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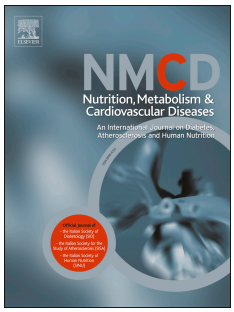

Salba-chia (*Salvia hispanica* l.) in the treatment of overweight and obese patients with type 2 diabetes: a double-blind randomized controlled trial

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Salba-chia (*Salvia hispanica* l.) in the treatment of overweight and obese patients with type 2 diabetes: a double-blind randomized controlled trial

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ABBREVIATIONS: ALA – alpha-linolenic acid, ALT – alanine aminotransferase, CVD – cardiovascular disease, DXA – dual energy x-ray absorptiometry, GLP-1 – glucagon-like peptide-1, Hs-CRP – high-sensitivity C-reactive protein, PT – prothrombin-time, T2DM – type 2 diabetes.

REGISTRATION: clinicaltrials.gov identifier: NCT01403571

ABSTRACT

Background: Preliminary findings indicate that consumption of Salba-chia (*Salvia hispanica* L.), an ancient seed, improves management of type 2 diabetes and suppresses appetite.

Objective: To assessed the effect of Salba-chia on body weight, visceral obesity and obesity-related risk factors in overweight and obese adults with type 2 diabetes.

Methods: A double-blind, randomized, controlled trial with two parallel groups involved 77 overweight or obese patients with type 2 diabetes (HbA_{1c}:6.5-8.0%; BMI:25-40kg/m^2). Both groups followed a 6-month calorie-restricted diet; one group received30g/1000kcal/day of Salba-chia, the other 36g/1000kcal/day of an oat bran-based control. Primary endpoint was change in body weight over 6-months. Secondary endpoints included changes in waist circumference, body composition, glycemic control, C-reactive protein, and obesity-related satiety hormones.

Results: At 6-months**,** participants on Salba-chia had lost more weight than those on control (1.9±0.5kg and 0.3±0.4kg, respectively; P=0.020), accompanied by a greater reduction in waist circumference (3.5±0.7cm and 1.1±0.7cm, respectively; P=0.027). C-reactive protein was reduced by 1.1±0.5mg/L (39±17%) on Salba-chia, compared to 0.2±0.4mg/L (7±20%) on control (P=0.045).Plasma adiponectin on the test intervention increased by 6.5±0.7%, with no change observed on control (P=0.022).

Conclusions: The results of this study, support the beneficial role of Salba-chia seeds in promoting weight loss and improvements of obesity related risk factors, while maintaining good glycemic control. Supplementation of Salba-chia may be a useful dietary addition to conventional therapy in the management of obesity in diabetes.

ClinicalTrials.gov Identifier:NCT01403571

INTRODUCTION

The prevalence of obesity continues to rise worldwide as does the incidence of type 2 diabetes (T2DM) (1). Many strategies have been employed for body weight reduction in this population, but a successful long-term strategy is an unmet clinical goal. Current pharmacological therapies aimed at weight loss are limited in efficacy and hindered by significant adverse effects (2). Therefore, an alternative behavior paradigm that is easy to implement and could reduce body weight while also providing health benefits beyond weight loss is urgently needed (3). The relative success of dietary management to induce weight loss has been more frequently ascribed to an individual's adherence to the prescribed calorie-restricted diet than to relative proportions of macronutrients, or even particular dietary patterns (4-6). Nevertheless, with adequate adherence, individual nutrients such as fiber (7), protein (8), and omega-3 fatty acids (9) have been credited with attenuating cardiovascular disease (CVD) risk factors and aiding in weight regulation. Thus, a dietary approach collectively utilizing efficacious nutrients while maximizing adherence is key to weight and CVD risk factor management.

