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Exploring the Potential Value of Nicandra Physaloides (L.) Gaertn Seed Meal Substitute in Prolonging Digestion Rate and Regulating Blood Lipid

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Abstract: *Object: Exploring the potential value of Nicandra Physaloides (L.) Gaertn seed meal substitute in prolonging digestion rate and regulating blood lipid.Methods: In this study, the metabolic rate of gastric contents in rats was determined by quantitative analysis, and the hypolipidemic effect was explored by detecting the serological indexes (insulin level, leptin, serum adiponectin, TC, TG, HDL, TNF- α, IL-6, etc.) in obese rats.Results: The experimental results show that the retention time of gastric contents could be effectively delayed by using Nicandra Physaloides (L.) Gaertn seed as substitute meal compared with ordinary meal substitute. It effectively reduced Lee's index, liver-body ratio, and total limb-body ratio in obese SD rats. In addition, it could not only effectively reduce the Lee's index, liver / body ratio, total limb ratio, oral glucose tolerance and insulin level of obese rats, but also effectively reduce the levels of serum TC and LDL-C in hyperlipidemic rats.*

Keywords: *Physaloides (L.) Gaertn seed, gastric retention time, weight loss, hyperlipidemia*

1. Introduction

In recent years, with the development of China's economy and the improvement of national living standards, the number of deaths caused by chronic non-communicable diseases such as cardiovascular disease and diabetes accounts for nearly 90% of the total deaths of Chinese residents. it has become a major public health problem in China and even in the world [1-5]. Worldwide, overweight and obesity are the main risk factors for chronic diseases. More than 50% of adults and about 20% of school-age children are overweight or obese, although many studies are exploring how to address this health risk. However, the problem of obesity and related chronic diseases has not been effectively controlled, which requires our further research.

Nicandra Physaloides (L.) Gaertn seed(NPGS)is an annual herb that is distributed in many provinces and autonomous regions in my country. At the same time, its wild distribution is very large, and its cultivation is relatively easy, so the price of the synthesized drug is relatively low. In China, it is used as a sedative, expectorant, antipyretic and antidote [6]. Studies have shown that its leaf extract can lower blood sugar and has anti-tumor effects; and its seeds contain pectin, which can be made into jelly for consumption [7]. In addition, many studies have shown that NPGS are rich in protein, carotenoids, vitamin A and vitamin C, and have also been found to be various biologically active substances such as lycopene, anthocyanins, chlorophyll and phenols [7, 8]. Blaner et al. found that vitamin A and related proteins play a role in the development and prevention of obesity and obesity-related diseases [9]. Zhu et al. found that lycopene helps prevent diabetes and obesity [10]. These studies all show that NPGS has a potential role in preventing the occurrence and development of obesity and metabolic diseases. However, related studies are rare and require further exploration.

The main purpose of this study is to explore the potential value of meal substitute made of NPGS in prolonging digestion rate and regulating blood lipid, and to discover the potential role of NPGS in obesity.

2. Methods

Experimental animals and feeding conditions: Clean male SD rats were used in the experiment and

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were kept in the SPF-level animal room at the Mudanjiang Medical University Pharmaceutical Research Center, with a temperature of around 20℃ and a humidity of around 60%. The rats had free access to drinking water throughout the experiment, and the animal room was kept clean.

NPGS meal substitute: NPGS meal was obtained by removing the outer layer of the seed and using freeze-drying methods, and the substitute was made using medical slow-release technology.

2.1 Investigating the gastric retention time of NPGS meal substitute compared to other substitutes

Ten clean male SD rats were randomly divided into five groups, with two rats in each group. The NPGS meal substitute group and five different temporary substitute groups were administered by oral gavage, with the NPGS meal substitute group receiving the same amount of substitute as the control group given another substitute with the same amount of NPGS meal. After 2 hours, or longer, each rat was killed and the stomach contents were examined to see how much of the gastric contents had been consumed. The amount and duration of gastric contents were recorded for each group of rats.

