Satiety And Glycemic Control Enhancing Properties Vary Between Functional Fibers, Mixed Salad, And A Novel Hydrogel (Gelesis100)


Gelesis, Boston MA, USA

INTRODUCTION

• The importance of fruits, vegetables, and wholegrains as part of a healthy diet is well documented, in part because of their abundance of naturally occurring dietary fibers. Demonstrated benefits of dietary fibers relevant to the management of overweight and obesity include reduced appetite and energy intake, prolonged absorption of nutrients, and reduced body weight.¹

• Ingestion of functional fibers and high-viscosity polysaccharides has been employed as a strategy to improve glycemic control, suppress appetite, and facilitate weight loss in patients with increased cardiometabolic risk.
  – Prospective studies suggest that consumption of fibers with higher viscoelastic properties were 2-4 fold more effective at reducing appetite and energy intake than fibers with lower viscoelastic properties.¹

• Superabsorbent hydrogels are three-dimensional cross-linked polymer networks capable of absorbing much larger quantities of fluids compared to linear structures of functional fibers, thus resulting in more rigid, elastic gel particles (Figure 1). Hydrogel technologies have been employed for a variety of therapeutic uses such as tissue engineering and enhanced drug delivery.

• Gelesis100 is a novel orally-administered, non-systemic hydrogel comprising a matrix of modified cellulose cross-linked with citric acid (both commonly used in foods; Figure 2) that is designed to mimic the three-dimensional structure of naturally occurring dietary fibers in vegetables.

• The purpose of this study was to compare the viscoelastic properties of Gelesis100, which is currently in clinical development for weight loss and glycemic control, versus common processed functional fibers and vegetables rich with natural fibers.

Figure 1: Comparison of superabsorbent hydrogels and linear processed functional fibers.
Figure 2: Gelesis100 is composed of modified cellulose (carboxymethylcellulose) and citric acid, both found in common foods.

METHODS

- Processed functional fibers (psyllium, guar gum, and glucomannan) and Gelesis100 were pre-hydrated in simulated gastric fluid (SGF)/H₂O 1:8 (V/V) media in a 1:160 (w/V) ratio, and vegetables (mixed salad greens, cucumbers) were subjected to mechanical mastication and then poured in SGF/H₂O 1:8 (V/V) solution in the same amount.

- Ten grams of hydrated and/or masticated samples were subjected to serial in vitro digestion in simulated gastric, small intestine, and colonic fluids (as described in Table 1) for 30-180 min each at 37°C in a glass beaker under mild mechanical mixing. Remnants of digested samples were poured onto an AERS rotational rheometer (TA Instruments) equipped with parallel plates (cross hatched configuration) for determination of elastic modulus (G') in triplicate.

Table 1: Composition of simulated gastrointestinal fluids.

<table>
<thead>
<tr>
<th>Simulated Fluid</th>
<th>Composition per 1,000 mL</th>
<th>Approximate pH</th>
<th>Digestion Time (min)</th>
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</thead>
<tbody>
<tr>
<td>Gastric (SGF)</td>
<td></td>
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<tr>
<td>1/8X</td>
<td>0.25 g NaCl, 0.4 g pepsin</td>
<td>-2.1</td>
<td>30</td>
</tr>
<tr>
<td>1/4X</td>
<td>0.5 g NaCl, 0.8 g pepsin</td>
<td>-1.8</td>
<td>90</td>
</tr>
<tr>
<td>1X</td>
<td>2.0 g NaCl, 3.2 g pepsin</td>
<td>-1.2</td>
<td>60</td>
</tr>
<tr>
<td>Small Intestine (SIF)</td>
<td>6.8 g KH₂PO₄, 10.0 g pancreatin (trypsin, amylase, lipase, ribonuclease, protease)</td>
<td>-6.8</td>
<td>120</td>
</tr>
<tr>
<td>Colonic (SCF)</td>
<td>6.8 g KH₂PO₄, 10.0 g pectinase</td>
<td>-6.8</td>
<td>30</td>
</tr>
</tbody>
</table>
RESULTS

