JEIMP
THE SCIENCE
Journal of
European Internal Medicine Professionals
J Eur Int Med Prof
2023, Volume 1(4)

10.5281/zenodo.10019780
Original Article

The Effect of Hot Pepper, Sumac, and Chewing on Gastric inhibitory peptide, Glucagon-like Peptide, and Cholecystokinin Hormone Secretion

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Received: 26.06.2023 **Accepted**: 03.07.2023 **Published**: 20.10.2023

ABSTRACT

Background: The influence of various dietary factors on metabolic responses and gastrointestinal function has been the subject of extensive research. In this study, we aimed to investigate the effects of capsaicin, chewing, and sumac on metabolic parameters and gastrointestinal function in healthy male volunteers.

Methods: A total of 33 healthy male volunteers aged 18 to 40 years were recruited for the study. Participants underwent four different experimental groups: capsaicin (n=10, a mixed meal containing 467 kcal [22% protein, 46% fat, 32% carbohydrates] and 1 g of capsaicin), chewing (n=11, chewed sugar-free and non-artificial sweetener gum for 5 minutes), sumac (n=7, a meal containing a total of 328 kcal [28% fat, 63% carbohydrates, 9% protein] and 2 g of sumac, and sumac with defecation groups (n=10, a meal containing a total of 328 kcal [28% fat, 63% carbohydrates, 9% protein] and 2 g of sumac. Metabolic parameters including glucose, insulin, Glucagon-like peptide-1 (GLP-1), glucose-dependent insulinotropic polypeptide (GIP), and cholecystokinin (CCK) levels were measured from blood at 0, 5, 10, 25, 45, 60, 120, and 180 minutes following digestion. Gastrointestinal function was assessed by monitoring bowel movements, stool consistency, and appetite levels. $p<0.05$ was assumed statistically significant.

Results: The addition of capsaicin did not result in significant changes in glucose, insulin, GIP, GLP-1, and CCK levels, as well as appetite and energy intake. Chewing sugar-free gum also had no significant effects on the examined parameters. Similarly, the consumption of sumac did not lead to significant alterations in glucose, insulin, GIP, GLP-1, and CCK levels, appetite, or energy intake. However, it was observed that sumac consumption for one week resulted in looser stools without affecting bowel movement frequency or appetite.

Conclusion: Our findings suggest that chewing or the inclusion of capsaicin, or sumac in the diet does not exert significant effects on metabolic parameters and appetite in healthy male volunteers. However, sumac consumption over a one-week period was associated with a change in stool consistency. Further investigations are required to elucidate the underlying mechanisms responsible for the observed effects and to explore the potential long-term implications of these dietary factors on metabolic and gastrointestinal health.

Keywords: Capsaicin, chewing, cumac, gastrointestinal function, metabolic parameters

INTRODUCTION

Nutrition is essential for maintaining a healthy lifestyle. The central centers regulating feeding behavior are located in the brain, particularly in the hypothalamus and its surroundings (1). Signals from adipose tissue, the gastrointestinal system, and other organs involved in metabolic events reach the central nervous system through neural and humoral mediators. Necessary adjustments are made, and then these signals are transmitted to the periphery through neural, endocrine,

and paracrine mediators (2).

Several hormones play a role in appetite regulation, including cholecystokinin (CCK), gastrin, ghrelin, gastric inhibitor peptide (GIP), glucagon-like peptide-1 (GLP-1), GLP-2, motilin, oxyntomodulin, postprandial insulin and hyperglycemia (PHI/PHV), pancreatic polypeptide (PP), peptide YY3-36 (PPY3-36), secretin, somatostatin, leptin, bombesin, gastrin-releasing peptide (GRP), and apolipoprotein A/V (APO-A/V) (3-6). Among these hormones, GIP is closely related to fat metabolism (7). Although the mechanisms of GIP secretion are not fully understood, various studies have observed that it is influenced by the type of meal and the composition of consumed fats (7,8). It is thought that sensory afferent nerves of the intestine and enteroendocrine cells play a role in this secretion (9).

The fact that GIP secretion starts to increase immediately after a meal (5-15 minutes) suggests that central mechanisms may also play a role in the control of hormone secretion (10). GIP is also present in saliva, and the amount of GIP in saliva decreases after meals (10). Chewing is probably decreasing GIP levels (11). Postprandial plasma levels of CCK can vary depending on the content of the food consumed. While both CCK and GLP-1 are involved in appetite regulation and satiety, their interactions and potential effects on each other are still being studied, and the precise relationship between postprandial CCK levels and GLP-1 remains unclear (12).