2.2 Effects of NPGS meal substitute as a meal substitute on blood glucose and lipid levels in nutritional obesity rats

Forty male SD rats were randomly divided into four groups: the blank control group, the nutritional obesity model group, the positive control group, and the NPGS meal substitute group.

All groups were fed a high-fat diet to create the nutritional obesity model (consisting of regular feed 60%, lard 8%, sucrose 5%, whole milk powder 5%, peanuts 8%, eggs 10%, salt 2%, cholesterol 2%), except the blank control group that received an equal amount of regular feed.

After the model was established, the positive control group was given orlistat gavage, the NPGS meal substitute group was given NPGS as a meal substitute, and the remaining groups were given equal volumes of saline via gavage.

2.2.1 Measurement of rat body fat percentage, Lee's index, liver-to-body weight ratio, and total fat-to-body weight ratio

During four weeks of continuous administration, rat weight and other measurements were taken to compute the body fat percentage, Lee's index, liver-to-body weight ratio, and total fat-to-body weight ratio.

2.2.2 Measurement of fasting Plasma Glucose (FBG) in rats and evaluation of oral glucose tolerance testing (OGTT)

After the experiment was completed, the rats fasted overnight and a tail vein blood sample was taken to monitor fasting blood glucose levels (FBG) using a blood glucose meter. The rats were then given oral glucose (2.0 g/kg body weight) to evaluate oral glucose tolerance test (OGTT). Blood glucose levels were monitored at 0, 30, 60, 120, and 180 minutes after glucose administration.

2.2.3 Determination of the Effects of NPGS Meal Substitute on Serum Insulin Levels, Leptin, Serum Adiponectin, TC, TG, HDL, TNF-α and IL-6

Collecting cardiac blood from rats, serum samples were sent to the Red Flag Hospital for testing. Total cholesterol (TC), triglycerides (TG), and high-density lipoprotein (HDL) levels were measured in the serum. Insulin, leptin, adiponectin, interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and monocyte chemoattractant protein-1 (MCP-1) levels were also measured to evaluate NPGS meal substitute's effects on insulin resistance, lipid metabolism, and chronic low-level inflammation levels as well as MCP-1 levels in the serum of rats fed a high-fat diet.

3. Results

3.1 The Gastric Retention Time of NPGS Meal Substitute and Other Substitutes

As is shown in **Figure 1**, within 10 hours, the remaining amount of NPGS meal substitute was greater compared to ordinary substitute.

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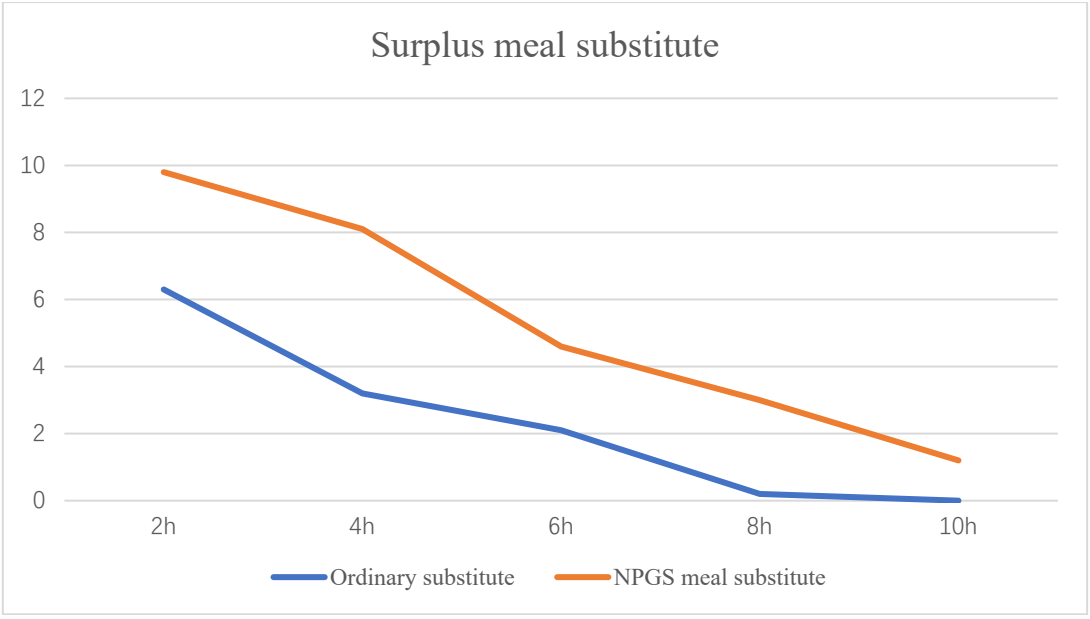

