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SHORT TERM EFFECTS OF A GREEN COFFEE EXTRACT, GARCINIA CAMBOGIA AND L-CARNITINE CONTAINING CHEWING GUM ON SNACK INTAKE AND APPETITE REGULATION

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ABSTRACT

Different studies have assessed the influence of chewing gum to aid control of appetite and reduce food intake.

Purpose: The aims of the present study were to evaluate the effects of chewing gum on satiety, food hedonics and snack intake, and to explore the potential effects of the combination of Garcinia Cambogia, green coffee extract and L-carnitine on satiety, when administered in a gum format.

Methods: This was a prospective study in which fifty seven subjects randomly received three kinds of treatments, in a cross-over design: 1) active gum; 2) placebo gum; and 3) no gum. Food preferences and appetite sensations were evaluated by means of the Leeds Food Preference Questionnaire and visual analog scales. Results: There was a significant reduction in low fat sweet snack intake with placebo gum and the active gum compared to no gum, and a reduction in high fat sweet snack intake with the active gum compared to placebo gum and no gum. Total caloric intake was only reduced in the active gum condition. Both the active and placebo gum conditions significantly reduced hunger and prospective food consumption and increased fullness compared to no gum, and were associated with a reduced wanting for sweet food in the LFPQ, consistent in a reduction in the relative preference for sweet snacks vs. savoury snacks.

Conclusion: This study supports the notion that chewing gum containing nutraceutical products might aid in the control over snack intake and reduce hunger sensations.

INTRODUCTION

Different studies have pointed out the influence of sensory factors on satiety. Already in classic studies it was postulated that orosensory stimulation caused by sweet food could result in a reduction in food intake and perceived hunger [1]. Moreover, Rolls & Rolls [2], evidenced that when people chew but don´t swallow certain food, it induces a reduction in the pleasure sensation related to the taste of that specific food compared to non-tasted foods, in what they describe as sensory specific satiety. More lately, numerous studies evidenced that oro-sensory exposure time plays a key role in the development of satiety [3-5].

In a study conducted in healthy volunteers, Lavin et al found that chewing sweet pastilles for 10 minutes reduces energy intake compared to jelly or a drink with the same content of sugar and calories, but consumed for a shorter period of time [6]. Similarly, in a study conducted in 60 healthy volunteers, chewing gum every hour after lunch significantly reduced subsequent snack intake [7]. Moreover, hunger perception and desire for sweet snacks were significantly reduced after chewing gum [7]. However, in another recent study, no differences were found in 24-hour energy intake in subjects that consumed chewing gum for more than 90 minutes a day compared to those who did not [8].

Besides these potential beneficial effects of chewing gum on satiety, it has been proposed that gum could be also used as a vehicle to administer drugs or natural compounds [9-10] based on its habitual use in Western societies [11]. Indeed, several nutraceutical products that claim to promote satiety are available in chewing gum format. However, as far as we know, most of them have failed to prove their efficacy in controlled trials [12].

Lisopresol ® is a nutraceutical mint flavored gum containing Garcinia Cambogia, green coffee extract and L-carnitine, that claims to aid to the control of snack intake. In previous

studies, we [13] and others found that Garcinia Cambogia containing products might increase postprandial satiety, possibly by means of increasing fat metabolism due to the inhibition of the key enzyme ATP-citrate lyase, that catalyzes the conversion of citrate into oxaloacetate and acetyl-CoA [14]. Similarly, other authors have attributed to chlorogenic acid – the main compound present in green coffee extract - the ability to reduce hepatic glucogenolisis by means of the inhibition of glucose-6-phosphatase, and to stimulate GLP-1 intestinal release, suggesting its potential effect on the satiety cascade [15-18]. However, to our knowledge, the effects of the combined use of Garcinia Cambogia and green coffee extract on appetite sensations have not been evaluated.

Consequently, the aims of the present study were to further evaluate the effects of chewing gum on appetite sensations, food hedonics and snack intake, and to explore the potential effects of the combination of Garcinia Cambogia, green coffee extract and L-carnitine on appetite, when administered in a gum format.

METHODS

Participants

Participants were recruited from the volunteer database of CESIM Foundation, in the city of Santa Rosa, La Pampa, Argentina. Fifty seven subjects (sixteen men, forty one women) completed the study. Of the 61 participants initially enrolled, data from 4 were not included in the final analysis for not completing all study visits. Sample size calculation was performed in order to be able to detect a 10% difference between treatments in fullness visual analog scale score.