Capsaicin is one of the main components of chili pepper (13). Thousands of transient receptor.potential vanilloid-1(TRPV1; capsaicin receptor) receptors are found on sensory nerves. Capsaicin activates the TRPV1 channel, which is predominantly expressed in sensory neurons. Activation of the TRPV1 channel leads to the influx of calcium ions (Ca2+) into the sensory nerve cells, resulting in depolarization and the generation of action potentials. However, the exact action of capsaicin on gastrointestinal motility is unclear (14,15).
Capsaicin increases blood flow in the gastrointestinal system. Its effects on fat absorption and energy are believed to occur through sympathetic activity. It has been shown that it has a positive effect on appetite and fat metabolism (16,17). It is thought that dietary chili pepper supplementation or using it as a food additive with an ideal dosage may be a tentative method for capsaicin to play its protective roles in metabolic health (18). Smeets et al. reported that an acute lunch containing capsaicin had no effect on satiety, energy expenditure, and peptide YY but increased GLP-1 and tended to decrease ghrelin (18). GIP, which is highly likely to undergo changes in its blood levels due to capsaicin administration, was not studied in these experiments.

Another spice that is expected to alter peptide hormones secreted from the intestine is sumac. It has been shown that sumac extracts lower blood sugar levels in humans and inhibit carbohydrate digestion enzymes such as amylase and alpha-glucosidase in vitro environments (19,20). It has been demonstrated that inhibitors of amylase and alpha-glucosidase, when given with or before a meal, increase GLP-1 levels and decrease GIP levels (21,22). Whether sumac has a similar effect is not yet known.

This study aims to investigate the effects of capsaicin, chewing, and sumac on metabolic parameters and gastrointestinal function in healthy volunteers by examining the influence of these dietary factors on various metabolic parameters such as glucose, insulin, GLP-1, GIP, and CCK levels. We also aim to assess the impact of capsaicin, chewing, and sumac on gastrointestinal function, including bowel movements, stool consistency, and appetite levels.

METHODS

Participants and Study Design

A total of 35 volunteers enrolled in the study. Twenty-five individuals were involved in peptide measurements, while 10 individuals were involved in stool characterization. Volunteers were recruited by posting advertisements explaining the experiment and its purpose at the Marmara University Faculty of Medicine Hospital. Those who responded to the advertisements were interviewed face-to-face, provided with detailed information, and enrolled in the study after giving written consent. The study received approval from the Marmara University Ethics Committee in June 2009 (Ethics Committee decision no. MAR-Y4-2009-0226, dated June 5, 2009). One participant who was involved in the chewing experiments was excluded from the study because they were diagnosed with type 2 diabetes. Another participant did not attend the experiments in the second week, so their data were not used. The total number of completed participants in the study is 33.
All participants' height.and.weight were measured, and their body mass index(BMI) was calculated (BMI = Body Weight (kg) / Height (m)²). Individuals with a BMI between 20-25 kg/m² were considered to have a normal weight, those with a BMI between 25-30 kg/m² were considered overweight, and those with a BMI above 30 kg/m² were considered obese.

Inclusion criteria: Healthy male volunteers between the ages of 18-40 without any known illnesses were included in the study.

Exclusion criteria: Individuals who have consumed water within the past 2 hours or have chewed gum, individuals who have smoked within the past 12 hours, individuals who have taken any medication within the past week, individuals who have had a febrile illness within the past week, individuals who have attempted

to follow any diet program within the past month, individuals who have experienced a weight change of more than 5% in the past 3 months, individuals with a BMI over 30 for meal-based studies, individuals who have consumed more than 210 grams of alcohol per week, and individuals with systemic illnesses.

Experimental Groups

Capsaicin group (n=10): A meal containing a total of 467 kcal was given. The meal consisted of 100 g of eggs, 10 g of butter, 30 g of low-fat cheese, and 70 g of white bread, with a composition of 22% protein, 46% fat, and 32% carbohydrates. The participants were given the meal with or without the addition of 1 g of capsaicin, with at least a one-week interval between the two conditions. Blood samples were taken at 0-5-10-25-45-60-120 and 180 minutes after the meal. Four hours after the meal, all participants were allowed to eat until they were full at a buffet, and the amount and type of food consumed were recorded. The participants' hunger and satiety levels were recorded using a visual scale before and after each meal. The Capsaicin content of the red pepper ingested with the meal was determined by a High-Performance Thin Layer Chromatography (E Yeşilada) using methanolic extracts at Yeditepe University Faculty of Pharmacy.

Chewing group (n=11): Participants chewed sugar-free and non-sweetened FALIM gum for 5 minutes. Blood samples were taken at 0-5-10-25-45 and 60 minutes after chewing. One participant was excluded from the study due to a new diagnosis of diabetes.

Sumac group (n=7): A meal containing a total of 328 kcal was given. The meal consisted of 350 g of potatoes, 10 g of olive oil, and unsweetened tea, with a composition of 28% fat, 63% carbohydrates, and 9% protein. The participants were given the meal with or without the addition of 2 g of sumac, with a one-week interval between the two conditions. Blood samples were taken at 0,10,30,60,90,120, and 150 minutes after the meal. Three hours after the meal, all participants were asked to eat until they were full at a buffet, and the participants' hunger and satiety levels were evaluated using a visual scale before and after both meals.