Figure 1: Residual amount of meal substitute in stomach at different time periods

3.2 Data of Lee's Index, Liver-to-Body Weight Ratio, Body Fat Percentage, and Total Fat-to-Body Weight Ratio in Rats

Table 1, Figure 1, Figure 2 and *Figure 3,* showed the effects of NPGS as a meal substitute on Lee's index, liver-to-body weight ratio, total fat-to-body weight ratio, and body fat percentage($\bar{x}$±s)n=10.

Lee's index: Compared to the saline group, the obesity group of rats had significantly higher data. Compared with the obesity model group, The NPGS group and the orlistat group were significantly lower than the obesity group.

Total fat-to-body weight ratio: Compared to the saline group, the obesity group had significantly higher data. Compared with the obesity model group, The NPGS group was significantly lower.

Body fat percentage: Compared to the blank control group, there was a significant difference in the obesity model group. The NPGS group was significantly different from the obesity group.

Liver-to-body weight ratio: The data from the four groups were similar, and there were no significant differences.

Table 1: Comparison of Lee's index, liver-to-body weight ratio, total fat-to-body weight ratio, and body fat percentage between groups

Groups	Lee's index	liver-to-body weight ratio	total fat-to-body weight ratio	Body fat percentage
Normal saline group	333.0±1.1	3.0±0.1	1.7±0.3	2.0±0.2
Obesity model group	350.1±0.2**	3.1±0.2	3.0±0.5**	4.2±0.2
Orlistat meal substitute group	331.3±0.5▲	2.8±0.2	2.4±0.2▲▲	2.6±0.4
NPGS meal substitute group	334.5±1.0▲	3.0±0.3	2.9±0.5▲	2.7±0.3

Note: Compared with the obesity model group, ▲P<0.05, compared with the obesity model group, ▲▲P<0.01.

Compared with the normal saline group, *P<0.05, compared with the normal saline group, **P<0.01.

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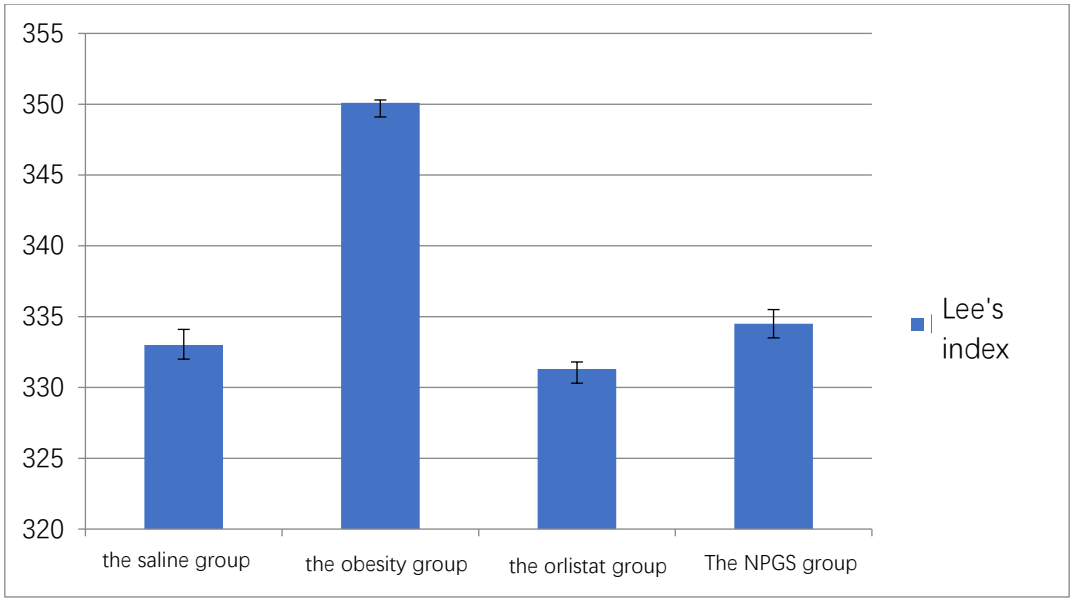