Salvia hispanica L. (Salba-chia), an ancient seed used as food and remedy by the Aztec civilization, is one of the highest whole food sources of dietary fiber and α-linolenic fatty acids (ALA) per total fat, exceptionally rich in minerals, and a good source of protein (10). Incorporating these components into the diet makes Salba-chia a prime contender in regulating body weight and possibly other comorbidities associated with diabetes. Our preliminary study demonstrated that supplementing 37g/day of Salba-chia to an isocaloric diet improved major and emerging CVD risk factors in T2DM (11), suggesting its cardioprotective potential, while maintaining weight. A subsequent study by our group demonstrated that Salba-chia acutely reduced postprandial glycemia when added to a meal and prolonged satiety (8). These

observations, taken along with the promising nutrient profile of the seeds and previous anecdotal participant reports on feeling of fullness provided a rationale for the present study.

Thus, the objective of the current study was to determine whether 6-month dietary incorporation of Salba-chia will induce a significant weight reduction compared to an oat bran-based control, when consumed in conjunction with a calorie-restricted diet, and added on top of conventional treatment in overweight and obese individuals with T2DM.

METHODS

Participants

Participants were recruited from a single Canadian academic center using existing patient databases and advertisements, between March 2012 and September 2013. Primary inclusion criteria consisted of: age between 35-75 years, presence of T2DM of ≥1 year duration, BMI between 25-40kg/m^2, HbA_{1c} between 6.5-8.0%, stable body weight with <10% reported change over the previous 3-months, and willingness to participate in either study group. Exclusion criteria included: use of insulin therapy, weight-lowering pharmacotherapy, ALA, dietary fiber, or fish oil supplementation, unstable angina, myocardial infarction or stroke within 6 months. The study was approved by the Research Ethics Board of St. Michael's Hospital. All participants provided written consent prior to study enrollment. This study was registered at ClinicalTrials.gov, identifier: NCT01403571.

Design

The study followed a 6-month randomized, double-blind, parallel design. The study was originally conceptualized as a 6 month weight-loss phase followed by a 6-month weight

maintenance phase; the weight-loss study results are reported here. Participants were randomized to one of two interventions using a computer-generated random number table, stratified according to sex. All participants were advised to follow a 500kcal reduced diet daily based on estimated energy requirements using the Harris-Benedict equation. Participants attended the clinic after randomization (0-month), at 2 weeks, and then every 6 weeks for 6-months to receive one-on-one 30min counseling sessions with a study dietitian. Sessions provided participants with advice on following an individualized energy-restricted diet, utilizing study supplements, and following dietary and lifestyle guidelines as outlined by the Canadian Diabetes Association for individuals with T2DM. At each visit, participants completed 3-day food records to assess adherence to the intervention and a symptoms diary to record adverse events. Participants were encouraged to maintain their usual lifestyle as well as maintain a constant level of physical activity throughout the study period, measured by pedometers.

Intervention

Participants were randomly assigned to receive daily either 30g/1000kcal of ground Salba-chia (Salba Smart Natural Products LLC, Centennial, CO, USA) or 36g/1000kcal of an oat bran-based control. Salba-chia (*Salvia hispanica* L.) is a single strain of an oily seed with a highly consistent nutritional composition. Salba-chia is lignin-free, low in available carbohydrate, a rich source of magnesium, calcium and iron, with a total antioxidant capacity of 84/g. The control supplement was conceptualized to act as a positive control, which comprised of a mixture of 25.7g oat bran (PepsiCo, Peterborough, Canada), 7.1g inulin fiber (Pure-le Natural, Barrie, Canada), and 3.2g maltodextrin (Whey-Factory.com, Canada) to match for total dietary fiber (≈10.5g) and energy content (≈115kcal) per day. Both supplements were provided in two forms:

approximately one third were baked into whole-wheat bread and the remainder was provided as a powder to be sprinkled onto food to reduce monotony. Interventions were similar in appearance, taste, and odor to maintain the double-blind study design. To minimize gastrointestinal side effects, both interventions were titrated over 2 weeks to reach the prescribed amounts. Participants were asked to return any non-consumed supplements or bread at each follow-up visit to assess adherence.

