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# Policaptil Gel Retard® reduces body weight and improves insulin sensitivity in obese subjects

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**PAPER**

## Abstract

Policaptil Gel Retard® (PGR), a natural fiber-based molecule, has been shown to prevent weight gain and ameliorate insulin-resistance indices in obese children and adolescents. The aim of this study was to compare the effects of 12 weeks of low calories and low glycemic index (LC-LGI) diet associated or not with the intake of PGR on anthropometric, bioimpedance, and metabolic parameters. Data from 20 obese adult subjects (10 per group) were analyzed. An LC-LGI diet with or without PGR intake reduced weight, BMI, and waist circumference. PGR intake elicited a reduction in fasting plasma insulin and insulin resistance index together with an improvement in insulin sensitivity.

*Keywords*: caloric intake; dietary fiber; glycemic index; Mediterranean diet; obesity

## Introduction

The World Health Organization (WHO) declared obesity as the largest global chronic health disease in adults (Frühbeck *et al*., 2013). Obesity is a metabolic disease (ICD-10 code), with epidemic proportions, becoming one of the leading causes of cardiovascular disease, disability, and death worldwide (Blüher, 2019).

Obesity is the result of individual behaviors and environmental factors leading to excessive caloric intake and inadequate physical activity. It is characterized by a pro-inflammatory milieu leading to hyperinsulinemia, hyperglycemia, and hyperlipidemia, which can foster insulin resistance and metabolic abnormalities (Ceriello, 2003; Finer, 2015; WHO, 2015).

Appropriate goals of weight management involve achieving a realistic weight loss (at least 5% of baseline body weight) to promote a reduction in health risks and should include, besides weight loss, weight maintenance and prevention of weight regain (Frühbeck *et al*., 2013).

To date, conventional treatment for obesity is based on nutritional therapy, low-calories and low-glycemic index (LC-LGI) diets, combined with regular physical activity.

Nevertheless, results of several clinical studies indicate that is not often feasible to achieve and maintain weight loss (Dwyer *et al*., 2000).

An elevated consumption of fibers slows down the absorption of carbohydrates, thus reducing the extent and the velocity of post-prandial blood glucose increase (Weickert and Pfeiffer, 2008).

For this reason, integrating an LC-LGI diet with the intake of natural fiber-based molecules, such as the polysaccharide complex PGR, might improve the success rate of dietary intervention.


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PGR is a patented complex of macromolecules produced by concentrating specific polysaccharide fractions obtained from: Cellulose, Opuntia Ficus indica, Amorphophallus Konjac, Althaea Officinalis, Linum Usitatissimum, Tilia Platyphyllos, and Cichorium Intybus.

PGR, with or without association with metformin, has been shown to prevent weight gain, and to ameliorate insulin-resistance indices, in obese children and adolescents (Stagi *et al*., 2016, 2017). Recently, it has been observed that a single intake of PGR is associated with a significant reduction in appetite, ghrelin, and triglycerides in the postprandial period in obese children (Fornari *et al*., 2020).

Guarino and coll. published results of a randomized controlled clinical trial showing that PGR supplementation and metformin have comparable effects in terms of glycemic control in obese adult subjects affected by metabolic syndrome (MS) or type 2 diabetes (T2D). Moreover PGR supplementation was associated with a greater serum lipid-lowering capacity and tolerability as compared to metformin (Guarino *et al*., 2021).

The aim of this study was to compare the effects of an LC-LGI diet plus PGR assumption versus an LC-LGI diet alone on anthropometric, bioimpedance, and metabolic parameters in obese adults.

## Materials and Methods

### *Study design and subjects*

This was a retrospective pilot single center study conducted at the Endocrine and Metabolic Disease Unit, Pescara Town Hospital, Italy.

Data of obese adults (Body Mass Index, BMI ≥ 30 kg/m$^2$; age ≥18 years) treated for at least 12 weeks with an LC-LGI diet with or without PGR in the period between 01/01/2016 and 31/12/2020 were retrospectively collected.

We excluded from analysis subjects with T2D, thyroid dysfunction, treated with medications associated with weight gain or weight loss, affected by genetic syndromes associated with obesity or by autoimmune, chronic, or systemic diseases.

Patient's data were anonymously extracted from an electronic medical record system (MyStar Connect/Smart Digital Clinic, Meteda Srl, San Benedetto del Tronto, Italy) and divided into two groups according to whether or not PGR was part of patients' treatment (LC-LGI diet plus PGR group/LC-LGI diet alone group).