Figure 2: Comparison of Lee's index between groups

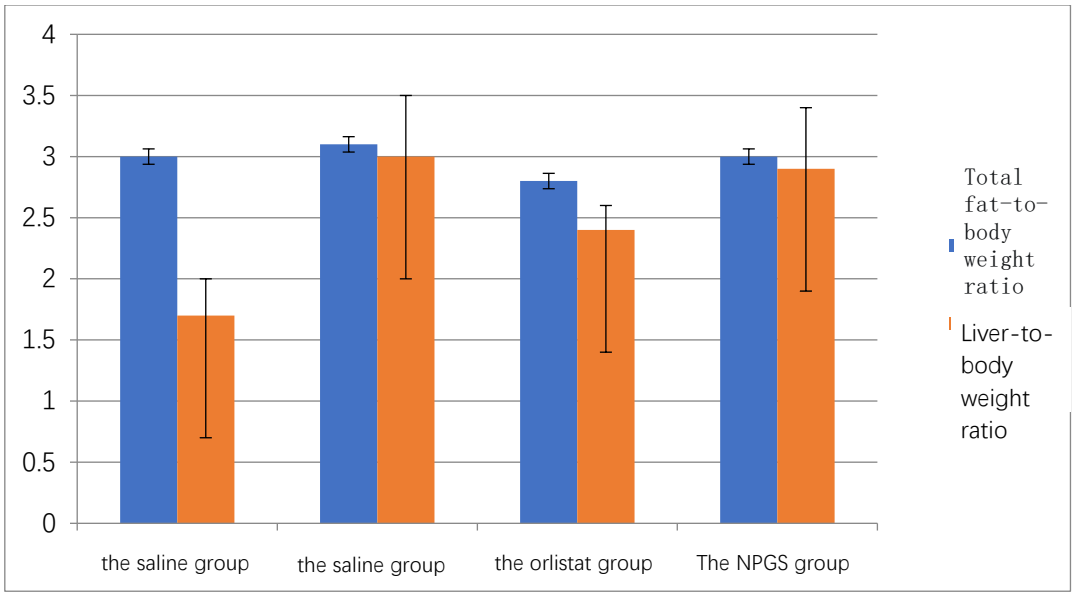

Figure 3: Comparison of liver-to-body weight ratio and total fat-to-body weight ratio between groups

3.3 Oral Glucose Tolerance Test (OGTT) and Fasting Plasma Glucose (FBG) of Rats

The effect of NPGS on glucose metabolism was evaluated. It can be seen from the statistical graph that after 1-4 weeks of NPGS dietary intervention, the FBG level of rats in the obesity model group was slightly decreased, but there was no statistical difference (Figure 4, $p>0.05$). Compared with the obesity model group, the blood glucose level in the NPGS meal substitute group was significantly reduced (Figure 5, $p<0.01$), indicating that the NPGS dietary intervention weakened the oral glucose tolerance of rats fed with high-fat diet.