Sumac and defecation groups (n=10): Participants were monitored for 15 days regarding their daily number of bowel movements, the type of stool according to the Bristol scale, and their hunger level before the evening meal and their satiety level after the evening meal. During one week, participants were given 2 g of sumac along with a desired meal. The participants' diet was not intervened during this study.

Determination of Hunger and Satiety Levels

Before starting each meal and immediately after finishing, participants were asked to indicate their level of hunger or satiety on a visual scale ranging from 1 to 10, where 0 represented very hungry and 10 represented very full.

Measurement of Energy Intake

In the capsaicin experiments, 4 hours after the initial meal, and in the sumac experiments, 3 hours after the initial meal, participants were provided with food and beverages in a pizzeria in the desired amounts, and all consumed items were recorded. The calorie content and distribution of macronutrients in the consumed meal were calculated using specialized software (Ebispro for Windows, Stuttgart, Germany; Turkish version: BeBiS, Version 6.1) with the assistance of a dietitian. The nutritional content of the food items in the software is derived from the German Food Code and Nutrient Database (Bundeslebensmittelschluessel; BLS) at a 97% rate, with the remaining data obtained from the USDA database.

Blood Sampling and Storage Conditions

Venous blood samples for GIP, CCK, and GLP-1 analysis were obtained from an indwelling venous catheter at specified time points as mentioned above. Aprotinin (AppliChem, Darmstadt, Germany, catalog no: A2132, 6511,52 g/mol, 6000 KIU/mg) was dissolved in physiological saline. Venous blood was collected into chilled tubes containing aprotinin (5000 KIU/ml of blood) and EDTA (1 mg/ml of blood; Merck, Darmstadt, Germany). The tubes were centrifuged at 4°C, and plasma was immediately stored at -20°C until assayed. Blood samples for glucose and insulin analysis were collected into blank tubes, centrifuged at 4°C, and measurements were done immediately.

Peptide determination

CCK, GIP, and GLP-1 measurements were conducted at the University of Copenhagen using the radioimmunoassay (RIA) method. CCK was determined using antibody 92128 in the biochemistry laboratory of the University of Copenhagen (23). GIP and GLP-1 were determined using antibodies R65 and 89390, respectively, in the clinical physiology laboratory of the University of Copenhagen (24).

Plasma concentrations of CCK, GIP, GLP-1, PYY, and PP were all measured by highly specific RIAs: CCK using the antibody 92128 (23), GIP using antibody R65, and GLP-1 using antibody 89390 by methods (24). Insulin concentrations were measured immunometrically (Modular E, Roche Diagnostics, Germany). Measurements were conducted in the clinical physiology laboratory of the University of Copenhagen.

Capsaicin Determination

The Capsaicin content of the red pepper ingested with the meal was determined by High-Performance Thin Layer Chromatography (E Yeşilada) using methanolic extracts at Yeditepe University Faculty of Pharmacy (25)

Insulin and Glucose Determinations

Insulin and glucose levels in the separated serum samples were analyzed immediately at the Marmara Biochemistry Center laboratory. Glucose levels were measured spectrophotometrically using the Roche-Hitachi 917 kit and the Roche Hitachi Modular Analytics device. Insulin was determined using the electrochemiluminescence immunoassay method with the Modular Analytics E170 device and the COBAS kit.

STATISTICAL ANALYSIS

The continuous data were expressed as mean and standard deviation, while categorical data were presented as median and range. Parametric tests were used for normally distributed continuous data, and nonparametric tests were used for non-normally distributed continuous data and categorical data.

In the experiments investigating the effects of sumac, chili pepper, and chewing, the area under the curve (AUC) of insulin, glucose, and peptide levels, obtained by plotting them against time, was calculated using the trapezoidal method. Differences between experimental days were analyzed using paired t-tests. The effect of time on changes in glucose, insulin, and peptide levels was evaluated using one-way ANOVA, while the combined effect of time and treatment was analyzed using two-way ANOVA. Additionally, the values obtained from experiments with and without chili pepper/sumac at each sampling time were compared using paired t-tests. In the sumac and defecation experiments, the daily number of stools and stool patterns for each participant were averaged for weeks with and without sumac, and the means were compared using paired t-tests. P-values less than 0.05 were considered statistically significant.

RESULTS

The number of participants in each experiment and the demographic and anthropometric characteristics of the participants are presented in Table 1.

The Effect of Chili Pepper

a. Effect on Serum Glucose and Insulin Levels

The changes in serum glucose and insulin levels before breakfast and during the following 180 minutes in the chili pepper experiments are summarized in. In the chili pepper experiments, serum glucose was significantly higher at 45 minutes compared to the baseline ($p<0.05$), while no significant increase in serum.glucose.was observed in the experiments without chili pepper. Consumption of chili pepper did not cause any significant differences in serum glucose levels at the time points of blood sampling, and the total area under the.glucose. curve was similar in both the chili pepper and non-chili pepper experiments. When considering the combined effect of time and treatment (two-way ANOVA), it was observed that the changes in glucose levels were time-dependent ($p<0.001$ for time, $p=0.90$ for treatment, and $p=0.99$ for time and treatment) (Figure 1).

