

Specification of Anti- Diabetes (Glycemic Control) Probiotics Capsule

1. Brief Introduction

Product Name: Anti- Diabetes (Glycemic Control) Probiotics Capsule

Product Specification: 60 capsules/bottle, 500mg/capsule

Directions: Take two (2) Glycemic Control Probiotics capsules daily during administration of metformin.

Caution: Consult physician if pregnant/nursing, taking medication, or have a medical condition. Keep out of reach of children.

Storage: store in a cool(below 4°C), dry place to maintain potency.

Potency: *Lactobacillus plantarum* HH-LP56(20 billion CFU/g), *Lactobacillus paracasei* HH-LP58 (20 billion CFU/g).

Other ingredients: Bitter melon extract, green tea extract, inulin, fructooligosaccharide.

Health benefits: improve gut health and the secretion of GLP-1.

2. Consumer Study

In the consumer study, 30 adults between the age 55 to 65 years were recruited to the study and asked to consume the Glycemic Control Probiotics capsule daily for 90 days and send the filled questionnaire. The table below demonstrates the

improvement of discomfort in the participants.

Table 1. Improvement of discomfort in the participants

Discomfort	% adults who felt improvement
Excessive thirsty	80%
Polyuria(excessive urination volume)	70%
Weight loss	80%

3. Probiotics and Diabetes

The effect of probiotics on glycemic control in individuals with diabetes has received increased attention in recent years. The addition of probiotics to metformin therapy is associated with improvement in T2DM outcomes.

Table 2. Common diabetes therapies

Therapy	Pros & Cons
Change life style	slowly
Inject insulin	Costly
Use hypoglycemic drugs	Side effects
Use probiotics	Safe and effective without side effects

4. Probiotic Mechanisms Affecting Glucose Homeostasis

- ① Increase serum levels of adiponectin
- ② Induce the secretion of GLP-1
- ③ Reduce insulin resistance
- ④ Improve inflammations
- ⑤ Improve immune system
- ⑥ Balance gut microbiota

Among them, inducing GLP-1 secretion is an important way for probiotics to regulate blood glucose. Therefore, we further analyzed the mechanism of GLP-1 on blood glucose.

5. Effects of GLP-1 on Glucose Homeostasis

GLP-1 is a peptide hormone deriving from the tissue-specific post-translational processing of the proglucagon peptide, which is produced and secreted by intestinal enteroendocrine L-cells. The most noteworthy effect of GLP-1 is its ability to promote insulin secretion in a glucose-dependent manner. In the stomach, GLP-1 inhibits gastric emptying, acid secretion and motility, which collectively decrease appetite. It can also repress hepatic gluconeogenesis, stimulate hepatic lipogenesis, improve glucose uptake, and hence, reduce postprandial plasma glucose levels via insulin.

6. Screening of Probiotics with Glycemic Control Activity

To obtain new LABs with glycemic control activity, we obtained four LAB isolates from traditional fermented food (such as pickle) by comparing their capacity in inducing GLP-1 secretion in rats. We identified them at the species level by 16S rDNA sequencing method. Specifically, two isolates, named *Lactobacillus plantarum* HH-LP56 and *Lactobacillus paracasei* HH-LP58 showed more promising probiotic potential than others because of their efficiency in glycemic control, resistance to acid and bile salts, and colonization ability.

7. Animal Study

Type 2 diabetes rat model was established using a high-fat diet and streptozotocin. Rats were divided into normal group, model group, metformin group, high-potency probiotic group (90mg/kg/d, HH-LP56: 2.0×10^{10} CFU/g and HH-LP58: 2.0×10^{10} CFU/g), low-potency probiotic group (90mg/kg/d, HH-LP56: 2.0×10^9 CFU/g and HH-LP58: 2.0×10^9 CFU/g). A 8-week oral gavage was performed in the rats, and levels of fasting blood glucose, serum GLP-1 and Peptide YY (PYY), and colon GLP-1 were tested.

8. Results

It can be seen from Table 3 that the FBG level in model group was significantly higher than that in normal group during the 4 weeks treatment, while the FBG level in metformin group and the high-potency probiotic group was significantly decreased at week 3, and the FBG of the low-potency probiotic group was significantly decreased at week 4.

