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Original

# Double blind randomized clinical trial controlled by placebo with a FOS enriched cookie on saciety and cardiovascular risk factors in obese patients

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**Abstract**

***Introduction:*** **It is essential to determine which snack foods are most affective for appetite control. The objective of the current study was to assess the responses of two different cookies on satiety and cardiovascular risk factors.**

***Material and Methods:*** **38 patients were randomized: group I (FOS enriched cookie, n=19) and group II (control cookie, n=19). Previous and after 1 month , the subjects rated their feelings of satiety/hunger with a test meal of 5 cookies.**

***Results:*** **After the test meal, the basal area under curve of the first hunger/satiety score was higher with satiety cookie than with control cookie, the data after 1 month of treatment was higher with satiety cookie than with control cookie, too. The score was higher than the fasting level for 20 minutes with satiety cookie and for 40 minutes with the same cookie, too. In satiety group, these scores (20 min and 40 min) were higher than control group before and after 1 month of treatment. The results were in the same way with the 100 mm 5-point visual satiety scale. Cardiovascular risk factors and dietary intake remained unchanged after dietary intervention.**

***Conclusion:*** **A FOS enriched cookie produced greater ratings of satiety than a control cookie, without effects on cardiovascular risk factors or dietary intakes.**

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Key words: *Cardiovascular risk factors. Cookies. FOS. Satiety. Obesity.*

**ENSAYO CLÍNICO RANDOMIZADO CONTROLADO CON PLACEBO DE UNA GALLETA ENRIQUECIDA EN FOS, ERFECTO SOBRE LA DACIEDAD Y FACTORES DE RIESGO CARDIOVASCULAR EN PACIENTES OBESOS**

**Resumen**

***Introducción:*** **Es importante evaluar el papel de los alimentos tipo «snacks» sobre el apetito. El objetivo de este trabajo fue evaluar la respuesta en términos de saciedad y el efecto sobre factores de riesgo cardiovascular de dos galletas diferentes.**

***Material y Métodos:*** **Se randomizaron 38 pacientes: grupo I (galleta enriquecida en FOS, n=19) y grupo II (galleta control, n=19). Antes de la intervención nutricional y tras un mes, a los pacientes se les valoró la saciedad con un test de prueba con 5 galletas.**

***Resultados:*** **Tras el test de prueba, el area bajo la curva del test de saciedad fue mayor con la galleta saciante que con la galleta control, detectándose el mismo resultado con el test trás 1 mes de ingerir las galletas. Analizando los diferentes tiempos, el score de saciedad mostró una puntuación superior en los tiempos 20 y 40 minutos frente al valor basal (tiempo 0) tras la ingesta de la galleta saciante, comparado con la galleta control. Los valores de saciedad en los tiempos (20 minutos y 40 minutos) fueron superiores que los que presentó la galleta control. Este resultado fue similar, al realizar el test tras 1 mes tomando la galleta saciante. Los resultados fueron similares al utilizar una escala visual de saciedad de 100 mm con 5 cuestiones. No se detectaron efectos sobre los factores de riesgo cardiovascular tras la intervención nutricional, ni sobre la ingesta dietética global.**

***Conclusion:*** **La galleta enriquecida en FOS produce mayores niveles de saciedad que la galleta control. Sin embargo no existieron efectos sobre los factores de riesgo cardiovascular ni la ingesta dietética global.**

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Palabras clave: *Factores de riesgo cardiovascular. Galletas. FOS. Saciedad y obesidad.*

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## Introduction

Snack foods are substantial contributors to daily energy intake. In a study, more than 85% of women reported snacking at least once per day and 53% of women reported snacking multiple times per day[1]. Researchers have demonstrated that subjects commonly choose bakery goods, sweets, milk products, chocolate and cookies during snacking episodes[2]. Some authors[3] observed that obese subjects consume snacks more frequently than healthy weight subjects. The composition of snack foods likely influences the overall impact that snacking has on metabolism and energy balance. Green et al[4] indicates that a high-carbohydrate snack is more likely to promote a lower total energy intake than if the snack is high in fat. Additionally, more stable blood glucose concentrations are associated with reduced appetite[5].

