Effects of Gelesis200, an oral superabsorbent hydrogel, on postprandial insulin response in people with prediabetes: an analysis of the LIGHT-UP study

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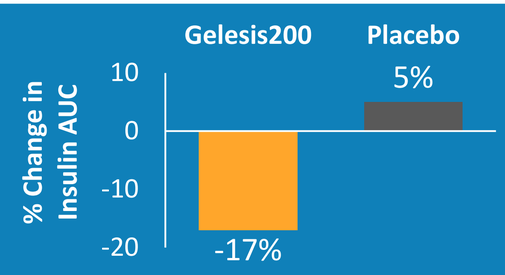
Administration of GS200 in people with prediabetes significantly improved postprandial insulin secretion independently of weight loss.



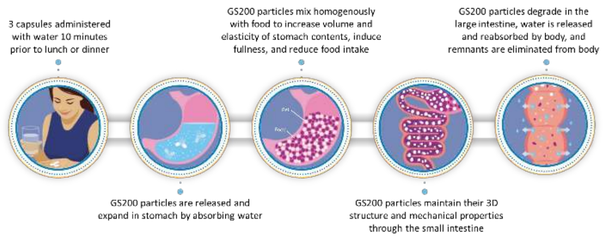
INTRODUCTION

- Postprandial hyperinsulinemia is associated with beta cell dysfunction and development of type 2 diabetes.
- GS200 is an investigational, non-systemic, oral superabsorbent hydrogel synthesized from modified cellulose to form a 3-dimensional matrix capable of holding large amounts of water in the gastrointestinal tract, with composition and firmness similar to raw vegetables. GS200 is taken as 3 capsules (2.10 g) prior to lunch and dinner and is designed to induce satiation and reduce food intake (Figure 1).
- LIGHT-UP (NCT03058029) was a randomized controlled trial to assess the effects of GS200 in people with a body mass index (BMI) of 27-40 kg/m^2 and prediabetes or type 2 diabetes.
- Within LIGHT-UP, changes in fasting insulin were evaluated as a secondary endpoint and changes in post-prandial insulin as an exploratory endpoint. This presentation focuses on these insulin-related analyses.

METHODS

- The LIGHT-UP study was conducted over 25 weeks in 254 participants with prediabetes or type 2 diabetes and a BMI of 27-40 kg/m^2. At study end, mean weight loss was 7.1% for GS200 vs. 4.6% for placebo (*P*=0.003).
- Fasting serum insulin (FSI) was measured in participants throughout the study.
- Participants with prediabetes, but not those with diabetes, completed a 2-hr oral glucose tolerance test (OGTT) at baseline and study end. Plasma glucose and serum insulin were measured at 15–30-minute intervals until 120 minutes following OGTT.
- Changes in FSI were analyzed from baseline to study end (Week 25) as a secondary endpoint in participants with baseline FSI ≥10 µU/mL using a repeated measures mixed model with outliers removed.
- Area under the curve (AUC) was calculated using the trapezoidal method and differences were assessed using ANCOVA model with weight loss as a covariate.

Figure 1: Gelesis200 hydrogel in the gastrointestinal tract.

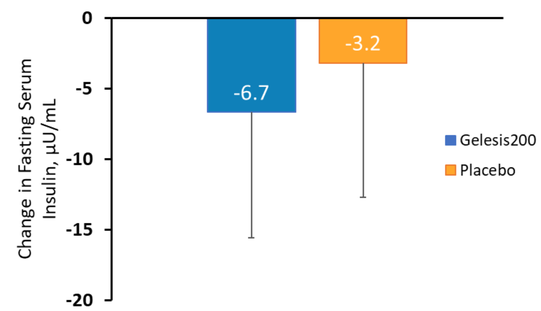


RESULTS

FASTING INSULIN

- Mean baseline FSI was 20.4±7.3 µU/mL for GS200 and 19.4±7.0 µU/mL for placebo.
- At study end, participants randomized to GS200 had significantly greater reductions in FSI compared to placebo (-26.0% vs. -9.1%; *P*=0.05).

Figure 2: Change in fasting serum insulin from baseline to study end.



