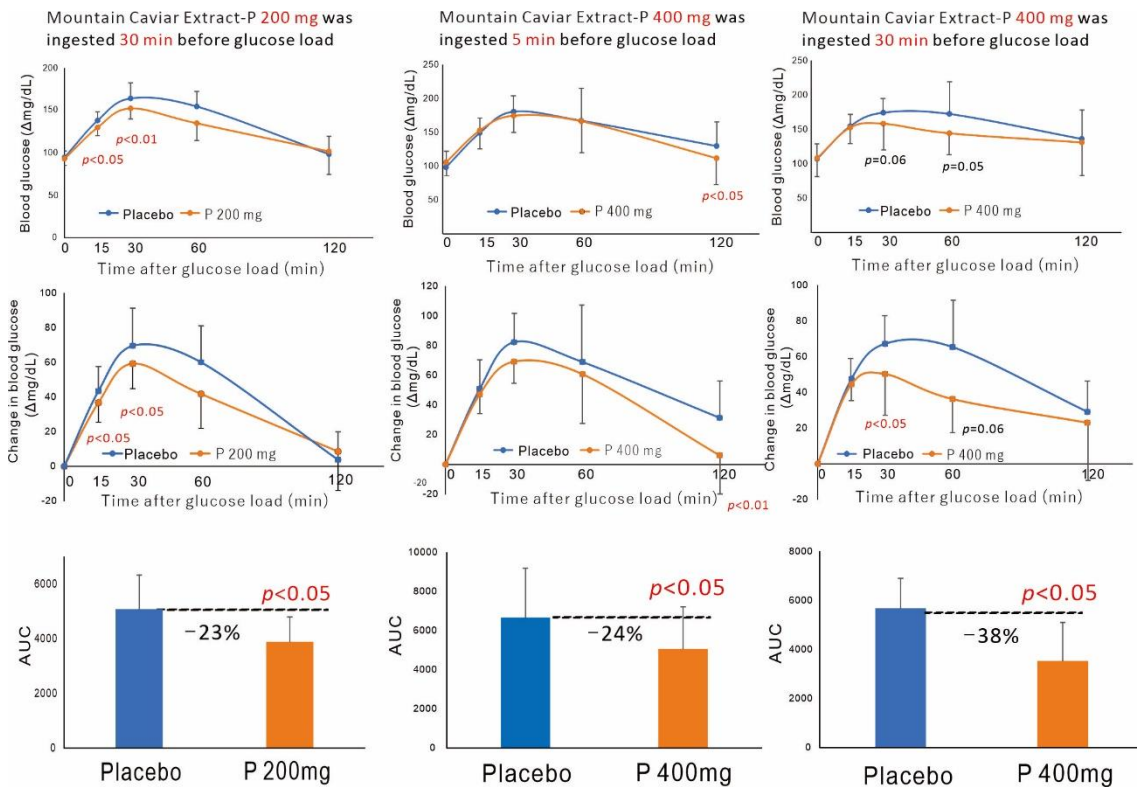


Figure 8. Effect of Mountain Caviar Extract-P on Human OGTT (50 g) Mean with the SD (n=7-10).

2) Steamed Rice-Loaded Study

We investigated the inhibitory effect of Mountain Caviar Extract on the rise in blood glucose level when eating rice. In the test, a pack of retort rice was ingested 30 minutes after ingestion of Mountain Caviar Extract-P (200 mg), and blood was collected over time to measure changes in blood glucose levels. As a result, the blood glucose level decreased significantly 30 minutes after ingestion of rice (Figure 9). Changes in blood glucose levels were significantly reduced at 30 and 60 minutes. A significant decrease was also observed in the area under the blood concentration curve (AUC).