Obesity now represents a major pandemic, with a multifactorial origin, showing an association with various cardiovascular risk factors, high mortality and high healthcare costs[6]. Therapeutic options for the treatment of obesity go through dietary management[7], drug therapy and bariatric surgery[8]. Despite the wide range of treatments, the first therapeutic step is the dietary treatment. This option has been proven effective in weight loss and improvement in cardiovascular risk parameters. One of the problems of dietetic therapy is the lack of patient adherence, and lack of perception of the benefits secondary to the control of cardiovascular risk factors. One possibility is included in the diet, snacks that include changes in composition as fiber to control satiety and dietary intake. Cookies are one of the foods that have been demonstrated to improve this cardiovascular risk. Several studies have demonstrated the usefulness of these foods, eg Romero et al[9] have proven useful in lowering cholesterol psyllium-enriched cookies. Other groups have shown improvements in cardiovascular risk factors with the use of cookies enriched in inulin or fructooligosaccharides (FOS)[10,11].

Since appropriate snacking may promote a healthy body weight or a control of satiety, it is essential to determine which snack foods are most affective for appetite control. Cookies enriched with FOS could be appropriated snacks. Fructooligosaccharides (FOS), oligofructose and inulin are the most common prebiotics commercially and those with a greater number of studies that have examined their actions on health and may present a potential role in controlling certain cardiovascular risk factors for obese patients[12].

The objective of the current study was to assess the responses of two different cookies similar in protein, fat and carbohydrate contents, while differing in fiber content, on satiety, subsequent food intake, and cardiovascular risk factors.

## Material and methods

Thirty eight obese subjects were recruited from the community, starting the recruitment in October 2011 and completed follow-up of patients in may 2012. Inclusionary criteria included being 25-60 years of age, having a body mass index (BMI) between 30 and 35 (kg/m$^2$), and being weight stable (less than 5% weight fluctuations) for past 3 months. Potential patients were excluded if they were pregnant, elevated blood glucose > 126 mg/dl, high cholesterol> 250 mg/dl, triglycerides> 250 mg/dl, blood pressure > 140/90 mmHg, and the taking of any of the following medications; statins, fibrates, resins, sulfonylureas, biguanides, thiazolidinediones, insulin, glucocorticoids, alpha blockers, converting enzyme inhibitors and angiotensin II receptor antagonists. These patients were studied in a Nutrition Unit. The general design of research was explained before the study began and all subjects provided written informed consent. The protocol has been approved by the Ethics Committee of the Center.

### *Procedure and satiety scores*

Patients were randomized (table of numbers) to one of the following two groups: cookie I (enriched with FOS, see table OI) (Gullón SL) and cookie II (control cookie, see table I). Each patient received a total of 10 cookies per day (total product 60 grams), completing a month of treatment. Cookie intake was controlled for a month, each week, and patients were instructed to eat cookies along the day. The methodology was double-blind, neither the patient nor the investigator who followed the patient knew the type of cookie.

Patients reported to the laboratory at the same time each day following a 10-h fast. Before starting the dietary intervention and at the end of the protocol were determined weight, fat mass, blood pressure, fasting blood glucose, C reactive protein (CRP), insulin, insulin resistance (HOMA-R), total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides.

**Table I**
*Composition of cookies (10 cookies –60 grams of product)*

| | *Control cookies* | *Saciety cookies* |
|---|---|---|
| **Proteins (g)** | 4,10 | 7,00 |
| **Carbohydrates (g)** | 46,98 | 31,4 |
| **Fats (g)** | 6,12 | 7,50 |
| Saturated (g) | 3,06 | 0,86 |
| Mono-unsaturated (g) | 2,44 | 4,99 |
| Poli-unsaturated (g) | 0,61 | 1,68 |
| **Cholesterol (mg)** | <5 | <5 |
| **Total fiber (g)** | 1,02 | 11,40 |
| *soluble fiber (g)* | 0,00 | 9,84 |
| FOS (g) | 0 | 9,84 |
| *Insoluble fiber* (g) | 1,02 | 1,56 |
| Hemicellulose (g) | 0,51 | 0,78 |
| Cellulose (g) | 0,51 | 0,78 |
| **Sodium (mg)** | 0,17 | 0,17 |
| **Kcal** | 261,0 | 247,8 |

FOS: fructooligosaccharides.

After arriving at the laboratory, the patients were interviewed to assure that they followed the dietary protocol prior the visit. The subjects rated their feelings of satiety/hunger using a scoring system graded from minus 10, to represent extreme hunger, to plus 10, to represent extreme satiety[13]. Subjects were shown a scale with 20 graduations and asked to indicate how they felt in respect of hunger or satiety by pointing to an appropriate place along the scale. The scale was punctuated with phrases describing various degrees of hunger and satiety, but subjects were free to choose any point along it.