Table 3. Effects of probiotics on FBG(mmol/L)

Group	Before Intervention	1-week	2-week	3-week	4-week
Model group	22.89 ± 2.01 ^a	23.99 ± 3.48 ^a	24.28 ± 3.01 ^a	25.34 ± 2.65 ^a	25.79 ± 3.03 ^a
Metformin group	22.05 ± 3.88	21.75 ± 2.45	20.45 ± 2.54	18.60 ± 3.01 ^b	17.67 ± 2.65 ^c
Low-potency probiotic group	22.78 ± 1.35	23.09 ± 2.85	24.30 ± 2.50	23.21 ± 1.66	21.34 ± 2.65 ^d
High-potency probiotic group	22.36 ± 3.01	21.99 ± 1.99	21.34 ± 2.01	19.53 ± 3.84 ^d	18.64 ± 2.05 ^c
Normal Group	5.34 ± 0.45	5.28 ± 0.38	5.04 ± 0.58	5.23 ± 3.27	5.30 ± 0.19

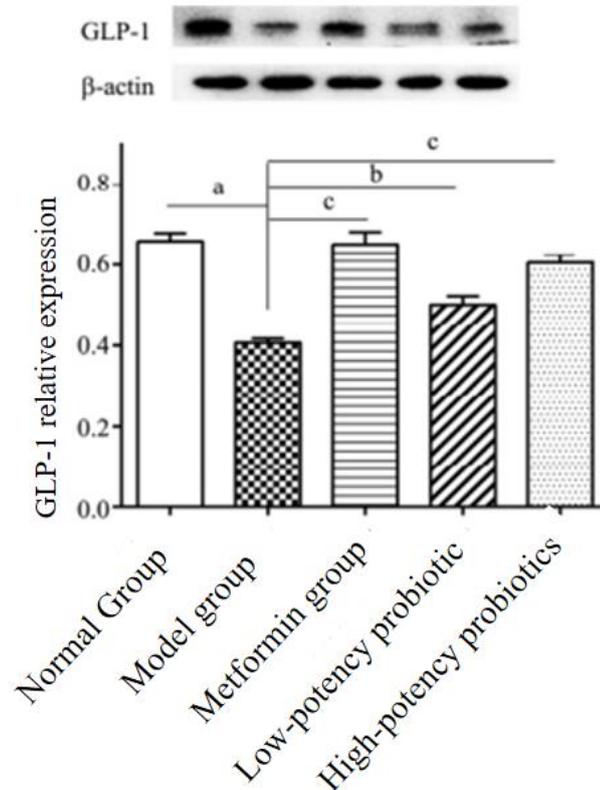
It can be seen from Table 4 that the levels of serum GLP-1 and PYY in model group was lower than that in normal group, while both probiotic treatment groups and metformin group showed higher level in GLP-1 and PYY comparing with model group.

Table 4. Effects of probiotics on GLP-1 and PYY(mmol/L)

Group	GLP-1 (pmol/L)	PYY (mmol/L)
Model group	3.60 ± 0.10 ^a	2.35 ± 0.20 ^a
Metformin group	4.89 ± 0.20 ^b	3.55 ± 0.08 ^b
Low-potency probiotic group	3.98 ± 0.18 ^b	2.89 ± 0.25 ^b
High-potency probiotic group	4.66 ± 0.12 ^b	3.41 ± 0.14 ^b
Normal Group	5.02 ± 0.11	3.75 ± 0.08

It can be seen from Figure 1 that both probiotic treatment groups and metformin group showed higher level in colon GLP-1 comparing with model group.

Figure 1. Effects of probiotics on colon GLP-1 level



In a conclusion, *Lactobacillus plantarum* HH-LP56 and *Lactobacillus paracasei* HH-LP58 showed strong ability in inducing GLP-1 secretion, suggesting that they have the potential to reduce blood glucose in diabetic patients.

9. Recommended Human daily intake

For a 70kg adult: 4.0×10^{10} CFU/day.

10. Other Ingredients

Bitter melon extract: bitter melon contains chemicals that acts like insulin to help reduce blood sugar levels.

green tea extract: green tea extract (GTE) can increase insulin sensitivity and lower blood glucose levels. **Inulin, fructooligosaccharide:** prebiotics.