We recruited normal and overweight subjects (body mass index 18.5 – 29.9 kg/m^2) aged 18–50 years, with teeth in a good state of repair, after an initial screening process to exclude those who were taking medication (except low dose estrogen oral contraceptives),

actively losing weight, reported a history of eating or psychological disorders, were active smokers or were intolerant to any of the study products (characteristics of the subjects are summarized in Table 1). Subjects were familiarized with the study procedures, and told that they would be participating in a study to investigate the effects of a chewing gum with or without a nutraceutical product on food preferences and snack intake, before giving their written consent. Anthropometric measurements and restraint, hunger susceptibility and disinhibition scores according to the Three Factor Eating Questionnarie [19] were evaluated during the screening visit. The study was approved by an independent Medical Ethical Committee (Comité de Ética Independiente Patagónico, CEIP, Santa Rosa, La Pampa, Argentina) and was performed in accordance with national regulations and the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Subjects did not receive any payment for their participation in the study.

Study Design

This was a prospective cross-over study in which each subject randomly received three kinds of treatments, spaced by at least three days: 1) active gum; 2) placebo gum; and 3) no gum. Treatments 1 and 2 were double-blind, whereas treatment 3 was open. The whole study was conducted in Fundación Centro de Salud e Investigaciones Médicas (CESIM), Santa Rosa city (La Pampa), Argentina.

On each experimental day, subjects were instructed to consume their normal breakfast at home and not to eat or drink (except water) until they attended the laboratory four hours later, between 12 noon and 1:30 p.m. for a fixed lunch. Breakfast characteristics were evaluated by means of a food diary in order to confirm that energy and nutrient content was the same in all study visits.

Lunch

Lunch consisted of sandwiches and fruit salad. The portions were adjusted according to the estimated total energy expenditure for each participant, to provide about 25% of total calories, with approximately 15% of calories as protein, 30% fat and 55% carbohydrate. During the following four hours, subjects were able to continue with their regular activities, with the exception that they could not eat or drink (except water) or perform strenuous physical activity until they return to the lab for the snack intake test.

Snack Intake Test

Snack products were clustered in four categories based on their taste (sweet/savoury) and fat content (high/low) (Table 2). Each subject selected one snack from a choice of three from each category by first ranking each snack from "most preferred" to "least preferred". On the experimental session, each subject received a tray with 4 bowls, each containing 100 g of the snack selected. They could ask for extra bowls if necessary. Ad libitum intake of snack product was measured by weighing remaining food in the bowls. Water was supplied ad libitum.

Appetite Sensations and Food Preferences

One hundred mm visual analog scales (VAS) were used to assess the appetite profile. The questionnaire was completed immediately before and after lunch, and every thirty minutes up to four hours post lunch. The scales were anchored with opposing extremes of feelings of hunger, fullness and prospective consumption of food. Subjects were instructed to make a single vertical mark at the appropriate point between the two anchors on each scale to indicate their subjective feelings.

Food preferences and their hedonic profile was assessed by a computerized task – the Leeds Food Preference Questionnaire (LFPQ) –, administered immediately before snack intake. The LFPQ measures explicit liking and implicit wanting responses according to the shared

sensory properties of a photographic array of foods. 16 images are chosen by the experimenter from a validated database to be either predominantly high (>50% energy) or low (<20% energy) in fat and sweet or savoury (non-sweet) in taste but similar in familiarity and palatability (Table 3). For the explicit measure of liking, foods were rated on 100 mm VAS according to "how pleasant would you find the taste of this food right now?" For the implicit measure, the same foods were presented in a series of 96 randomized pairs and participants had to "select the food which you most want to eat right now" as quickly and accurately as possible. Reaction times for all responses were recorded and used to compute mean response times for each food type after adjusting for the frequency of selection and overall mean response time [20]. During the latter procedure, choice frequency was also recorded for each food type.

Gum Condition

In the active gum condition, subjects were provided with a Lisopresol® containing gum (ELEA Laboratories S.A.C.I.F., Buenos Aires, Argentina), composed by a combination of 200 mg Garcinia Cambogia (with an average content of 60% of hydroxycitric acid and less than 2 mg caffeine), 20 mg L-carnitine, 100 mg of green coffee extract (45 mg of clorogenic acid content) and B6 vitamin (0,26mg), mint flavored. In the placebo condition, subjects were provided with a placebo containing gum, similar in appearance and taste to the active gum.