A 100 mm 5-point visual satiety scale[14] was used, too. The patients were instructed to place a single vertical line representing their feeling of 5 questions on the scale in each question (grade of hunger, grade of satiety, grade of fullness, desire to eat some food, desire to eat something fatty, salty, sweet or savory). The scale was anchored at 0 with «nothing at all» and at 100 with «a large amount».

Both hunger/satiety scores were recorded before a test meal of 5 cookies, immediately after it, and at 20 and 40 minutes after starting it. The patients were told that test food (5 cookies) was taken in less than 10 minutes with 150 ml of water.

*Biochemical determinations*

Blood samples were centrifuged for 7 min at 4ºc immediately after each collection and it was stored in cryogenic vials at -70ºC. Serum total cholesterol and triglyceride concentrations were determined by enzymatic colorimetric assay (Technicon Instruments, Ltd., New York, N.Y., USA), while HDL cholesterol was determined enzymatically in the supernatant after precipitation of other lipoproteins with dextran sulphate-magnesium. LDL-cholesterol was calculated using Friedewald formula. Plasma glucose levels were determined by using an automated glucose oxidase method (Glucose analyser 2, Beckman Instruments, Fullerton, California). Insulin was measured by enzymatic colorimetry (Insulin, WAKO Pure-Chemical Industries, Osaka, Japan) and the homeostasis model assessment for insulin resistance (HOMA-R) was calculated[15].

*Anthropometric measurements*

Body weight was measured to an accuracy of 0.1 Kg and body mass index computed as body weight/(height$^2$) (kg/m$^2$). Waist (narrowest diameter between xiphoid process and iliac crest) and hip (widest diameter over greater trochanters) circumferences to calculate waist-to hip ratio (WHR) were measured, too. Tetrapolar body electrical bioimpedance was used to determine body composition[16]. An electric current of 0.8 mA and 50 kHz was produced by a calibrated signal generator (Biodynamics Model 310e, Seattle, WA, USA) and applied to the skin using adhesive electrodes placed on right-side limbs. Resistance and reactance were used to calculate total body water, fat and fat-free mass.

Blood pressure was measured twice after a rest period of 10 minutes with a random zero mercury sphygmomanometer (Omron, London, United Kingdom), and averaged.

*Dietary intervention*

Before and after intervention, patients received prospective serial assessment of nutritional intake with 3 days written food records. All enrolled subjects received instruction to record their daily dietary intake for three days including a weekend day. Handling of the dietary data was by means of a personal computer equipped with personal software, incorporating use of food scales and models to enhance portion size accuracy. Records of intake and consumption of cookies were reviewed by a dietician and analyzed with a computer-based data evaluation system. National composition food tables were used as reference[17]. The exercise allowed was aerobic, which was previously done by patients before entering the study, mainly walking. At dietary intervention, patients were asked whether they considered their bowel habits have changed over who had previously shown a quantitatively and qualitatively. For a qualitative evaluation, they were asked whether they considered that the introduction of the cookie in the diet would have produced diarrhea or constipation.

*Statistical analysis*

The sample size was calculated to detect a difference in satiety score[14] of 2 mm after treatment with a 90% power and an alpha error of 5% (n = 18 in each group). The results were expressed as mean (standard deviation). The normality of variables was analyzed by the Kolmogorov-Smirnov. Quantitative variables with normal distribution were analyzed with Student's t test paired and unpaired. Variables without normal distribution were analyzed with Wilcoxon W-test. ANOVA test was used as needed with Bonferroni test as post hoc test. Qualitative variables were analyzed with chi-square with Yates correction when appropriate, and Fisher's test. The area under the response curve (AUC) for both hunger/satiety scores with the test food (5 cookies) was calculated using the trapezoidal method. The strategy of analysis was by intention to treat. P less than 0.05 was considered statistically significant. All statistical analyses were performed using SPSS (version 15.0).