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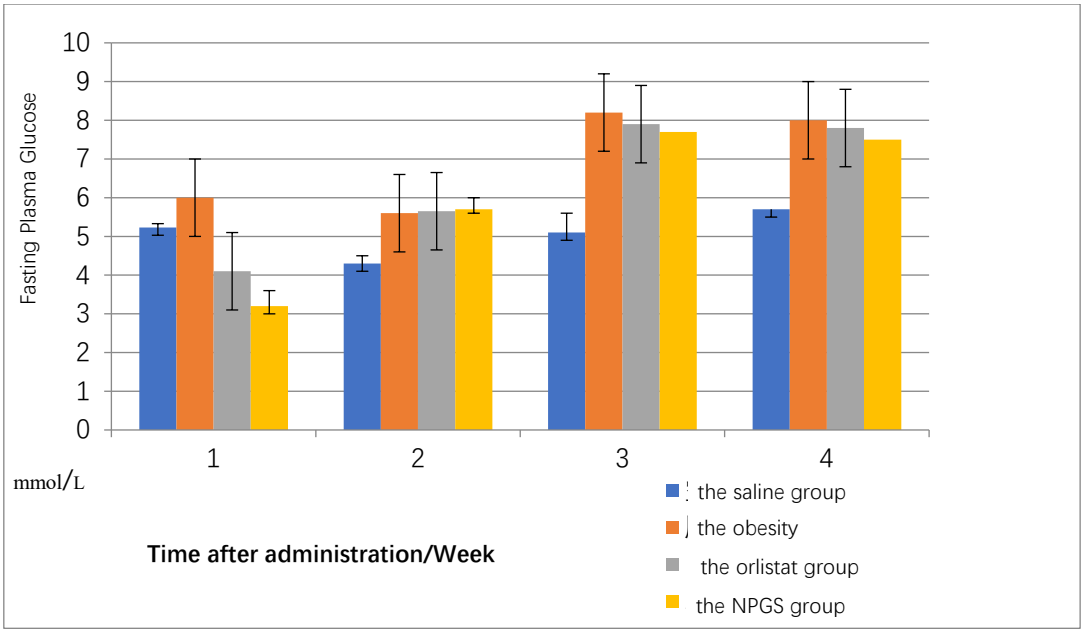