During the gum conditions, subjects were instructed to chew gum for at least 15 minutes every hour, starting 45 minutes after breakfast, computing a total of eight gums (four gums before lunch and four gums before snack intake). In the no gum condition, subjects were instructed to rest for at least 15 minutes every hour, instead of chewing gum. At the end of

every study session, empty gum containers were returned to the lab to evaluate the compliance with the study instructions.

Statistical Analysis

Data were analyzed using SPSS for Windows (version 17.0, SPSS Inc, Chicago, IL) and presented as mean SE, unless stated otherwise. The significance was set at $P < 0.05$. Total snack intake and the composite analysis of snack intake according to its fat content and taste were compared by means of repeated measures ANOVA. Snack intake pattern was analyzed by using 3 x 2 x 2 (three treatment conditions, 2 tastes and 2 fat contents) fully within-subject ANOVA. Pre lunch (time -1) subjective appetite sensation VAS were analyzed by means of repeated measures ANOVA. Subjective appetite sensation VAS excursions (from time 0 to pre-snack) were analyzed by using 3 x 9 (three treatment conditions, 9 time points) fully within-subject ANOVA. Food preferences were evaluated by computing the bias for sweet taste (sweet > savoury) and bias for high fat (high fat > low fat) scores for explicit liking, implicit wanting and choice frequency. The fat bias was calculated as the mean score for low fat foods subtracted from the mean score for high fat foods. The sweet bias was calculated as the mean score for savoury foods subtracted from the mean score for sweet foods. Explicit liking, implicit wanting and choice frequency results of the LFPQ were analyzed by using repeated measures ANOVA.

RESULTS

Participant characteristics

Mean restraint, disinhibition and hunger scores according to the TFEQ data were normally distributed, however 16 subjects were considered restrained eaters (i.e. presented more than 11 points on the restraint scale). Five rated more than 9 points on the disinhibition scale and 21 rated more than 7 points on the hunger scale. As exclusion of the 16 volunteers that

144 rated more than 11 points on the restraint scale did not significantly modify the results, the
145 data presented corresponds to all studied subjects.

146 **Snack intake**

147 Total snack intake was significantly lower in the active gum condition compared to placebo
148 gum or no gum (Figure 1). No significant differences were observed between placebo gum
149 and no gum regarding total snack intake.

150 Snack intake selection was significantly different among conditions ($F=5.034$, $p=0.008$),
151 characterized by a reduction in low fat sweet snack intake with placebo gum and the active
152 gum compared to placebo, and a reduction in high fat sweet snack intake with the active
153 gum compared to placebo gum and no gum. No significant differences were observed
154 between conditions in low fat and high fat savoury snack intake, although there was a non
155 significant tendency towards lower high fat savoury snack intake with the active gum
156 compared to no gum (Figure 2).

157 In the composite analysis of snack intake according to its fat content, the active gum
158 condition was associated with a significant reduction in caloric intake from high fat snacks
159 compared to no gum and placebo, meanwhile no significant differences were observed
160 between conditions regarding caloric intake from low fat snack intake (despite the
161 reduction reported in low fat sweet snack intake with active and placebo gums) (Figure
162 3A). Despite a non significant tendency towards lower savoury snack intake after the active
163 gum treatment, no differences were observed in savoury snack intake among conditions
164 (Figure 3B). Conversely, sweet snack intake was significantly lower in the active gum
165 condition (Figure 3B).

166 **Appetite ratings**

167 **Pre-lunch ratings**

Chewing gum with or without active ingredients was associated with a lower pre-lunch hunger perception compared to no treatment (mean difference active gum vs no gum -7.89±2.96, 14.6%, p = 0.01; placebo gum vs no gum -10.55±3.46 mm, 18.2%; p = 0.004). No significant differences were observed between active and placebo gum (p = 0.41, NS) (Table 4). Similarly, prospective food consumption ratings were also significantly lower in the chewing gum arms compared to no gum (Table 4) and pre-lunch fullness perception was higher in the chewing gum arms compared to no treatment (mean difference active gum vs no gum 7.89±3.22, 31.0%, p = 0.018; placebo gum vs no gum 5.80±2.98 mm, 22.8%; p = 0.057, NS), although only the active gum reached statistical significance. No significant differences were observed between active and placebo gum in this regard (p = 0.57, NS).