Data relative to body weight, BMI, waist circumference, bioimpedance data, fasting plasma glucose (FPG), plasma insulinemia levels and insulin resistance index (Homeostatic Model Assessment for Insulin Resistance, HOMA-IR), and sensitivity index (Quantitative Insulin Sensitivity Check Index, QUICKI) before and after 12 weeks of treatment were collected.

The study was conducted in compliance with the Declaration of Helsinki and European Guidelines on Good Clinical Practice. Ethical approval (ethical code PE 08) was obtained from the Chieti and Pescara Provinces Ethics Committee.

### *Bioimpedance analysis and insulin sensitivity*

Bioimpedance analysis was performed using a BC-420 MA Class III body composition analyzer (Class III: compliant with the European Directive on medical devices) and the European NAWI standard relating to nonautomatic weighing instruments, Tanita, Tokyo, Japan. Body composition was evaluated by the instrument through a frequency of 50 kHz. The margin of error for the measurements performed corresponded to ±2%, which corresponds to a variation of approximately ±0.5% of the fat mass measurement in a standard figure (Esparza-Ros *et al*., 2019).

Insulin resistance (HOMA-IR) and sensitivity (QUICKI) indexes were calculated according to the following formulas as previously reported:

- HOMA-IR: FPG (expressed in mg/100 mL) × fasting insulin (expressed in μU/mL)/405 (Matthews *et al*., 1985);
- QUICKI: 1/(log (fasting insulin μU/mL) + log (FPG mg/dL.) (Katz *et al*., 2000).

### Dietary intervention

A personalized diet plan prescription was elaborated taking into consideration the subject's ideal body weight, lifestyle, eating habits, food preferences, and working shifts.

The energy intake was fixed by reducing by 25% the estimated caloric intake, which was calculated on the basis of food history and basal metabolism assessed by bioimpedance analysis.

The total amount of energy intake never fell below 1200 kcal per day.

The diet composition was formulated in compliance with the indications provided by the Italian Recommended Dietary Allowances (RADs) (SINU, 2019):

- carbohydrates 50–53 % kcal/day (<10% simple sugars);
- lipids 25–30 % kcal/day (<10% saturated fatty acids);
- protein 15–20 % kcal/day (about 0.9 g/kg/day);
- fibers at least 30 g/day.

The alimentary plan consisted of three main meals (breakfast, lunch, dinner) and one to three snacks (variable according to subject's habits) to avoid prolonged fasting between main meals (>5 h).

The low glycemic index was guaranteed by the presence of a balance among macronutrients and fibers. Moreover, dieticians strongly encouraged consumption of low glycemic index foods.

As per clinical practice, all subjects were encouraged to accumulate at least 30 min or more of moderate-intensity physical activity per day and underwent a follow-up visit every month to monitor weight changes, compliance with physical activity, diet and supplement prescribed for the entire duration of the treatment.

### PGR supplementation

PGR® is a patented complex of macromolecules produced by Aboca Spa Company (Sansepolcro, Arezzo, Italy). This complex contains specific polysaccharide fractions obtained from: Cellulose, Opuntia Ficus indica, glucomannan (Amorphophallus konjac), Althaea officinalis, Linum usitatissimum, Tilia platyphyllos, and Cichorium intybus.

The PGR group patients consumed three PGR tablets with a large glass of water before their two main meals for a period of at least 12 weeks.

### Statistical analysis

Variables distribution normality was checked using the Shapiro–Wilk test. Normally distributed data are shown as mean values ± standard deviation (SD), while data with nonnormal distribution are presented as median values and interquartile ranges.

Since the distributions of most of the quantitative variables were significantly different from the normal distribution (Shapiro-Wilk test), nonparametric tests were used. The Wilcoxon signed rank test was used to compare baseline and follow-up parameters within the study group. The Mann Whitney U test was used to compare differences between independent groups. Differences with $P < 0.05$ were considered statistically significant.

Statistical analysis was performed using the statistical software package Stata (version 16.1, StataCorp, 4905 Lakeway Drive, College Station, TX, USA).

## Results

### Baseline characteristics

The primary demographic, clinical, and biochemical characteristics of the two study groups are shown in Table 1. All baseline characteristics were similar in both groups.

### *Effects of 12-week intervention of* an *LC-LGI diet versus* an *LC-LGI diet plus PGR*

*Anthropometric measurements*

After 12 weeks of intervention, there was a significant reduction in body weight, BMI, and waist circumference both in patients following an LC-LGI alone diet and in those on an LC-LGI diet plus PGR, as shown in Figure 1 and Table 2. The magnitude of the intervention effects on these parameters was not different between the two groups (Table 2).

