# ATTIVA, A NOVEL SUPERABSORBENT BIODEGRADABLE HYDROGEL, INCREASES THE FEELING OF SATIETY IN HUMANS

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## INTRODUCTION

Obesity (body mass index (BMI) ≥ 30) is becoming a major global health problem. It is estimated that over 310 million subjects worldwide are obese.

Treatment of obesity includes hypocaloric diet, exercise, behavior modification, drug therapy, intragastric balloon, and bariatric surgery. The therapeutic benefit of all currently available anti-obesity tools is limited by their marginal efficacy and variable tolerability and safety profiles.

A need exists for a product that is able to reduce stomach volume in a manner comparable to bariatric surgery or intragastric balloon, but with a risk-benefit profile acceptable to the entire population of obese subjects. By reducing stomach volume, a novel treatment could have the same efficacy as bariatric surgery without the associated surgical morbidities and mortality.

Attiva is a novel superabsorbent biodegradable hydrogel obtained from cellulose derivatives (food-grade materials).

Attiva was invented by Dr. Alessandro Sannino (University of Salento, Lecce, Italy) together with Dr. Luigi Ambrosio (National Research Council of Italy, Naples, Italy) and Dr. Luigi Nicolais (University of Naples, Naples, Italy).

Attiva is able to swell in the stomach and the small intestine in the presence of water and gastrointestinal fluids. By occupying the gastric and intestinal cavities and by delaying gastric emptying, Attiva can induce a feeling of satiety that lasts until the hydrogel is degraded in the colon and expelled in the feces (**Figure 1**).

**Figure 1.** Physical properties of Attiva.

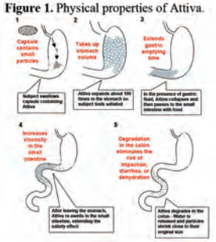



**Figure 2.** First meal effect: Placebo-adjusted change in satiety scores (%) at 30 and 60 minutes after breakfast, lunch, and dinner, with Attiva.

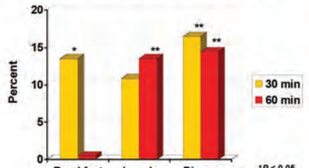
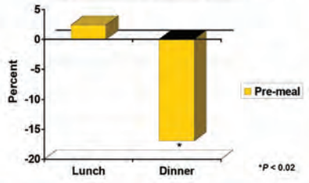



**Figure 3.** Second meal effect: Placebo-adjusted change in hunger score (%) before lunch and dinner, with Attiva administered before breakfast and lunch.




## OBJECTIVE

The aim of this study was to assess the effects of a single administration of Attiva on satiety and hunger in humans.

## SUBJECTS

Ninety-five subjects were studied (**Table 1**).

**Table 1.** Clinical characteristics of the 95 study subjects.

| Gender (number) | | Age (years) | | BMI* | |
|---|---|---|---|---|---|
| Male | Female | Mean ± SD | Range | Mean ± SD | Range |
| 22 | 73 | 41 ± 12 | 19-67 | 31.1 ± 7.5 | 18.0-55.9 |

*Twenty-one subjects had normal (or subnormal) BMI, 22 were overweight, and 52 were obese.

The study was conducted by Drs. Roberto Tacchino and Serena Marchisella (Gemelli Hospital, Rome, Italy).

## METHODS

Study subjects were randomly divided into 3 groups (Groups A, B, and C) and received 2 g of Attiva (5 oral capsules) versus placebo before breakfast, lunch, and dinner, in a double-blind, cross-over fashion. There was a 3-day interval between each administration of Attiva for each subject (**Table 2**).

**Table 2.** Study design.

| Meal | Day 1 | Day 4 | Day 7 |
|---|---|---|---|
| Breakfast | Group A (*Attiva*) | Group A (*Placebo*) | Group A (*Placebo*) |
| | Group B (*Placebo*) | Group B (*Attiva*) | Group B (*Placebo*) |
| | Group C (*Placebo*) | Group C (*Placebo*) | Group C (*Attiva*) |
| Lunch | Group A (*Placebo*) | Group A (*Placebo*) | Group A (*Attiva*) |
| | Group B (*Attiva*) | Group B (*Placebo*) | Group B (*Placebo*) |
| | Group C (*Placebo*) | Group C (*Attiva*) | Group C (*Placebo*) |
| Dinner | Group A (*Placebo*) | Group A (*Attiva*) | Group A (*Placebo*) |
| | Group B (*Placebo*) | Group B (*Placebo*) | Group B (*Attiva*) |
| | Group C (*Attiva*) | Group C (*Placebo*) | Group C (*Placebo*) |

For each subject, meals consisted of habitual intake and were consumed at home.

Satiety was assessed using a self-administered questionnaire immediately, and 30 and 60 minutes after meal. The questionnaire included 5 options to score the feeling of satiety: not at all (score 0), a little (score 1), enough (score 2), very (score 3), and very much (score 4).