Post-lunch ratings

As expected, hunger and prospective food consumption ratings significantly increased and fullness rating significantly decreased between 0 and 4 hours after lunch across all three conditions (p ‹ 0.0001). Hunger ratings increased to a lesser extent over time after chewing the active (15.07 – 50.65 mm, mean difference -5.32±2.25 mm, p = 0.02) or placebo gum (16.02 – 50.77 mm, mean difference -5.83±1.95 mm, p= 0.004) compared to no gum (18.79 – 63.11 mm) (condition time interaction F = 3.26, p = ‹ 0.0001), but no significant differences were observed between the active and placebo gum (Figure 4 A). Similar results were obtained regarding prospective food consumption (condition time interaction F = 3.10, p = ‹ 0.0001) (Figure 4 B).

In accordance with the other appetite ratings, fullness decreased to a lesser extent along four hours after lunch after chewing the active gum (71.18 – 41.07 mm, mean difference 5.54±2.50 mm, p = 0.03) or placebo gum (71.93 – 37.79 mm, mean difference 6.12±2.23

mm, p= 0.008) compared to no gum (69.00 – 27.19 mm) (condition time interaction F = 2.87, p = ‹ 0.0001) (Figure 4 C). No significant differences were observed between active and placebo gum.

Food preferences and hedonic profile

No significant differences were observed between conditions regarding explicit liking and implicit wanting bias for high fat foods. Conversely, there was a significant change in implicit wanting bias for sweet foods consistent with a reduction in the relative selection of sweet snacks vs savoury snacks in the active and placebo gum conditions compared to no gum. No differences were observed in explicit liking bias for sweet foods (Table 5). While there were no significant changes in the choice frequency score for any of the food categories of the LFPQ with the placebo gum compared to no gum, the active gum condition was associated with a significant decrease in low fat sweet choice frequency and a corresponding increase in low fat savoury snack selection in the LFPQ compared to no gum (Table 5).

DISCUSSION

The design of the present study, with two different gum conditions (active and placebo gum) and a no gum condition contributes to our knowledge of the effects of chewing gum on snack intake and appetite sensations, per se, separated from the possible effects of the compounds present in the active treatment. Regarding the effects of chewing placebo gum on ad libitum snack intake, several results deserve special attention. Specifically, while there was a reduction in low fat sweet snack intake in the placebo gum condition compared to no gum, this was not reflected in a significant change in total caloric intake. This might be explained, at least in part, by the absence of significant changes observed in the selection of other types of snack, that might reduce the impact of this subtle effect on low fat sweet

snack intake relative to total caloric intake. Interestingly, these results might reconcile some discrepancies reported in other studies that evaluated the effects of chewing gum in free living and laboratory conditions. For instance, Julis and Mattes [21] did not find any effect of chewing gum on spontaneous food intake in a free living study where subjects could freely choose the amount and type of snack to eat after a fixed meal. On the other hand, in a very well designed laboratory study, Hetherington and Regan [22] found that chewing gum was associated with a subtle but statistically significant reduction in snack intake (of approximately 25 kilocalories less from sweet snack intake compared to no gum and 11.5 kilocalories less from salted snacks). However, these results were obtained following a study protocol that required that subjects attend the lab on four different occasions (two in the chewing gum condition and two with no gum consumption), and on each visit they were given access to only one kind of snack (savoury in one visit and sweet in the other), so, although it allowed to test the effects of chewing gum on caloric intake from savoury and sweet snack intake, it did not allow for the evaluation of the effects of this intervention on snack selection, as was possible in the free living study of Julis and Mattes or in the present study.

Interestingly, the active gum condition was associated to a significant reduction in total energy intake from snacks, mainly as a consequence of a reduction in caloric intake from low fat and high fat sweet snacks. Taking into account that this effect was significantly different than the one observed in the placebo condition, it supports the hypothesis that snack intake reduction does not stem from orosensory stimulation or mechanical effort caused by chewing gum per se, as the active and placebo gum shared organoleptic properties. Conversely, other mechanisms should be further evaluated, especially the role of the active ingredients present in Lisopresol gum. For instance, it has been reported that

chlorogenic acid – the main compound present in green coffee extract – might increase GLP-1 intestinal secretion in vivo [23] and in vitro [24]. Interestingly, intracerebroventricular injection of exendin-4 (a long acting GLP-1 agonist) in rats reduces intake of a palatable high fat diet [25], and chronic treatment with the GLP-1 agonist exanatide reduces sweet taste preference in rats [26], suggesting that GLP-1 stimulation might mimic the effects in food preference observed in the present study. However, future studies will be needed to test this hypothesis, as GLP-1 levels were not evaluated in the present study.