## Results

Thirty eight patients were included in the protocol (fig. 1, Consort diagram), 36 patients finished the

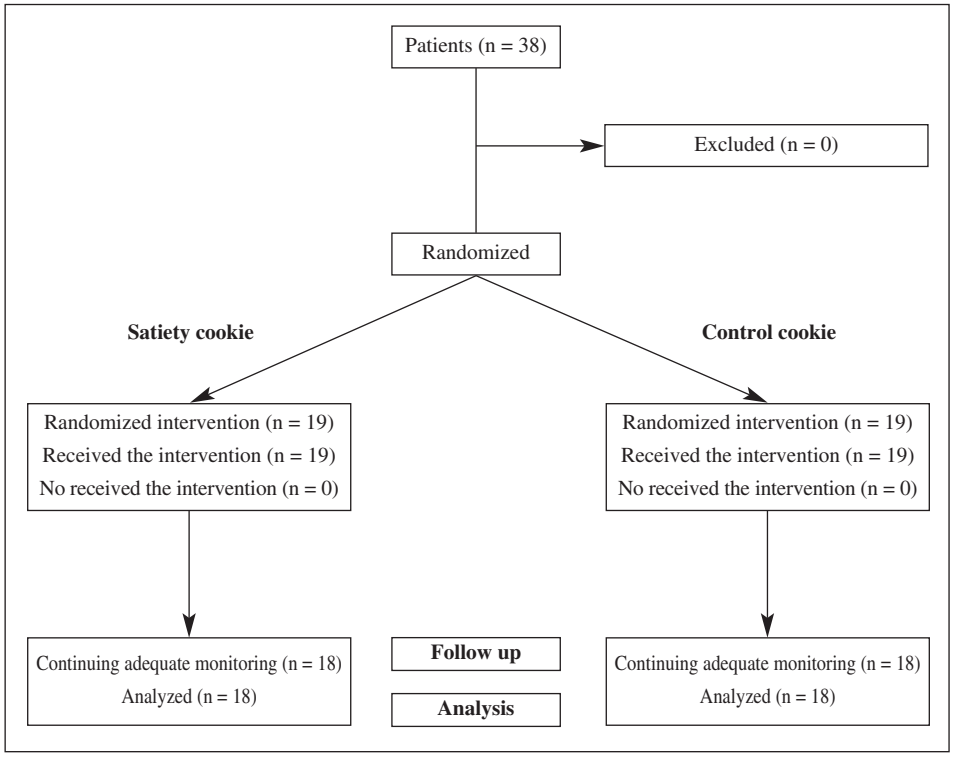


*Fig. 1.—Consort diagram.*

**Table II**
*Biochemical and antropometric parameters*

| | *Satiety cookie* | | *Control Cookie* | |
|---|---|---|---|---|
| *Parameters* | *Basal* | *1 month* | *Basal* | *1 month* |
| BMI | 35.9 ± 3.4 | 35.7 ± 3.3 | 39.2 ± 7.2 | 38.9 ± 5.8 |
| Weight (kg) | 92.3 ± 11.3 | 91.6 ± 1.4 | 106.4 ± 16.2 | 105.54 ± 20.1 |
| Fat mass(kg) | 37.8 ± 12.3 | 37.6 ± 12.6 | 39.2 ± 5.9 | 38.9 ± 5.8 |
| WHC | 0.93 ± 0.08 | 0.92 ± 0.08 | 0.96 ± 0.06 | 0.96 ± 0.04 |
| SBP (mmHg) | 131.4 ± 15.3 | 129.4 ± 12.7 | 134.4 ± 18.5 | 130.3 ± 16.5 |
| DBP (mmHg) | 81.0 ± 20.3 | 80.6 ± 8.2 | 81.3 ± 10.3 | 81.0 ± 9.6 |
| Glucose (mg/dl) | 103.8 ± 16.9 | 104.8 ± 10.3 | 103.3 ± 14.9 | 104.4 ± 12.1 |
| Total-ch. (mg/dl) | 210.2 ± 45.1 | 204.2 ± 38.1 | 215.2 ± 44.4 | 217,1 ± 47.5 |
| LDL-ch. (mg/dl) | 128.4 ± 40.2 | 123.4 ± 37.4 | 136.8 ± 34.7 | 135.6 ± 38.5 |
| HDL-ch. (mg/dl) | 57.5 ± 14.1 | 54.4 ± 14.3 | 53.2 ± 16.3 | 53.1 ± 16.2 |
| TG (mg/dl) | 145.5 ± 48.4 | 151.1 ± 50.3 | 129.2 ± 53.4 | 140.6 ± 60.6 |
| Insulin (mUI/L) | 13.1 ± 8.2 | 13.8 ± 10.4 | 12.9 ± 9.5 | 14.2 ± 6.6 |
| HOMA-R | 3.8 ± 2.1 | 4.3 ± 4.1 | 3.5 ± 3.0 | 3.4 ± 2.3 |
| CRP(mg/dl) | 4.7 ± 4.4 | 6.6 ± 7.1 | 9.0 ± 7.5 | 8.3 ± 7.8 |