Serum insulin levels were significantly higher than the baseline at 25 and 45 minutes in the experiments without chili pepper ($p<0.05$), and at 25, 45, and 60 minutes in the chili pepper experiments ($p<0.01$, $p<0.05$, and $p<0.01$, respectively). There were no significant differences in insulin values at the time points of blood sampling between the experiments, and the area under the insulin curve did not differ between the two experiments (Table 2). When evaluating the combined effect of time and chili pepper (two-way ANOVA), it was found that the changes in insulin levels were only influenced by time ($p<0.0001$ for time, $p=0.55$ for chili pepper, and $p=1$ for time and chili pepper).

b. Effect on Plasma Peptides (GIP, GLP-1, and CCK)

CCK: In the control experiments, plasma CCK levels increased above baseline at 45-180 minutes ($p<0.01$). In the chili pepper experiments, plasma CCK levels increased at 25-180 minutes ($p<0.01$) and remained elevated at 180 minutes ($p<0.05$). There was no significant difference in plasma CCK levels between the time points of blood collection. The area under the CCK curve was similar in both experimental groups. Plasma CCK levels showed a significant time-dependent change, while they were not affected by chili pepper ingestion (Two-way ANOVA, time: $p<0.001$, chili pepper: $p=0.75$, time*chili pepper: $p=0.90$) (Figure 1).

Table 2. Serum glucose and insulin levels in the chili pepper experiments

Time, minute	0	5	10	25	45	60	120	180	AUC†	AUC†
Glucose mg/dl									mg/dl/min	
Capcaicine free	89.60±18.65	88.50±20.17	91±17.8	106.7	105,6±23,9	100±30.5	93.2±22.9	93.8±17.4	96.92±21.89	98.62±23.12
Capcaicine	89.3 ±10.53	87.9 ±9.34	91.8±10.8	105.6±12.36	108.7±19.10	104.2±21.2	89.1±12.8	92.0±8.40	96.35±12.4	99.2±14.6
Insulin mIU/ml									mIU/ml/min	
Capcaicine free	6.98± 4.86	11.55± 9.2	16.78± 9.8	46.65± 63.3	45.69±42.18	43.63±34.46	19.3±14.23	9.1±5.0	26.79± 2.17	
Capcaicine	5.9±2,86	7.0± 4.0		42.9±36.15	35.96± 30.1	44.53± 5.98	14.85±11.2	7.96±4.08	24.17±12.93	

The data, presented as mean ± standard deviation, was analyzed using nonparametric paired t-test. The area under the curve (AUC) was calculated for each participant. † Significant difference compared to baseline ($p<0.05$)