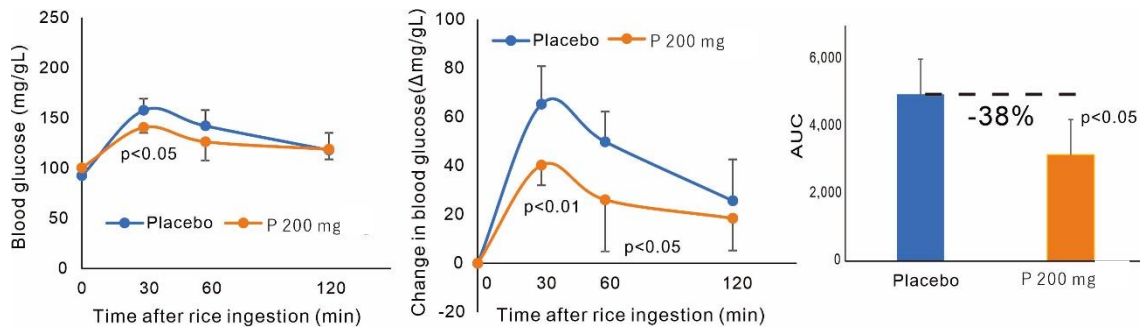


Figure 9. Effect of Mountain Caviar Extract-P on Blood Glucose after Rice Ingestion. Mean with the SD (n=4).

3) Fructose-Loaded Test

We investigated the effect of Mountain Caviar Extract-P on the rise in blood glucose level when ingested fructose. In the test, 30 minutes after ingesting of Mountain Caviar Extract-P (200 mg), fructose (30 g) was ingested. Blood was collected over time to measure changes in blood glucose levels. As a result, the increase in blood glucose level caused by fructose intake was very mild (Figure 10). Mountain Caviar Extract showed a tendency to suppress the increase in blood glucose at 30 minutes after ingestion of fructose.

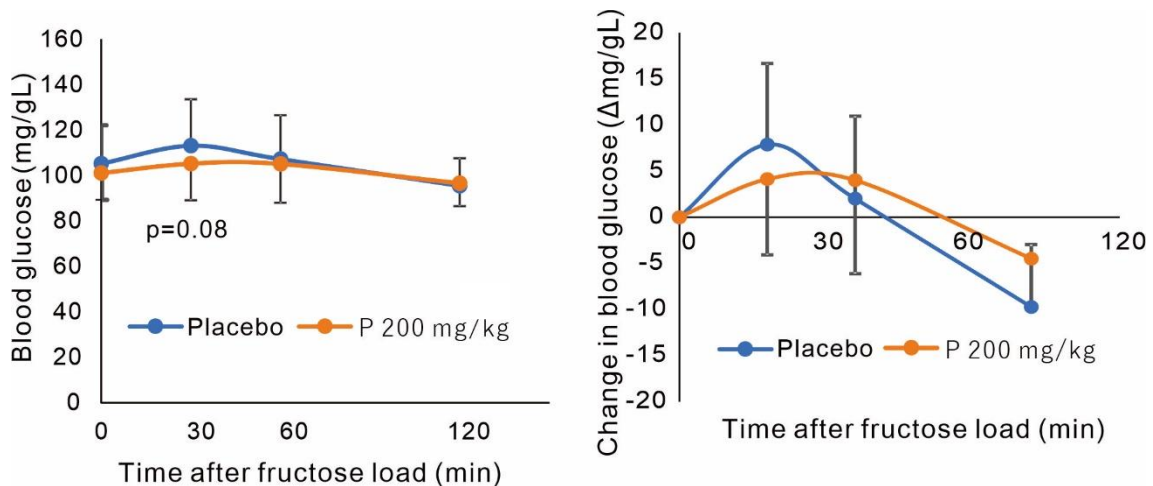


Figure 10. Effect of Mountain Caviar Extract-P on Blood Glucose after Fructose Ingestion. Mean with the SD (n=8).

5. Stability of Mountain Caviar Extract

(1) Heat stability

We heated Mountain Caviar Extract at 100 and 120°C for 2 hr to examine heat stability. As a result, momordin Ic content was not changed. Thus momordin Ic seems to be stable at the temperature on processing foods (Fig. 11).