*Body composition variables*

The effects of an LC-LGI diet and an LC-LGI diet plus PGR on body composition measurements are shown in

**Table 1. Baseline demographic, clinical, and biochemical characteristics of the two study groups.**

| Parameters | LC-LGI diet (n = 10) | LC-LGI diet plus PGR (n = 10) | P value |
|---|---|---|---|
| Age (years) | 54.5 ± 26 | 59.5 ± 11 | ns |
| Gender (M/F) | 2/10 | 4/6 | ns |
| Height (cm) | 160 ± 14 | 165 ± 5 | ns |
| Weight (kg) | 90.8 ± 12.5 | 97.1 ± 20.1 | ns |
| BMI (kg/m2) | 35.6 ± 8.9 | 36.7 ± 6.6 | ns |
| WC (cm) | 115.5 ± 29 | 111 ± 8.5 | ns |
| FM (kg) | 37.8 ± 10.4 | 45.3 ± 11.3 | ns |
| FFM (kg) | 50.9 ± 22.7 | 53.7 ± 10.1 | ns |
| MM (kg) | 48.3 ± 21.6 | 51 ± 9.9 | ns |
| TBW (L) | 36 ± 1.5 | 38.5 ± 7.7 | ns |
| FPG (mg/dL) | 95.5 ± 13 | 102.5 ± 10 | ns |
| Fasting Insulin (µU/mL) | 18.5 ± 8 | 14.7 ± 7.8 | ns |
| HOMA-IR | 4.5 ± 2.8 | 3.7.4 ± 1.9 | ns |
| QUICKI | 0.31 ± 0.03 | 0.31 ± 0.02 | ns |
| PGR (weeks) | – | 13 ± 1 | – |

Data shown as medians ± IQR. Abbreviations: IQR, interquartile range; LC-LGI, low-calorie and low-glycemic index; PGR, Policaptil Gel Retard; ns, not significant; BMI, body mass index; WC, waist circumference; FM, fat mass; FFM, fat free mass; MM, muscle mass; TBW, total body water; FPG, fasting plasma glucose; HOMA-IR, homeostatic model assessment for insulin resistance; QUICKI, quantitative insulin-sensitivity check index.