BMI: body mass index. WHC: waist to hip circumference. SBP: Systolic blood pressure. DBP: diastolic blood pressure. Ch: Cholesterol. LDL: low density lipoprotein. HDL: High density lipoprotein. TG: triglycerides. CRP. C reactive protein. HOMA-R: homeostasis model assesment. No statistical differences.

study. The 2 patients excluded from the analysis had taken less than 80% of the prescribed cookies. The distribution was in group 1 (4 males and 14 females) with a mean age of 45.3 ±16.1 years and the control group 2 (5 males and 13 females) with a mean age of 50.8±16.2 years. No differences in gender and age distribution of patients were observed.

*Biochemical and anthropometrical parameters*

Values of anthropometric and biochemical parameters were shown in table II. No differences were detected in biochemical and anthropometrical parameters with dietary intervention. With respect to the anthropometric parameters after the introduction of

**Table III**
*Dietary intakes*

| | *Satiety cookie* | | *Control Cookie* | |
|---|---|---|---|---|
| *Parameters* | *Basal* | *1 month* | *Basal* | *1 month* |
| BMI | 35.9 ± 3.4 | 35.7 ± 3.3 | 39.2 ± 7.2 | 38.9 ± 5.8 |
| Energy (kcal/day) | 1944.9 ± 499 | 1853.3 ± 509 | 2134.2 ± 447.1 | 2266.2 ± 556.3 |
| CH (g/ day) | 204.4 ± 60.1 | 195.5 ± 60.7 | 222.2 ± 62.8 | 241.1 ± 55.9 |
| Fat (g/ day) | 83.3 ± 27.5 | 73.9 ± 25.7 | 99.3 ± 34.9 | 97.9 ± 48.4 |
| Fat-S (g/ day) | 21.3 ± 9.7 | 17.5 ± 9.3 | 29.6 ± 10.5 | 26.5 ± 7.8 |
| Fat-M (g/ day) | 36.5 ± 11.2 | 34.7 ± 10.4 | 40.4 ± 10.3 | 43.5 ± 11.1 |
| Fat-P (g/day) | 8.6 ± 3.7 | 10.5 ± 5.4 | 12.1 ± 3.9 | 10.2 ± 4.5 |
| Protein (g/day) | 92.9 ± 34.4 | 96.7 ± 27.5 | 96.3 ± 27.2 | 97.8 ± 19.3 |
| Total Fiber (g/day) | 18.4 ± 5.7 | 28.6 ± 6.1* | 17.8 ± 7.9 | 16.9 ± 6.1 |
| Soluble fiber (g/day) | 6.2 ± 0.8 | 14.5 ± 2.3 | 5.9 ± 2.9 | 5.2 ± 2.2 |
| FOS (g/day) | 3.8 ± 1.8 | 11.5 ± 1.8* | 3.5 ± 2.1 | 3.1 ± 1.8 |
| Insoluble fiber (g/day) | 11.6 ± 4.1 | 12.4 ± 4.5 | 12.3 ± 5.9 | 11.7 ± 3.9 |
| Cholesterol (mg/day) | 431.2 ± 197.2 | 384.5 ± 252.1 | 371.5 ± 214 | 320.2 ± 145.8 |
| Sodium (mg/day) | 1536.2 ± 684.1 | 1544.1 ± 762.3 | 1642 ± 584 | 1512.9 ± 424.3 |
| Exercise (hs./week) | 3.4 ± 3.2 | 3.5 ± 3.1 | 4.1 ± 2.8 | 3.9 ± 2.6 |

CH: Carbohydrates. Fat-S: fat saturated. Fat-M: fat mono-unsaturated. Fat-P: Fat poly-unsaturated. FOS: Fructoolygosacharides.
(*) statistical differences in the some cookie group after intervention.