- **Gelesis100 vs. Processed Functional Fibers (Figure 3A and Figure 4)**
  - Throughout 180 min digestion in SGF, the G’ of Gelesis100 (range: $594 \pm 20$ to $950 \pm 10$ Pa) was maintained orders of magnitude higher than glucomannan (range: $27 \pm 2$ to $49 \pm 3$ Pa), which had the highest elastic modulus of any functional fiber tested.
  - This pattern was maintained during 120 min digestion in SIF (range: $257 \pm 3$ to $302 \pm 5$ Pa for Gelesis100 versus $42 \pm 2$ to $50 \pm 4$ Pa for glucomannan).
  - While G’ of glucomannan and guar gum were maintained during a final 30 min digestion in SCF, Gelesis100 lost its elastic modulus ($G' \sim 1$).

- **Gelesis100 vs. Vegetables (Figure 3B and Figure 4)**
  - Throughout digestion in SGF and SIF the G’ pattern of Gelesis100 (range: $257 \pm 3$ to $950 \pm 10$ Pa) was remarkably consistent with that of masticated mixed salad greens (range: $105 \pm 11$ to $2,074 \pm 101$ Pa) and cucumber (range: $72 \pm 11$ to $6,493 \pm 200$ Pa), and all three lost their elastic moduli in SCF.

Figure 3: Comparison of elastic modulus between Gelesis100 and processed functional fibers (panel A) and vegetables (panel B). Data presented as log-transformed G’ values in pascals.

Figure 4: Visual comparison of Gelesis100, processed functional fibers, and vegetables following hydration or mastication.
Although it has been long established that weight loss of 5 to 10% can lower the risk of weight-related comorbidities, realization of this benefit from dieting is frequently derailed by biologic feedback mechanisms that stimulate appetite, reduce dietary compliance, and ultimately lead to a rebound of energy intake and weight gain. Consequently, this has prompted efforts to understand how and to what extent eating behavior, digestion and metabolism are influenced by the rheological properties of food and/or food additives, in addition to their inherent caloric value and macronutrient composition. Several properties of natural fibers, including viscosity and elasticity, appear to confer benefits of appetite control and weight loss. However, less than 3% of individuals in the United States consume recommended amounts. Thus, efforts to compensate for inadequate dietary intake include supplementation with processed functional fibers which have linear structures and lower viscoelastic properties.

In this in vitro model of GI digestion, Gelesis demonstrated viscoelastic profiles that were orders of magnitude superior to that of common processed functional fiber supplements (psyllium, guar gum and glucomannan), and were remarkably similar to the profiles of the masticated vegetables tested. This latter observation is consistent with the components and structure of the hydrogels (Figure 1), which when hydrated in the GI system, results in individual gel particles that are fluid-containing 3D cellulosic matrices, akin to plant cells.

Increasing the elasticity of ingested meals has been shown to increase feelings of fullness in humans. Similarly, acute dosing of Gelesis100 in humans increased subjective feelings of satiety and decreased feelings of hunger in subjects who were overweight and had obesity, and chronic dosing of Gelesis100 elicited weight loss and improved glycemic control. The data observed in this study provides in vitro mechanistic evidence for these phenomena in humans, and suggests that Gelesis100 may elicit sensations of satiety and fullness by mimicking the physical properties of ingested vegetables.

In this in vitro model of GI digestion, Gelesis100 demonstrated viscoelastic profiles that were similar to masticated vegetables, and were orders of magnitude superior to that of common processed functional fiber supplements. These data provide evidence that Gelesis100 mimics the physical properties of ingested vegetables, which may in turn confer satiety-inducing, weight-loss, and glycemic-control benefits to patients with obesity or diabetes.

REFERENCES