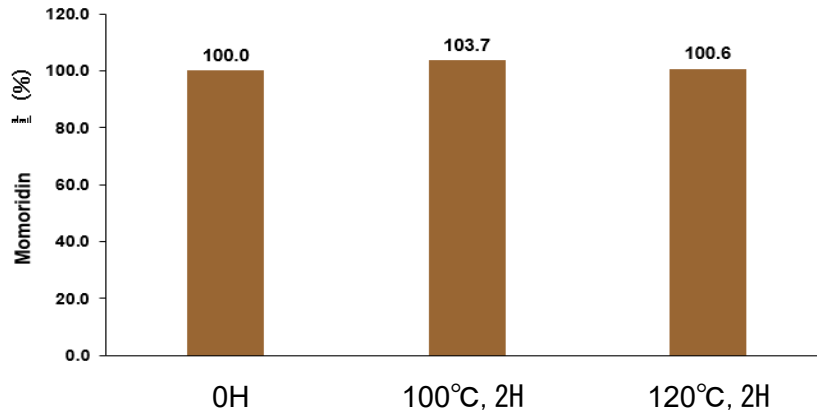


Figure 11. Heat Stability of Mountain Caviar Extract (Initial value: 100%)

(2) pH Stability

After dissolving Mountain Caviar Extract-P in water, pH was adjusted. The momordin Ic content was measured after storage at room temperature for 1 week under non-shading conditions. As a result, there was no decrease in momordin Ic content. From these results, momordin Ic was found to be stable at a wide range of pH from acidic to alkaline.

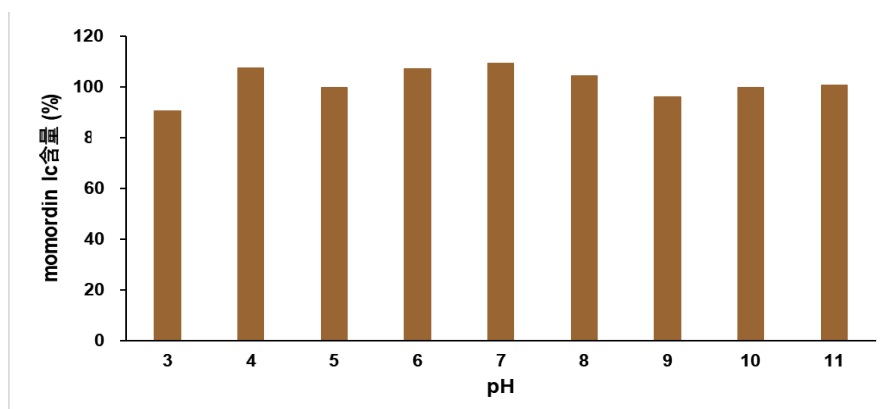


Figure 12. Stability of Dissolved Mountain Caviar Extract in Different pH Condition (Initial value: 100%)

6. Nutrition facts

Per 100g edible portion	P	Method
Water (g)	3.4	Ambient pressure heating and drying method
Protein (g)	5.0	Combustion method, constant: 6.25
Fat (g)	6.1	Acid decomposition method
Ash (g)	2.2	Direct ashing method
Carbohydrate (g)	83.3	*1)
Sugar (g)	82.9	*2)
Energy(kcal)	407	*3)
Sodium (mg)	119	Atomic absorption spectrometry
Sodium chloride equivalent (g)	0.30	*4)

*1) $100 - (\text{water} + \text{protein} + \text{fat} + \text{ash})$

*2) 計算式 : $100 - (\text{water} + \text{protein} + \text{fat} + \text{fiber} + \text{ash})$

*3) Calorie conversion constant : protein 4; lipid 9; carbohydrate 4; dietary fiber 2

*4) Sodium Conversion from Na

Facility : SUNATECH

Date : Sep. 29, 2022

No. : 220913632-001-01

7. Safety

(1) Residual Agricultural Chemical

We examined residual agricultural chemicals for 534 chemicals in Mountain Caviar.