**Table IV**
*Satiety/hunger using a scoring system graded from minus 10, to represent extreme hunger, to plus 10, to represent extreme satity*[13]

| | *Satiety cookie* | | *Control Cookie* | |
|---|---|---|---|---|
| *Parameters* | *Basal* | *1 month* | *Basal* | *1 month* |
| AUC Score (mm) | -1.8 ± 6.1# | -5.0 ± 6.7# | -8.1 ± 8.5 | -9.7 ± 6.0 |
| Score before test meal (mm) | -2.4 ± 2.4 | -3.3 ± 2.9 | - 2.7 ± 2.8 | -2.5 ± 2.8 |
| Score 20 min after test meal (mm) | -0.2 ± 2.2*# | -0.8 ± 3.3*# | -2.9 ± 3.1 | -2.6 ± 3.3 |
| Score 40 min after test meal (mm) | 0.8 ± 3.1*# | -0.7 ± 3.1*# | -2.5 ± 2.7 | -2.3 ± 2.8 |

AUC: Area under curve.
(*) statistical differences in the some cookie group and in the same time (basal or 1 month) with score before test meal.
(#) statistical differences between groups in the same time (basal or 1 month)

cookies on the patient's usual diet, did not change any parameter (table II). This finding is logical because the inclusion of patients in the protocol did not alter total energy intake from their diet. With respect to the biochemical values after the introduction of cookies on the patient's usual diet, it was not detected changes neither patients with enriched cookies nor patients with control cookie.

*Dietary intake effects*

In the evaluation of dietary intake variables, no statistically significant differences between baseline values of the two groups of cookies were detected (table III). With respect to the values after the introduction of cookies on the patient's usual diet, it was detected in patients with satiety cookies a significantly increased of total fiber and soluble fiber dietary intakes, as expected. It was not detected any significant change in food intake in patients who received the control cookie (table III). The number of cookies given per patient per month was 300 cookies. The number of consumed cookies after a month of intervention was 272.2±22.1 (97.2%) in patients in the control cookie and 270.3±13.98 in patients in the satiety cookie enriched (96.5%), without statistical differences.

*Satiating effects*

Immediately before the test meal, the basal hunger/satiety score (13) (table IV) was similar with satiety cookie and control cookie (-2.4±2.4 points vs -2.7±2.8 points;p>0.05), the data after 1 month of treatment was similar in both groups (-3.3±2.9 mm vs -

**Table V**
*The 100 mm 5-point visual satiety scale*[14]

| | *Satiety cookie* | | *Control Cookie* | |
|---|---|---|---|---|
| *Parameters* | *Basal* | *1 month* | *Basal* | *1 month* |
| «how is your grade of hunger?» | | | | |
| AUC Score (mm) | 77.0 ± 53.2[#] | 86.9 ± 70.9[#] | 108.2 ± 92.9 | 110.6 ± 88.1 |
| Score before test meal (mm) | 40.0 ± 29.4 | 48.0 ± 31.8 | 33.4 ± 31.9 | 41.5 ± 30.4 |
| Score 20 after test meal (mm) | 18.5 ± 22.1*[#] | 29.2 ± 24.9*[#] | 36.8 ± 31.3 | 33.4 ± 27.8 |
| Score 40 after test meal (mm) | 18.5 ± 17.8*[#] | 29.7 ± 25.3*[#] | 37.9 ± 30.3 | 33.9 ± 27.7 |
| «how is your grade of satiety?» | | | | |
| AUC Score (mm) | 169.7 ± 57.1[#] | 159.6 ± 58.7[#] | 117.2 ± 98.8 | 108.2 ± 87.9 |
| Score before test meal (mm) | 45.5 ± 27.6 | 37.5 ± 26.1 | 42.1 ± 33.1 | 37.4 ± 27.4 |
| Score 20 after test meal (mm) | 62.0 ± 25.1*[#] | 60.8 ± 21.0*[#] | 38.2 ± 33.1 | 47.4 ± 29.8 |
| Score 40 after test meal (mm) | 61.5 ± 17.2*[#] | 60.3 ± 22.7*[#] | 37.7 ± 33.3 | 48.3 ± 29.1 |
| «how is your grade of fullness?» | | | | |
| AUC Score (mm) | 156.7 ± 57.1[#] | 148.1 ± 52.7[#] | 95.7 ± 88.8 | 101.6 ± 43.9 |
| Score before test meal (mm) | 42.0 ± 26.2 | 30.8 ± 22.1 | 35.7 ± 33.9 | 32.3 ± 24.4 |
| Score 20 after test meal (mm) | 55.0 ± 23.1*[#] | 59.2 ± 19.8*[#] | 29.6 ± 30.5 | 45.8 ± 26.8 |
| Score 40 after test meal (mm) | 59.0 ± 17.4*[#] | 58.1 ± 24.6*[#] | 30.5 ± 29.3 | 48.2 ± 27.1 |
| «What is your desire to eat some food?» | | | | |
| AUC Score (mm) | 125.5 ± 69.1 | 133.6 ± 62.7 | 145.9 ± 90.8 | 145.3 ± 73.9 |
| Score before test meal (mm) | 57.0 ± 31.2 | 50.8 ± 28.1 | 42.9 ± 31.9 | 48.3 ± 27.4 |
| Score 20 after test meal (mm) | 34.0 ± 28.1*[#] | 38.6 ± 26.0*[#] | 51.4 ± 32.5 | 45.3 ± 7.8 |
| Score 40 after test meal (mm) | 34.5 ± 27.2 *[#] | 44.2 ± 25.6* | 51.9 ± 30.8 | 46.3 ± 24.1 |
| «What is your desire to eat something salty, sweet or savory?» | | | | |
| AUC Score (mm) | 125.7 ± 85.1 | 143.6 ± 79.7 | 162.2 ± 97.8 | 150.5 ± 79.9 |
| Score before test meal (mm) | 51.0 ± 32.6 | 51.4 ± 30.1 | 52.1 ± 34.3 | 51.5 ± 30.4 |
| Score 20 after test meal (mm) | 36.5 ± 33.1*[#] | 46.4 ± 28.9 | 55.7 ± 32.8 | 49.1 ± 27.8 |
| Score 40 after test meal (mm) | 37.5 ± 31.7*[#] | 45.8 ± 29.7 | 54.3 ± 32.5 | 46.6 ± 27.1 |