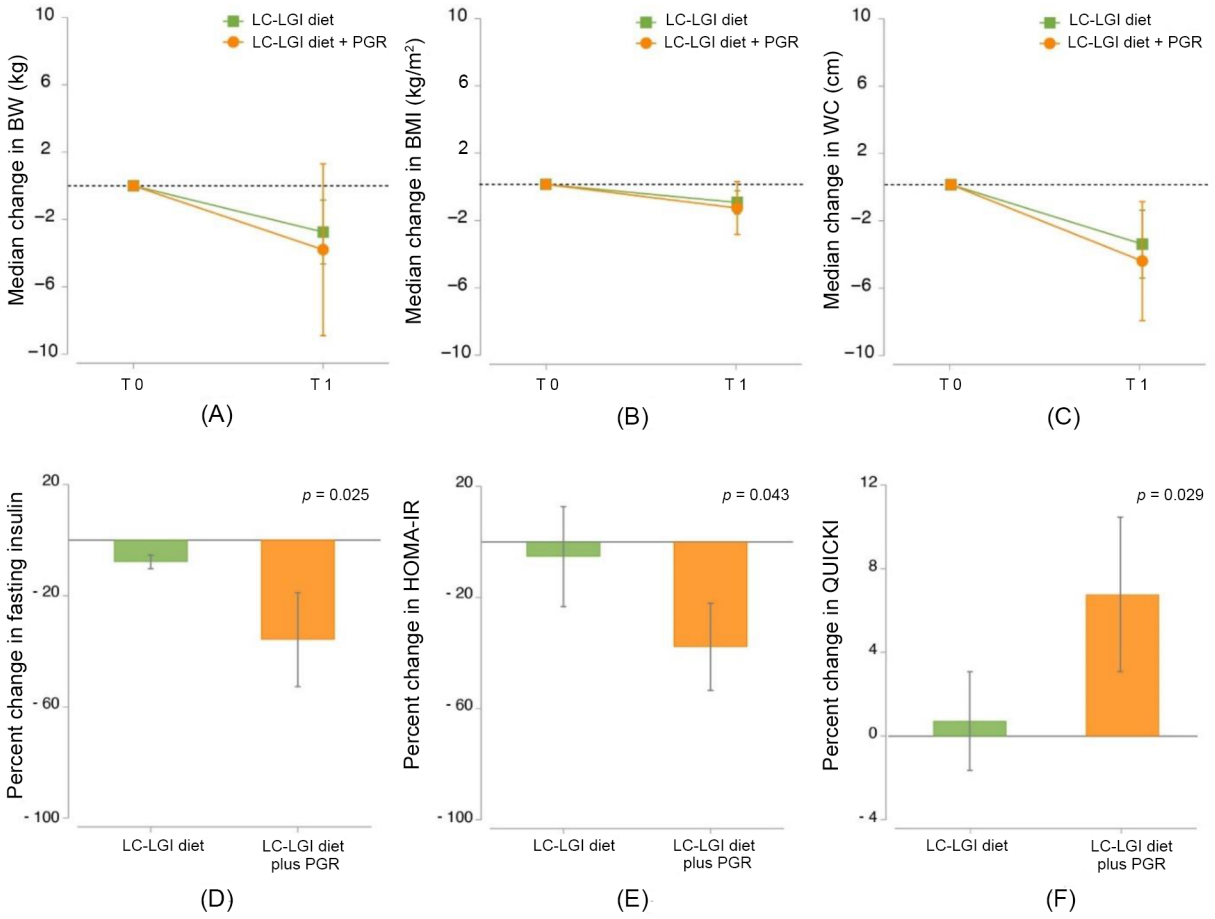


**Figure 1. Median change from baseline (T0) in (A) body weight (BW), (B) body mass index (BMI), and (C) waist circumference (WC) to 12 weeks (T1) in obese subjects treated with an LC-LGI diet or an LC-LGI diet plus PGR. Change in (D) fasting insulin, (E) HOMA-IR, and (f) QUICKI after 12-week intervention of an LC-LGI diet versus an LC-LGI diet plus PGR.**

Table 2. Fat mass (FM) and muscle mass (MM) slightly decreased after 12 weeks in the LC-LGI group. However, the difference between the two study groups with respect to FM, fat free mass (FFM), and MM loss was not statistically significant. There was no change in Total Body Water (TBW) in the study subjects (Table 2).

*Metabolic profile*

FPG did not change after 12 weeks of intervention in both study groups.

Compared to an LC-LGI diet, the LC-LGI diet plus PGR elicited a greater decrease in fasting insulin (–1.5 ± 1 vs –5.8 ± 4.3, P = 0.025, Table 2) and HOMA-IR index (–0.2 ± 0.9 vs –1.5 ± 1, P = 0.043, Table 2), with a percent change from baseline of –36 % and –37 %, respectively (Figure 1d and 1e).

QUICKI was significantly ameliorated in an LC-LGI plus PGR group (0.31 ± 0.02 vs 0.33 ± 0.02, P < 0.001, Table 2) with an increase of 7.1 % (Figure1f) but not in LGI group. The difference between the two study groups with respect to QUICKI was statistically significant (P = 0.029), as shown in Table 2.

## Discussion

This retrospective pilot study shows that while an LC-LGI diet both with or without PGR intake reduce, as expected, weight, BMI, and waist circumference, as compared to the diet only intervention, 12 weeks of PGR intake induce a significant improvement in insulin circulating levels, in insulin resistance calculated by HOMA-IR index, as well as in insulin sensitivity calculated according to QUICKI.

These effects of PGR may be related to a reduction in the post meal glycemic and insulinemic peaks as suggested by Stagi and collaborators who demonstrated an amelioration of HOMA-IR in obese children and adolescents after 1 year of PGR intake (Stagi *et al*., 2016, 2017). Moreover, Greco and colleagues recently observed an improvement