Figure 4: FBG levels in each group

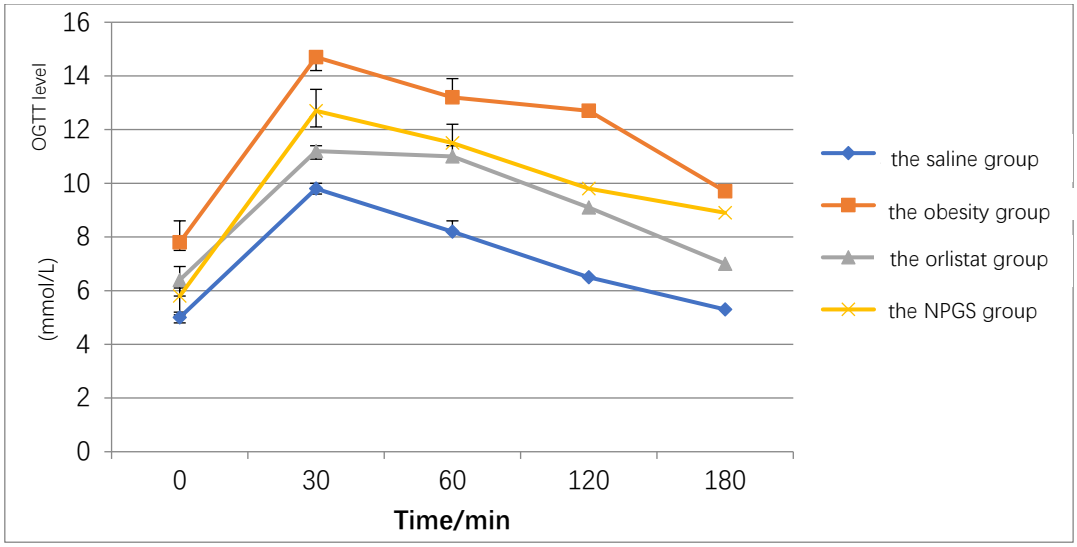

Figure 5: OGTT levels in each group

3.4 Detection of various indicators in rat serum

Table 2: The effects of rat TG, TC, and HDL (mmol/L) ($\bar{x}\pm s$) n=10

Groups	TC	TG	HDL
Normal saline group	1.44±0.18	0.86±0.24	0.92±0.14
Obesity model group	2.55±0.25**	2.63±0.66**	0.92±0.21
Orlistat meal substitute group	1.95±0.21▲	1.74±0.35▲▲	1.10±0.25
NPGS meal substitute group	2.12±0.43▲	2.11±0.42▲	1.08±0.14

Note: Compared with the obesity model group, ▲P<0.05, compared with the obesity model group, ▲▲P<0.01; compared with the normal saline group (i.e. the blank control group), **P<0.01.

NPGS intervention had no significant effect on serum insulin levels in rats (Table 2, Table 3,Figure 6 and Figure 7), but TC and TG levels significantly decreased. This indicates that NPGS intervention can improve insulin resistance in rats fed with high-fat diets. The evaluation of NPGS intervention on

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lipid metabolism is shown in Table 3. NPGS intervention increased adiponectin levels ($p<0.05$) and serum leptin levels ($p<0.01$). The effect of NPGS intervention on TC and LDL-C was most significant. Therefore, it could be concluded that NPGS intervention can alleviate hyperlipidemia in rats with high-fat diets.