AUC: Area under curve.
(*) statistical differences in the some cookie group after intervention.
([#]) statistical differences between groups in the same time (basal or 1 month).

2.5±2.8 mm;p>0.05), too. After the test meal, the basal AUC of this hunger/satiety score was higher with satiety cookie than with control cookie (-1.8 ±6.1 $mm^2$ vs -8.1±8.5 $mm^2$;p<0.05), the data after 1 month of treatment was higher with satiety cookie than with control cookie (-5.0 ±6.7 $mm^2$ vs -9.7±6.0 $mm^2$;p<0.05), too. The score was higher than the fasting level for 20 minutes with satiety cookie and for 40 minutes with the same cookie, too. In satiety group, these scores (20 min and 40 min) were higher than control group before and after 1 month of treatment.

The results were in the same way with the 100 mm 5-point visual satiety scale[14] (table V). When asked «how is your grade of hunger?» at the 20 min and 40 min, subjects rate that they wanted to eat less with satiety cookie. In satiety group, these scores (20 min and 40 min) were lower than control group at basal time and after 1 month of treatment. After the test meal, the basal AUC of this question score was lower with satiety cookie than with control cookie, the AUC data after 1 month of treatment remained lower with satiety cookie than with control cookie, too.

When asked «how is your grade of satiety? and «How is your grade of fullness? (table V) at the 20 min and 40 min, subjects rate that they wanted to eat less with satiety cookie. In satiety group, these scores (20 min and 40 min) were higher than control group at basal time and after 1 month of treatment. After the test meal, the basal AUC of this question score was higher with satiety cookie than with control cookie, the AUC data after 1 month of treatment remained higher with satiety cookie than with control cookie, too.

When asked «What is your desire to eat some food? and «What is your desire to eat something salty, sweet or savory? (table V) at the 20 min and 40 min, subjects rate that they wanted to eat less with satiety cookie. In satiety group, these scores (20 min and 40 min) were lower than control group at basal time and after 1 month

of treatment with the first question and only at basal time with the second question. After the test meal, AUC of these question score remained unchanged.

*Side effects*

With respect to monitoring the effects on the digestive tract, two patients in the group of control cookies (11.0%) and one patient (5.5%) in the satiety group referred episodes of diarrhea during the month of treatment. Two patients (11.0%) in the control group and 2 patients in the satiety cookie group (11.0%) referred have constipation during the month of intervention.