**Table 2. Comparison of differences between baseline and 12 weeks in anthropometric, body composition, and metabolic parameters between the LC-LGI diet and LC-LGI plus PGR groups.**

| Parameters | LC-LGI diet | | | LC-LGI plus PGR | | | LC-LGI vs LC-LGI plus PGR |
|---|---|---|---|---|---|---|---|
| | Baseline (T0) | Follow-up (T1) | Change (ΔT0-T1) | Baseline (T0) | Follow-up (T1) | Change (ΔT0-T1) | P value |
| Weight (kg) | 90.8 ± 12.5 | 88.3 ± 9.5 | −2.8 ± 1.9* | 97.1 ± 20.1 | 92.8 ± 22.6 | −3.8 ± 5.1** | 0.393 |
| BMI (kg/m2) | 35.6 ± 8.9 | 33.8 ± 9.5 | −1.1 ± 0.7* | 36.7 ± 6.6 | 36.1 ± 8.1 | −1.4 ± 1.6** | 0.413 |
| WC (cm) | 115.5 ± 29 | 111 ± 28 | −3.5 ± 2* | 111 ± 8.5 | 105.5 ± 9 | −4.5 ± 3.5** | 0.518 |
| FM (kg) | 37.8 ± 10.4 | 36.3 ± 9.4 | −1.5 ± 1* | 45.3 ± 11.3 | 45.4 ± 12.5 | −1.6 ± 3.8 | 0.837 |
| FFM (kg) | 50.9 ± 22.7 | 50.7 ± 22.4 | −1 ± 0.3 | 53.7 ± 10.1 | 49.5 ± 10.8 | −1.5 ± 2.8 | 0.517 |
| MM (kg) | 48.3 ± 21.6 | 47.8 ± 21.5 | −0.6 ± 0.1* | 51 ± 9.9 | 49.3 ± 10.6 | −1 ± 2.35 | 0.731 |
| TBW (L) | 36 ± 1.5 | 35.5 ± 2.5 | −0.5 ± 0.3 | 38.5 ± 7.7 | 37.5 ± 9.3 | −0.25 ± 1.9 | 0.865 |
| FPG (mg/dL) | 95.5 ± 13 | 91 ± 22 | 2.5 ± 10 | 102.5 ± 10 | 95.5 ± 11.5 | −5 ± 12.5 | 0.402 |
| Insulinemia (μU/mL) | 18.5 ± 8 | 19 ± 11 | −1.5 ± 1 | 14.7 ± 7.8 | 9.3 ± 3.3 | −5.8 ± 4.3** | ***0.025*** |
| HOMA-IR | 4.5 ± 2.8 | 4.5 ± 3.6 | −0.2 ± 0.9 | 3.7.4 ± 1.9 | 2.3 ± 0.8 | −1.5 ± 1** | ***0.043*** |
| QUICKI | 0.31 ± 0.03 | 0.31 ± 0.04 | 0.00 ± 0.01 | 0.31 ± 0.02 | 0.33 ± 0.02 | 0.02 ± 0.01** | ***0.029*** |

Data are shown as medians ± IQR. Wilcoxon signed rank test was used for intragroup comparisons (baseline vs follow-up). For intergroup analyses (LC-LGI diet vs LC-LGI plus PGR) the Mann Whitney U test for independent groups was applied. *P < 0.05; **P < 0.001. Abbreviations: IQR, interquartile range; LC-LGI, low-calorie and low-glycemic index; PGR, Policaptil Gel Retard; BMI, body mass index; WC, waist circumference; FM, fat mass; FFM, fat free mass; MM, muscle mass; TBW, total body water; FPG, fasting plasma glucose; HOMA-IR, homeostatic model assessment for insulin resistance; QUICKI, quantitative insulin-sensitivity check index.

of parameters defining metabolic syndrome in a mouse model fed with high-fat diet treated with PGR (Greco *et al.*, 2020).

Similar results were obtained by Guarino and colleagues in adults in whom PGR supplementation induced a better effect on serum lipid and tolerability as compared to metformin (Guarino *et al.*, 2021).

It is worth noting that in our study, similar observation has been made in a clinical setting, without the "trial effect," thus confirming the potential effectiveness of PGR as a valid clinical tool in obesity management.

Insulin resistance and hyperglycemia are known risk factors of cardiovascular disease (Laakso and Kuusisto, 2014). Therefore, a treatment that improves insulin action leading to a considerable amelioration of metabolic profile in obese subjects could represent an efficacious strategy in the prevention of cardiovascular disease.

The small sample size is the main limitation of our study. Furthermore, even if our short observation period suggests an effect of PGR in improving the carbohydrate metabolism, we cannot exclude a concomitant effect given by the weight loss obtained through an LC-LGI diet. A randomized placebo-controlled study would be useful to better single out the effects of this macromolecular complex.

For all these reasons, further studies with suitable study design on larger samples with a longer follow-up period are needed to confirm our preliminary results.

## Conclusions

PGR associated with a low calorie and low glycemic index diet may be useful to reduce body weight and improve insulin sensitivity in adult subjects affected by obesity.

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