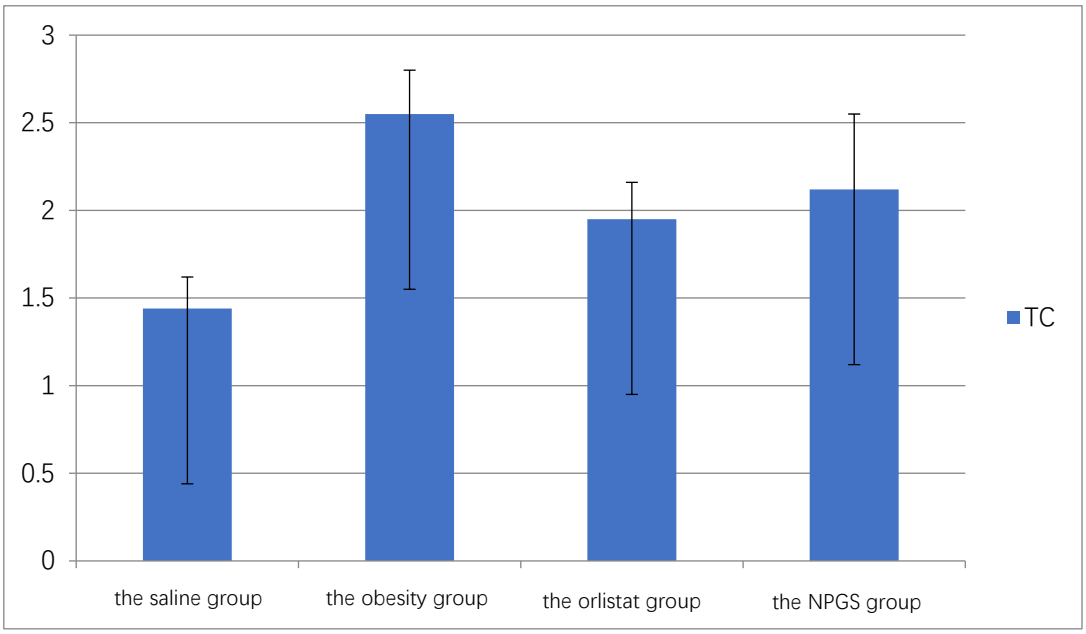

Figure 6: TC levels in each group

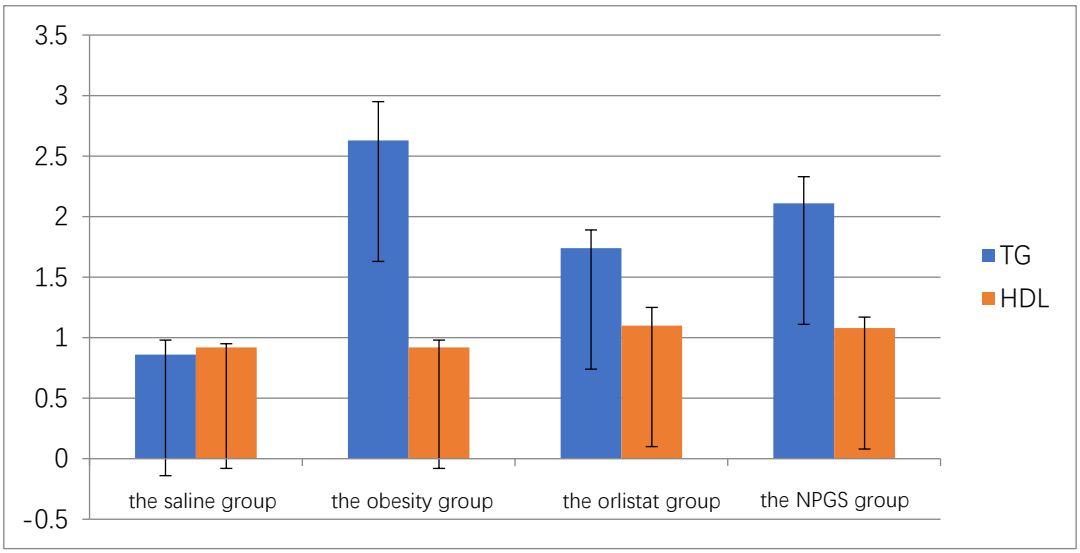

Figure 7: TG and HDL levels in each group

Table 3: Levels of insulin, leptin, adiponectin, IL-6, TNF-α, MCP-1 in rats Table 3 Effects of insulin, leptin, adiponectin, IL-6, TNF-α, and MCP-1 levels (mmol/L)

	Normal saline group	Obesity model group	Orlistat meal substitute group	NPGS meal substitute group
Lnsulin	6.21±1.53	17.21±2.90	13.56±2.87	15.65±3.02▲
Lleptin	22.89±4.22	58.56±7.43	47.76±5.98*	52.75±6.86**
Adiponectin	885.34±28.54	788.60±54.74	889.50±46.80**	804.45±54.33
IL-6	6.43±2.05	28.54±5.42	20.54±4.05▲▲	24.65±6.30**
TNF-α	17.88±4.53	80.42±8.41	61.89±13.03*	67.00±8.95▲▲
MCP-1	42.42±5.43	73.94±4.02	52.53±5.32▲▲	59.43±3.86**

Compared with the obesity model group, ▲P<0.05, compared with the obesity model group, ▲▲P<0.01; compared with the normal saline group (i.e. the blank control group), **P<0.01.

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4. Conclusion

This study showed that NPGS intervention can delay gastric retention time compared to regular meal substitute. It effectively reduced Lee's index, liver weight ratio, and total limb ratio in obese model SD rats. NPGS meal intervention also effectively weakened the oral glucose tolerance in rats fed with high-fat diets and improved insulin resistance. Furthermore, NPGS intervention significantly lowered serum TC and LDL-C levels in rats with hyperlipidemia. These findings demonstrate that NPGS intervention could slow down gastric metabolism rate, reduce body weight, and lower lipid levels.

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