Hunger was assessed using the same type of questionnaire before meal.

Symptoms that occurred during the study were recorded through a questionnaire. Statistical analysis was performed with a paired t-test.

## RESULTS

Attiva significantly increased the feeling of satiety at 30 minutes after breakfast and dinner (**Table 3**), and at 60 minutes after lunch and dinner (**Table 4**).

**Table 3.** Satiety scores (mean ± SD) at 30 minutes post-meal.

| Meal | Attiva | Placebo | *P* value |
|---|---|---|---|
| Breakfast | 1.85 ± 0.93 | 1.63 ± 0.95 | 0.037 |
| Lunch | 1.84 ± 1.14 | 1.66 ± 0.87 | 0.071 |
| Dinner | 1.98 ± 0.97 | 1.70 ± 1.01 | 0.004 |

**Table 4.** Satiety scores (mean ± SD) at 60 minutes post-meal.

| Meal | Attiva | Placebo | *P* value |
|---|---|---|---|
| Breakfast | 2.13 ± 1.00 | 2.12 ± 0.83 | 0.960 |
| Lunch | 2.35 ± 1.06 | 2.07 ± 0.86 | 0.007 |
| Dinner | 2.46 ± 1.12 | 2.15 ± 0.99 | 0.006 |

The administration of Attiva before lunch significantly decreased the feeling of hunger before the subsequent dinner (**Table 5**).

**Table 5.** Hunger scores (mean ± SD) before lunch and dinner following Attiva/Placebo administration before breakfast and lunch, respectively.

| Time | Attiva | Placebo | *P* value |
|---|---|---|---|
| Before lunch | 1.71 ± 1.00 | 1.67 ± 0.83 | 0.702 |
| Before dinner | 1.47 ± 1.16 | 1.77 ± 0.98 | 0.011 |

The placebo-adjusted effects of Attiva on satiety (first meal effect) and hunger (second meal effect) are reported in **Figure 2** and **Figure 3**, respectively.

Treatment with Attiva was safe and well tolerated. Fifteen subjects (15.8%) reported at least 1 symptom during the study. No detailed information was recorded as to whether the symptoms occurred after the administration of Attiva or placebo (or both).

Gastrointestinal symptoms were reported in 13 (13.7%) subjects during the study (**Table 6**).

**Table 6.** Gastrointestinal symptoms during Attiva/Placebo administration in 95 subjects.

| Symptoms* | Number of subjects | Percentage of subjects |
|---|---|---|
| Nausea | 7 | 7.4 |
| Constipation | 4 | 4.2 |
| Stomach ache | 4 | 4.2 |
| Vomiting | 1 | 1.1 |
| Diarrhea | 1 | 1.1 |

*No information was recorded as to whether the symptoms occurred after the administration of Attiva or placebo.

Three subjects (3.2%) reported more than 1 gastrointestinal symptom during the study: two reported 2 symptoms (stomach ache and diarrhea, nausea and constipation) and 1 reported 3 symptoms (nausea, vomiting, and stomach ache).

Of the 7 subjects who reported nausea during the study, all had a medical history of at least 1 gastrointestinal disorder (esophagitis, epigastralgia, colitis, constipation, and proctitis). In 2 of them, nausea was present just before the administration of the investigational product. Two subjects had 2 episodes of nausea.

Non-gastrointestinal symptoms (isolated headaches) were reported in 2 (2.1%) subjects during the study. One subject had 5 episodes of headaches.

No serious adverse event was observed during the study.

Considering that the prevalence of nausea, constipation, and stomach ache (the most commonly reported symptoms in this study) is reported to be around 6.8-10.7%, 17.0-25.9%, and 10.3-20.0%, respectively, in untreated overweight/obese subjects, and around 3.1-12.7%, 4.4%, and 11.0%, respectively, in placebo-treated overweight/obese subjects, the safety profile of Attiva reported in this study can be regarded as very good, even if all the gastrointestinal symptoms are attributable to the administration of Attiva.

## DISCUSSION

The results of this study demonstrate an increased post-meal feeling of satiety with Attiva and are in agreement with Attiva's physical properties.

The results also demonstrate that Attiva has a second meal effect, since its administration before lunch significantly decreases the feeling of hunger before the subsequent dinner.

The absence of a demonstrated effect on the feeling of hunger before the subsequent lunch can be explained by the fact that small amounts of food are consumed by the subjects at breakfast, and, therefore, the delayed gastric emptying property of Attiva cannot be fully operative.

## CONCLUSION

A single administration of Attiva, a novel superabsorbent biodegradable hydrogel, significantly increases the post-meal feeling of satiety in humans.

The administration of Attiva before lunch significantly decreases the feeling of hunger before the subsequent dinner.

The treatment is safe and well tolerated.

Attiva's effects on satiety and hunger, if confirmed by long-term studies, will support Attiva as a potential anti-obesity product.