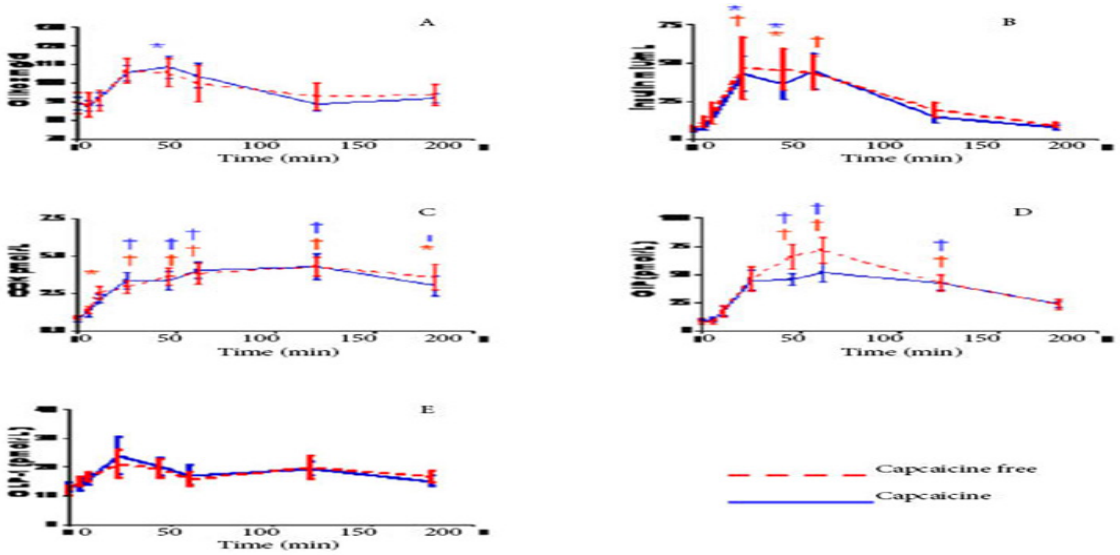

Figure 1. Response of glucose (A), insulin (B), CCK (C), GIP (D), and GLP-1 (E) during a 180-minute period in experiments with spicy pepper (blue solid line) and without spicy pepper (red dashed line), following the consumption of a mixed meal containing 467 kcal (22% protein, 46% fat, 32% carbohydrates). Glucose was significantly higher at 45 minutes in the spicy pepper experiment, while insulin was higher at 25 and 45 minutes in the non-spicy pepper experiment and at 25, 45, and 60 minutes in the spicy pepper experiment compared to baseline. CCK levels were higher at 45-180 minutes in the non-spicy pepper experiments and at 25-180 minutes in the spicy pepper experiments, while GIP response was higher at 45-120 minutes in all experiments compared to baseline. GLP-1 levels did not exceed the baseline. The consumption of spicy pepper did not result in significant changes in the examined parameters. †p<0.01, *p<0.05 compared to baseline.

GIP: In both the control and chili pepper experiments, plasma GIP levels increased above baseline at 25, 45, 60, and 120 minutes. There was no significant difference between the total integrative GIP response and the plasma GIP levels at the examined time points between the two experiments. Plasma GIP levels showed a significant time-dependent change, while they were not affected by chili pepper ingestion (Two-way ANOVA, time; p<0.0001, chili pepper; p=0.128, time*chili pepper; p=0.40) (**Figure 1**).

GLP-1: There was no significant increase in plasma GLP-1 levels compared to the baseline in all experiments. There was no significant difference in GLP-1 levels between the examined time points in the experiments, and the area under.the.curve was similar. The two-way ANOVA test did not show any significant difference related to time or chili pepper ingestion (Two-way ANOVA, time; p=0.22, chili pepper: p=0.30, time*chili pepper; p=0.90) (**Table 3**).

c. Effects on appetite and total energy intake

There were no significant differences in the degree of hunger before breakfast or before lunch between the non-spicy pepper and spicy pepper experiments (**Figure 2**). Similarly, there were no differences in hunger ratings before and after the buffet meal between the experiments. There were no significant differences in total energy intake or the distribution of energy intake according to food groups during the buffet meal.

Effect of Chewing

a. Impact on serum glucose and insulin levels

Chewing sugar-free gum for five minutes did not significantly alter glucose and insulin values at 0, 5, 10, 25, 45, and 60 minutes compared to baseline levels.

b. Influence on plasma peptides (GIP, GLP-1, and CCK)

Table 3. Plasma levels of CCK, GIP, and GLP-1 in chili pepper experiments

Time, minute	0	5	10	25	45	60	120	180	AUC† (0-180)	AUC (0-120)	AUC (0- 75)
CCK pmol/L									pmol/L/min		
Capcaicine free	0.90±0.41	1.37±0.76	2.51±1.39	2.93±1.32	3.60±1.83	3.83±2.26	4.27±1.92	3.59±2.75	3.14±1.92		
Capcaicine	0.83±0.55	1.21±0.88	2.13±0.93	3.35±1.67	3.33±1.92	4.05±1.68	4.27±2.75	3.01±.,01	3.37±1.90		
GIP pmol/L									pmol/L/min		
Capcaicine free	4.50±4.51	7.88±4.83	17.25±14.35	50.00±26.29	69.20±2.,47	71.55±34.88	46.00±19.30	25.16±10.72	43.91±21.50	47.29±23.23	55.33±27.80
Capcaicine	6.55±5.01	8.22±4.71	19.12±11.19	51.33±25.03	48.87±9.59	53.88±21.90	44.10±19.77	23.55±8.06	43.85±19.84	41.02±16.08	48.29±16.63
GLP-1 pmol/L									pmol/L/min		
Capcaicine free	12.38±3.95	14.88±4.62	16.71±4.68	18,16±9.21	15.90±4.30	15.77±7.17	16.25±4.30	14.83±3.81	16.07±5.94	14.76±5.57	
Capcaicine	14.10±5.49	16.11±5.66	17.50±4.75	17.55±4.90	17.42±4.11	16.00±4.92	18.22±6.03	15.11±5.23	15.96±7.24	15.75±3.69	

N=10, the data were expressed as mean±standard deviation and compared using nonparametric paired t-tests. The area under the curve (AUC) was calculated.†

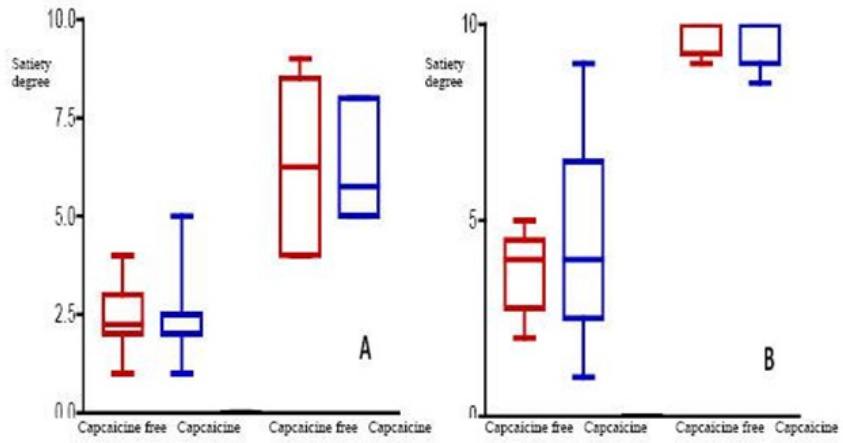

Figure 2. Degree of fullness perceptions before and after (A) breakfast and (B) lunch in the non-spicy pepper (red) and spicy pepper (blue) experiments. Consuming spicy pepper did not significantly alter the feeling of fullness.