POSTPRANDIAL INSULIN

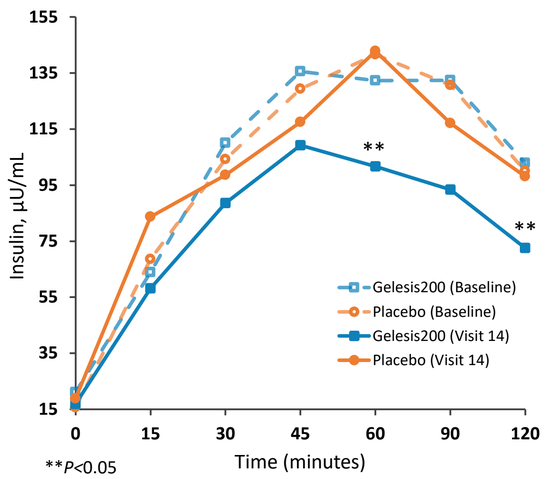
- Baseline statistics for participants with prediabetes that completed the baseline and Week 25 2-hr OGTT are in Table 1. Participants were 59.5% female, aged 47.1±11.7 years, with a fasting glucose of 104.6±10.4 mg/dL.
- Baseline insulin AUC$_{0\text{-}120}$ was similar for both groups (13006±6895 µU/mL for GS200 and 13234±8269 µU/mL for placebo).

Table 1: Baseline demographics and glycemic parameters for the LIGHT-UP prediabetes OGTT cohort.

Parameter	Gelesis200 (*n* = 42)	Placebo (*n* = 42)
Age, years	46.4±11.9	47.8±11.6
Female	61.9% (26/42)	57.1% (24/42)
Fasting Glucose, mg/dL	106.6±10.5	102.7±10.0
HbA1c, %	5.5±0.4	5.4±0.4
HOMA-IR	5.4±3.1	3.9±2.6
Insulin AUC$_{0\text{-}120}$, µU/mL	13006±6895	13234±8269
Glucose AUC$_{0\text{-}120}$, mg/dL	18806±4273	17257±3233

- At Week 25, insulin AUC$_{0\text{-}120}$ was significantly lower for participants on GS200 (10299±4653 µU/mL) compared to placebo (13036±9484 µU/mL), a mean difference of -22.0±10.5%, *P*=0.04 (Figure 3).
- Participants on GS200 had a greater reduction in postprandial insulin during OGTT at T$_{60}$ (-35.0±13.1 vs. -1.5±12.8 µU/mL for placebo, *P*=0.05) and T$_{120}$ (-30.9±11.6 vs. 0.5±11.4 µU/mL for placebo, *P*=0.04).
- Participants on GS200 also had a greater reduction in insulin C$_{max}$ vs. placebo (mean difference: -47.3±21.1 µU/mL, *P*=0.03).

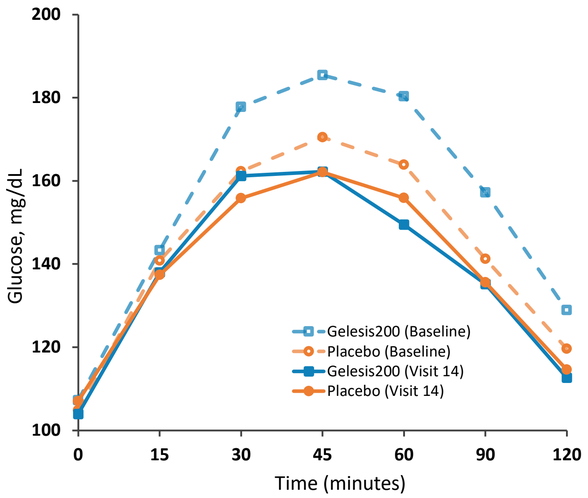
Figure 3: Changes in postprandial insulin for GS200 and placebo.



**P<0.05

- Changes in glucose AUC$_{0\text{-}120}$ were not significantly different between GS200 and placebo (-1420±444 mg/dL vs. -881±439 mg/dL, respectively) (Figure 4).
- HOMA-IR decreased by 0.3±0.9 for GS200 and increased by 0.9±0.9 for placebo, a mean difference of -1.2±1.3, however this was not statistically significant.

Figure 4: Changes in postprandial glucose for GS200 and placebo.



CONCLUSIONS

- In participants with prediabetes or type 2 diabetes, administration of GS200 significantly reduced fasting serum insulin compared to placebo.
- Administration of GS200 in participants with prediabetes significantly improved postprandial insulin secretion independently of weight loss.
- These findings suggest that GS200 may impact the progression of prediabetes to type 2 diabetes and may favorably impact metabolic syndrome, however further studies are needed.

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