## Discusion

Results of our study indicate that a FOS enriched cookie promotes greater satiety than control cookies, but daily food consumption, cardiovascular parameters and anthropometric parameters are not significantly affected.

Other previous studies comparing more versus less satiating foods have found that higher fiber and protein contents promote greater satiety, while more fat and sugar typically promote less satiety. Berti et al[18] demonstrated that pasta and bread with high fiber contents decrease energy intake relative to lower fiber foods. Holt et al[19]. determined that fiber and protein contents were associated with increased satiety and that fat and sugar contents were associated with lower satiety for a variety of snack foods, protein rich foods, bakery products, breakfast foods, protein rich foods, carbohydrate-rich foods, and fruits. In other study, boiled potatoes were demonstrated to be more satiating than French fries, which may have been partially influenced by the greater glycemic response of the boiled potatoes[20]. One hypothesis to explain the effect of these fiber enriched foods on satiety is the potential effects on bowel, as softer stools, increased bulk, and facilitate mobility providing a laxative effect[21], these symptoms could influence feelings of satiety. Gastrointestinal symptoms were assessed in our study and there are no differences between both groups.

No significant difference in food consumption was detected at the end of the FOS enriched cookie trial versus the control cookie trial. This result was unexpected given the difference in satiety scores. Many factors can affect food consumption following a pre-load that can alter subsequent food intake. These factors include food weight[22], food volume[23] and food portion size[24]. Additionally, the eating environment, which includes the number of distractions[25] and people present[26], affects food intake and may have contributed to variability in intake that limited our power to detect a significant difference. Some authors[27] propose that although monitoring food intake in a laboratory setting, as our design, may provide some valuable information, the outcomes are less than reliable and should not be overly generalized to appetite responses in more realistic conditions. In the other hand, hunger and satiety are subjective sensations and there is no generally accepted way of measuring them. Previous human interventional studies examining FOS and satiety have produced inconsistent results. A study in healthy subjects demonstrated enhanced satiety after consumption of 8g FOS supplements twice daily for two weeks[28]. In contrast, consumption of 8 g of FOS in a meal-replacement bar one to two times a day for two days did not affect appetite rating[29]. The different doses and the type of FOS supplement could explain these unclear results. Thus, our results corroborated that if FOS were to have an effect on appetite it is more likely to occur in doses over 9 g per day and included in a food as cookies.

The lack of effect on cardiovascular risk factors has been described in the literature, too. If we analyze the literature we found a number of problems in analyzing the effect of FOS on lipid profile and glucose metabolism. For example, we could mention, the heterogeneity of the populations (obese, diabetic, hyperlipidemic, healthy subjects, gender of the sample), secondly the daily amount of fiber administered and the type of prebiotic, which can vary from pure inulin to fructooligosaccharides (FOS) and finally the variability in the time of intervention performed. For example, one of the earliest studies was conducted with 12 healthy men, found no effect on the lipid profile by adding to the daily diet of 20 g FOS[17]. Similarly, in a study with 12 healthy volunteers also in various stages of intervention with inulin, FOS and galacto-oligosaccharides (GOS), there were no effects on LDL cholesterol, triglycerides, HDL cholesterol[30]. However, the results were significant when inulin was used in the interventions[31-33]. So, we could summarize this group of studies, noting that in the literature beneficial effects on triglycerides and cholesterol LDL by administering inulin have been detected, without effects with FOS. Most of this effect may be due to increased loss of bile salts in the feces, which can range between 20 and 80%, producing secondarily a decrease in total body cholesterol[31].

Tolerance towards FOS enriched cookies was good and explains the excellent compliance observed. Cookies could be a good food form to improve consumption of this type of fiber. One question may arise from our study: which mechanism could FOS modulate satiety? In rats, FOS supplementation increase satiety through the promotion of intestinal synthesis and portal release of GLP-1[34]. Nevertheless, all fermentable dietary fiber do not have the same potency to increase satiogenic peptides: for example, inulin is fermented in distal colon, whereas FOS is fermented in the proximal colon. The second type of fiber is able to produce the effects of OFS in terms of secretion and mRNA modulation[35].

Overall, selection of a FOS enriched cookie produced greater ratings of satiety and lower ratings of

hunger than a control cookie, without effects on cardiovascular risk factors, anthropometric parameters and dietary intakes. Future researches to more comprehensively discover snack foods that are most likely to promote satiety and a significant effect on dietary intakes.

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