Chewing sugar-free gum for five minutes did not result in a significant change in plasma peptide levels at 0, 5, 10, 25, 45, and 60 minutes.

Sumac's Effect

a. Impact on serum glucose and insulin levels

Glucose: Fasting plasma glucose levels were similar between the experiments with and without sumac. The mixed meal significantly increased plasma glucose levels compared to baseline at 30 minutes on both sumac and non-sumac experiment days ($p<0.01$). There was no significant difference in glucose values between the two experimental groups at the time points of blood collection. Similarly, the area under the curves obtained by plotting glucose values over time was similar for both sumac and non-sumac experiment days. In two-way analyses, time significantly influenced glucose levels ($p<0.0001$), while sumac consumption did not have a significant effect ($p=0.35$). When both variables were evaluated together, there was no significant difference between the experiment days ($p=0.66$).

Insulin: Fasting serum insulin levels were similar between the experiments with and without sumac. The mixed meal, whether consumed alone or with sumac, significantly increased serum insulin levels at 30 and 60 minutes compared to baseline ($p<0.01$). There was no significant difference in insulin measurements between the experiments at the time points of blood collection.

The area under the curve obtained by plotting insulin values over time did not differ between the experiments with and without sumac. When time and sumac consumption were evaluated together, it was observed that time significantly influenced insulin levels ($p<0.0001$), while sumac consumption did not have a significant effect($p=0.60$), and there was no interaction between time and sumac ($p=0.99$).

CCK: Fasting plasma CCK levels were similar between the experiments with and without sumac. The mixed meal significantly increased plasma CCK levels at 30 and 60 minutes in the experiments without sumac ($p<0.01$) and at 60 and 90 minutes in the experiments with sumac ($p<0.05$) compared to baseline. The plasma CCK level in the experiments with sumac showed a slightly delayed and prolonged elevation compared to the control experiments, but there was no.significant. difference between the two experiment days at the time points of blood collection. The area under the curve was similar in both experiments. Two-way analyses showed that only time had a significant effect on plasma CCK levels ($p=0.02$), sumac did not have a significant effect ($p=0.67$), and there was no significant interaction between the two factors ($p=0.43$).

GIP: The mixed meal, whether consumed with or without sumac, significantly increased plasma GIP levels at 30, 60, 90, and 120 minutes compared to baseline ($p<0.01$ at 30, 60, and 90 minutes, and $p<0.05$ at 120 minutes for both experiments). There was no significant difference. between the experiment days in terms of the total GIP response or the time points of blood collection. Time had a significant effect on plasma GIP levels ($p<0.001$), while sumac consumption did not have a significant effect, either alone ($p=0.43$) or in combination with time ($p=0.96$).

GLP-1: Plasma GLP-1 levels did not increase above baseline levels in both the experiments with and without sumac. There was no significant difference between the experiment days in terms of the total integrative GLP-1 response or the GLP-1 levels at the time points of blood collection. Two-way analyses showed that time ($p=0.15$), sumac ($p=0.59$), and the interaction between time and sumac ($p=0.88$) did not significantly affect plasma GLP-1 levels.

The effect of sumac on appetite and total energy intake

There was.no.significant difference in terms of hunger levels before breakfast or before lunch between the control experiments and the experiments with sumac.

Similarly, there was.no difference in hunger levels before and after the buffet meal between the experiments. There was no significant difference in total energy intake or the distribution of energy intake according to food groups during the buffet meal.

The effect of sumac on defecation

The stool consistency, as assessed by the Bristol Stool Scale, had a median score of 3 during the control week. However, during the week when 2 grams of sumac were consumed daily, the stool consistency had a median score of 4, and the difference between the weeks was statistically significant ($p < 0.05$). The average number of daily bowel movements was 0.59 during the week without sumac consumption, while it was 0.53 during the week with sumac consumption. However, this difference was not statistically significant ($p = 0.17$).

There was.no.significant difference in the subjective feeling of fullness evaluated before and after dinner between the control week and the week with sumac consumption.

DISCUSSION

This study investigated the potential effects of chili peppers and sumac on various physiological processes, including blood sugar levels, intestinal peptides, appetite, and bowel habits. However, the results did not show significant changes in these parameters compared to the control experiments. These findings suggest that the dosage or duration of use may play a role in eliciting the desired effects. Further research is needed to explore the optimal dosage, duration, and specific components of these spices to fully understand their potential health benefits.