No residual agricultural chemicals were detected,

Test trustee : Vasitech Co., Date : August 19, 2022

Test No. : P-2190408019

Sample name: Mountain caviar

(2) Acute toxicity (LD₅₀)

Mountain Caviar Extract-P (2,000 mg/kg), the maximum allowable amount that does not burden animals, was orally administered to ICR male and female mice (6 weeks old) under fasting. Then we observed the mice for 14 days. As a result, no deaths or abnormalities in weight transition (compared with the control group) were observed, and no macroscopic abnormalities of organs were observed in the autopsy performed after the

study. Therefore, the LD50 level (oral administration) of Mountain Caviar Extract-P in mice is more than 2,000 mg/kg for both sexes.

(3) Mutagenicity (Ames test)

Ames tests were performed on Mountain Caviar Extract (without dextrin) using *Salmonella typhimurus* TA98, TA100, TA1535, TA1537 and *E. coli* WP2. As a result, there was no increase in the number of mutant colonies at concentrations of 19.5 to 5,000 µg/plate in both the direct method and the metabolic activation method. From these results, it is considered that Mountain Caviar Extract is not mutagenic.

8. Recommended dosage

Based on the results of clinical trials, we recommend 200 to 400 mg of Mountain Caviar Extract-P for daily usage.

9. Application

	Application	Claims	Examples
Food	Functional food for blood sugar control	Suppression of postprandial hyperglycemia	Beverages, hard & soft capsules, tablets, candies, chewing gums, chocolates, wafers, jellies, ham, sausage, etc.

10. Packaging

Mountain Caviar Extract-P

1 kg, 5kg

Interior packing: Aluminum bag

Exterior packaging: Cardboard box

11. Storage

Avoid high temperature and humid. Store in cool, dry dark place.

12. Example

Mountain Caviar Extract -P

Maltodextrin, mountain caviar extract

PRODUCT STANDARD

PRODUCT NAME : **Mountain Caviar EXTRACT-P**
(FOOD)

This product is extracted with aqueous ethanol from fruits of *Kochia scoparia* (L.). It contains a minimum of 2.0% momordin Ic. This powder is water-soluble.

<u>Appearance</u>	Yellow greenish white to pale yellowish brown powder with slightly characteristic odor.									
<u>Momordin Ic</u>	Min. 2.0 %	(HPLC)								
<u>Loss on Drying</u>	Max. 10.0 %	(Analysis for Hygienic Chemists, 1 g, 105°C, 2 hr)								
<u>Purity Test</u>										
<u>(1) Heavy Metals (as Pb)</u>	Max. 20 ppm	(Sodium Sulfide Colorimetric Method)								
<u>(2) Arsenic (as As₂O₃)</u>	Max. 2 ppm	(Standard Methods of Analysis in Food Safety Regulation, The Third Method, Apparatus B)								
<u>Standard Plate Counts</u>	Max. 1×10 ³ cfu/g	(Analysis for Hygienic Chemists)								
<u>Moulds and Yeasts</u>	Max. 1×10 ² cfu/g	(Analysis for Hygienic Chemists)								
<u>Coliforms</u>	Negative	(Analysis for Hygienic Chemists)								
<u>Composition</u>	<table border="0" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="text-align: left; border-bottom: 1px solid black;"><u>Ingredient</u></th> <th style="text-align: right; border-bottom: 1px solid black;"><u>Content</u></th> </tr> </thead> <tbody> <tr> <td>Maltodextrin</td> <td style="text-align: right;">75%</td> </tr> <tr> <td style="border-bottom: 1px solid black;">Mountain Caviar Extract</td> <td style="text-align: right; border-bottom: 1px solid black;">25%</td> </tr> <tr> <td>Total</td> <td style="text-align: right;">100%</td> </tr> </tbody> </table>		<u>Ingredient</u>	<u>Content</u>	Maltodextrin	75%	Mountain Caviar Extract	25%	Total	100%
<u>Ingredient</u>	<u>Content</u>									
Maltodextrin	75%									
Mountain Caviar Extract	25%									
Total	100%									
<u>Expiry date</u>	2 years from date of manufacturing.									
<u>Storage</u>	Store in a dry, ventilated location. Keep away from high temperature and sunlight.									

ORYZA OIL & FAT CHEMICAL CO., LTD. striving for the development of the new functional food materials to promote health and general well-being.

From product planning to OEM - For any additional information or assistance, please contact :

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