Another compound present in the active gum that deserves further attention is hydroxycitrate, the active ingredient of Garcinia Cambogia. Consistent with our findings, in a study conducted by Westerterp-Plantenga and Kovacs [27], the administration of 900 mg/day of hydroxycitrate to overweight subjects significantly reduced 24 hour energy intake, mainly due to a reduction in energy intake between meals, without affecting satiety perception. However, in a recent study from our lab conducted in healthy volunteers supplemented with a nutraceutical product containing Garcinia Cambogia and Ascophyllum nodosum extract, we evidenced a significant reduction in hunger perception, but energy intake did not change compared to placebo [13].

Regarding appetite ratings, chewing gum was associated to a reduction in hunger and prospective food consumption and an increase in fullness perception that was evidenced four hours after breakfast and along four hours after lunch.

Taking into account that these suppressive hunger effects were observed after chewing placebo or the active gum, these results support the notion that chewing gum per se might be an effective aid to reduce hunger perception. This is in agreement with the results

reported by Hetherington and Boyland [28] in normal and restrained eaters [23] that demonstrated that chewing gum reduced postprandial hunger perception compared to no gum. Nevertheless, other authors failed to prove any effect of chewing gum on hunger perception [21-22], suggesting that methodological aspects may account for the observed results. Specifically, it is important to mention that in Julis and Mattes studies, the study intervention consisted of only a single gum-chewing episode. Conversely, in the Hetherington and Boyland study [7, 23], subjects were instructed to chew gum every hour for three hours, and in the present study appetite profile was evaluated after chewing four gums prior to lunch and for four hours after lunch, with a total of eight gums consumed in the day. This suggests that repeated chewing gum exposure might be needed in order to promote satiety. This is consistent with the notion of sensory specific satiety (the relative decrease in pleasure aroused by a food just eaten to satiation in contrast to uneaten foods) [29], as it has been reported that there is a direct relationship between the duration of oral sensory exposure and satiety ratings [20,30].

Regarding food hedonics, it is important to mention that meanwhile chewing the active and placebo gum was associated with a reduction in the relative selection of sweet snacks in the LFPQ, only the active gum was associated to a change in low fat sweet and low fat savoury snack choice frequency. This suggests that the active gum condition may influence food preferences by means of a mechanism different to oro-sensory stimulation, as these effects were not observed in the placebo gum condition. Nevertheless, future studies are needed in order to further address this issue.

CONCLUSION

In conclusion, chewing gum hourly during the day reduces hunger sensations and increases fullness in normal and overweight subjects. Meanwhile this effect was not accompanied by changes in snack intake with the use of a placebo containing gum, chewing a gum containing green coffee extract, Garcinia Cambogia and L-carnitine was also related to a significant reduction in energy intake from snacks in our experimental conditions, mainly through a reduction in high fat sweet snack intake. Although future studies are needed in order to further evaluate the mechanisms involved in this effect, this study supports the notion that chewing gum containing nutraceutical products might be an aid to control snack intake and reduce hunger sensations.

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373

374 **Figure Legends**

375 **Fig. 1** Total energy intake from snacks. Data shows mean (± SE) energy intake (kcal) from
376 snacks after no gum (open bar), placebo gum (dotted bar) and active gum (closed bar)
377 conditions. n = 57. ** p ‹ 0.01 vs. no gum; # p ‹ 0.05 vs. placebo gum.

378 **Fig. 2** Snack intake pattern. Data shows mean (± SE) energy intake (kcal) from snacks
379 classified by its fat content and taste (low fat savoury, high fat savoury, low fat sweet and
380 high fat sweet) after no gum (open bar), placebo gum (dotted bar) and active gum (closed
381 bar) conditions. n = 57. **Condition effect ‹ 0.01.

382 **Fig. 3** Composite analysis of energy intake from snacks classified by its fat content (panel
383 A) and taste (panel B). Data shows mean (± SE) energy intake (kcal) from snacks after no
384 gum (open bar), placebo gum (dotted bar) and active gum (closed bar) conditions. n = 57. *
385 p ‹ 0.05 vs. no gum; ** p ‹ 0.01 vs. no gum; ## p ‹ 0.01 vs. placebo gum.

386 **Fig. 4** Subjective appetite along four hours after meal. Data shows mean (± SE) visual
387 analog scale score for hunger (panel A), prospective food consumption (panel B) and
388 fullness (panel C) after no gum (open circles), placebo gum (closed triangles) and active
389 gum (closed boxes) conditions. N = 57.