Spices have been used for centuries in various geographical regions, both to enhance the flavor of dishes and to treat various illnesses. Recent studies conducted in various disciplines have begun to shed light on the biological/physiological basis of the healing or digestive effects of spices, demonstrating that they may possess certain properties that could potentially be used as medicine (26,27).

Some of the mechanisms that regulate the secretion of intestinal peptides involved in appetite and gastrointestinal function depend on the perception of luminal nutrients (28,29). Structures involved in this perception include enteroendocrine cells, interneurons, extrinsic nerves, the central nervous system, and taste receptors located in enterocytes. Numerous studies have shown the role of sensory afferent nerves in the secretion of GLP-1, GIP, and CCK, which have been shown to have an impact on appetite and metabolism (30,31). However, it should be noted that there are likely other known and unknown mechanisms involved in the secretion of these peptides.

Animal studies have suggested that the presence of GIP is a prerequisite for the development of adipose tissue and obesity (32,33). To date, no human study has been conducted to investigate whether chili peppers affect GIP secretion. In our study, we investigated the effect of a single meal with added chili peppers on peptides that are secreted from the intestines and have an impact on appetite and metabolism, over a period of 2 hours following the meal, in healthy volunteers. We used a mixed meal that was richer in fat compared to a regular meal in order to stimulate GIP secretion further. According to our results, the administration of 1 g of chili pepper with a relatively fat-rich mixed meal did not cause a significant change in glucose, insulin, CCK, and GLP-1 levels. It flattened the GIP curve, but there was no significant difference in the integrated GIP response between with and without chili pepper. The perceived satiety level determined by a visual scale and the energy content of the meal consumed freely in the buffet did not differ between the experimental days, two hours after this meal. Our findings are not consistent with the results of previous studies. The reason for this discrepancy may be that the amount of capsaicin in the chili pepper used was insufficient to produce an effect. Although we provided a standardized amount of chili pepper by weighing it, we were unable to determine the capsaicin content in the chili pepper used, so we could not compare our study results with other studies. Our findings do not provide insights into the effects of long-term continuous use. The observed flattening in the GIP curve suggests that investigating the effects of larger amounts and longer durations of use would be necessary.

We also investigated whether mechanical stimuli originating from the mouth have any effects on the secretion of intestinal peptides. Various studies have suggested that visual perception of food, odor perception of food, and sham feeding can alter the secretion of intestinal peptides through central mechanisms (34-36). Although the presence of GIP in saliva and its increase with sham feeding have been previously demonstrated, the effect of mechanical stimulation without food contact on plasma GIP secretion is unknown. In our study, we did not observe any changes in plasma peptide levels due to mechanical stimulation without food contact. We did not investigate GIP levels in saliva or total protein content in saliva. Our study is the first to investigate the effect of mechanical stimulation on plasma peptides, and there is no comparable data for comparison.

For the secretion of intestinal peptides that affect appetite and metabolism, nutrients in the lumen need to be present in their broken-down form, absorbed, or bound to a receptor. The secretion of GLP-1 requires glucose binding to the glucose transporter in enterocytes in addition to central reflex mechanisms. The breakdown of carbohydrates and their binding to the transporter is

sufficient for secretion; they do not need to be absorbed. The secretion of GIP is primarily stimulated by fats, and both the breakdown and absorption of fats are required for its stimulation (29,36). CCK secretion is associated with both carbohydrates and fats (38). In order for its secretion to occur, in addition to central reflex mechanisms, the absorption of fatty acids containing more than 10 carbon atoms is necessary.

Sumac is a commonly used spice, and it is a plant with approximately 250 species (39). Various species of sumac have been extracted, and their contents have been determined in Turkey (40). There are numerous experimental studies showing the anti-fibrinogen antiapoptotic, anti-inflammatory, antioxidant, leukopenic, cytotoxic, and hypoglycemic effects of extracts obtained from Sumac (38,40). It is known that sumac extracts exhibit antioxidant effects in diabetics (41-43). The mechanism of action on blood sugar is known to involve the inhibition of alpha-glucosidase and amylase, thereby preventing the breakdown and absorption of carbohydrates (21,44). Since other alpha-glucosidase inhibitors have been used in the treatment. of diabetes, and it has been shown that they increase the secretion of intestinal peptides with incretin-like properties, which are stimulated by carbohydrates in the lumen, it is possible for sumac to have a similar effect.

Based on this possibility, we investigated the effects of consuming 2 grams of sumac with a carbohydrate-rich mixed meal in terms of blood sugar, intestinal peptides, appetite, and total energy consumption in the next meal. There was no difference in glucose, insulin, GIP, GLP-1, CCK responses, appetite, and energy consumption between the sumac and control experiments. The CCK response appeared slightly later and was slightly lower in the Sumac experiment, but the difference was not statistically significant. In this experiment as well, the analysis of the components of the sumac we used was not performed, and the species of the sumac plant was not determined.

To date, no study has been conducted investigating the effects of single-dose sumac consumption on blood sugar. Previous studies have demonstrated hypoglycemic effects using sumac extracts in humans or in vitro environments. However, hypoglycemic effects only occur with long-term use in diabetic patients. The lack of hypoglycemic effect of sumac in this study may be due to the dosage used, single-dose administration, or a small number of subjects. Another possibility is that some species of sumac may have stronger enzyme inhibition properties. It may be more appropriate to evaluate the sumac species used in Turkey and test those that are effective in vitro in humans. The effects of sumac on appetite and the amount of food consumed in the next meal have not been investigated so far. The lack of changes in this study does not provide insights into the effects of continuous and higher doses of sumac use. Sumac is also known to have potential effects on altering carbohydrate digestion in the lumen and exhibiting antibacterial properties (45-47). Therefore, we investigated its effects on bowel habits. Continuous use of 2 grams of sumac for one week did not change the frequency of bowel movements but softened the stool consistency. The observed effect in our experimental setup does not provide information on whether it is related to intestinal flora, carbohydrate digestion, direct mucosal irritation, or any other effect of sumac. This study did not investigate intestinal flora, stool osmolarity, carbohydrate digestion, and antioxidant capacity.

Limitations of the Study

1.Dosage and duration: The study used a single dose of chili pepper and sumac, and the effects were measured over a relatively short period of time (2 hours). The study does not provide insights into the effects of long-term or higher doses of spice consumption.

2.Lack of human GIP study: While animal studies have suggested the role of GIP in adipose tissue development, no human study has been conducted to investigate the effect of chili peppers on GIP secretion. This limits the understanding of the potential impact of chili peppers on GIP levels.

3.Mechanical stimulation: The study investigated the effect of mechanical stimulation on plasma peptide levels without food contact. However, it did not measure GIP levels in saliva or total protein content in saliva, making it challenging to compare the findings with other studies.
4.Lack of analysis and identification: The study did not analyze the specific components or species of the sumac used, limiting the understanding of its potential effects. Different species of sumac may have varying properties, and further investigation is needed to determine their efficacy.
5.Limited sample size: This may limit the statistical power and generalizability of the results.

6.Lack of comprehensive analysis: The study did not investigate several factors related to the effects of spices, such as intestinal flora, stool osmolarity, carbohydrate digestion, and antioxidant capacity. These additional analyses could provide a more comprehensive understanding of the mechanisms and effects of spices on physiological processes.

7.Lack of comparison data: The study mentions the absence of comparable data for certain measurements, making it difficult to contextualize and compare the findings with previous studies.

Conclusion

The spices used in the doses we administered did not alter the secretion of intestinal peptides with single-

dose use, but one week of sumac consumption softened stool consistency. Our findings suggest that evaluating the effects of long-term and high-dose use may lead to the discovery of a potential treatment for diabetes and/or constipation.

DECLARATIONS

Ethical approval: This is a Specialization Thesis and was approved by the Marmara University ethical committee (Decision No: MAR-Y4-2009-0226, Date: 5 June 2009).

This study was conducted in agreement with the Declaration of Helsinki-Ethical principle for medical research involving human subject

Conflict of interest: The authors declare no conflicts of interest.

Acknowledgments: We are thankful to Marmara University clinical research committee for their financial support (Project no.: SAG-C-TUP-171209-0336). Warm thanks to Marmara University gastroenterology institute Zeki Yollu vakfı for support of the shipping price. Peptide determinations were made free of charge at Copenhagen University Biochemistry and Clinical Physiology Laboratories. Very warm thanks to Prof. Dr. Erdem Yeşilada who supported the measurement of capcaisin before he passed away.

Authors also thank Burçin Sağlam, Davut Bilgin, Hüseyin Yıldız, Fatih Akbay, Ferhat Ekinci, Mahmoud Bhais, Mohammad Abu shaaban, Mohammed Abu Awwad, Walid Karim, Aydan Mütiş, Semiha Akbulut, Zakiye Likoğlu, Sare Merve Dörterler, Bilgin Selin, Bamanga Hauwa Amal, Toklong Filam Moses, Yapas Aysulu for assitance and participation and Seyfi Üstünsoy , Medeni Arpa, Rodi Kardaş from biochemsitry department and our technician Ayfer Urun who hepled in centrifusion as well as our Dietitian Esra Gunes who helped in diet content mesaurement.

Funding: This thesis Project was supported by the ‘’Marmara University clinical research committee ‘’for their financial support (Project no.: SAG-C-TUP-171209-0336).

This manuscript is the revised and developed version of the yet unpublished conference presentation entitled “***The effect of hot pepper and sham feeding on the secretion of incretin hormones***,” first orally delivered at the 27th Gastroenterology week (24-28 October 2010) Congress in Antalya.

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