Data Collection

The primary endpoint was change from baseline in body weight at 6-months, compared to control. Secondary end points included change in waist circumference, glycemic parameters (HbA_{1c} and fasting glucose), percentage body fat, body composition, satiety-related hormones (ghrelin and adiponectin), and plasma fatty acids, and high-sensitivity C-reactive protein (hs-CRP). Safety parameters included urea, creatinine, alanine aminotransferase (ALT), prothrombin-time (PT), and participant-reported symptoms. Anthropometric measurements, 3-day food records, and symptom diaries were collected at each visit. Hematological measures were collected at 0-, 3-, and 6-months. Satiety hormones and body composition were measured at 0- and 6-months. Plasma fatty acids, to assess adherence, were collected at the study end.

Analytical Assessment

Height was measured with a wall-mounted stadiometer (Perspective Enterprises, Portage, MI). After voiding the bladder and removing excess clothing and shoes, body weight was measured using a calibrated beam scale (402KL Physician Beam Scale, Health-O-Meter). Waist circumference was determined using an non-stretch tape measure, midway between the lowest rib and the iliac crest when unclothed. Body composition (% body fat, android and gynoid fat) was analyzed by Dual Energy X-Ray Absorptiometry (DXA) scan using the Lunar Prodigy

DF+10095. Whole blood analysis of HbA_{1c} was performed using HPLC (Tosoh HLC-723 analyzer). Beckman SYNCHRON LX System was used to analyze serum glucose. Serum hs-CRP was analyzed using the Beckman SYNCHRON LX System via turbidimetry. High molecular-weight adiponectin and acetyl ghrelin were assessed using their respective ELISA kits (CVs 5.5%). Safety parameters including serum ALT, PT, and serum creatinine and urea were analyzed using the Beckman SYNCHRON-LX System. Plasma fatty acids were determined by gas liquid chromatography (12). Food records were analyzed using ESHA Food Processor SQL (Version 9.8, Salem, OR, USA).

Statistical Analysis

Statistical analyses were performed using the Number Cruncher Statistical System (NCSS) 2000 software (NCSS Statistical Software, Kaysville, Utah). All measurements were tested for normality using the Shapiro-Wilk test. As normality was rejected for hs-CRP, Mann Whitney U test was used. Participant characteristics were expressed as mean ± SD, while all other measurements were presented as mean ± SEM. For primary and secondary measurements, ANCOVA was conducted to assess differences between and within intervention and control groups in the mean change from baseline to 6-months. The ANCOVA analysis for body weight and waist circumference were adjusted for its corresponding baseline values. Outcomes where intermediate measures were collected, the differences between means at each time point were assessed. Additionally, repeated-measures ANCOVA were conducted to assess differences between intervention and control, with time as the repeated factor. All comparisons, except for satiety related hormones, were adjusted for age, participant's sex, BMI, and medication use. Satiety-related hormones were adjusted for baseline values, change in weight from baseline, and

change in BMI from baseline in addition to potential confounders identified in the literature: ghrelin was adjusted for % body fat (13) and adiponectin was adjusted for participant's sex (14). For missing data, a modified intention to treat analysis was used. To avoid bias that may have resulted from omitting data from participants who had completed more than half of the study protocol, participants who completed up to week 18 were included in the final analysis. Missing values at baseline (0-month) or end of intervention (6-month) were imputed as intermediate values (3-month) or with 6-week or 18-week values, respectively, if available. Missing values for the intermediate visits were imputed using an average of the measurements at the previous and subsequent visits.

Given previous observations from weight loss studies in individuals with T2DM, a sample size of 31 participants per intervention group would provide 80% power to detect a difference of 2.9kg in mean weight change from baseline, relative to control, assuming a standard deviation of 4kg between two parallel intervention groups at a level of $P<0.05$, using a two-tailed approach (15). Assuming 20% attrition rate, a total of 77 participants was to be enrolled.

RESULTS

The mean baseline characteristics of the randomized participants were similar for both interventions **(Table 1)**. All participants followed the experimental protocol with little difficulty. A total of 357 participants were screened by telephone to identify 77 eligible participants, out of which 84 completed the 6-month study protocol. A total of 10 participants withdrew in the control group, with 3 occurring after week 18, and 13 participants withdrew from the Salba-chia group, with 1 occurring after week 18. Among all participants who withdrew, 3 reported transient gastrointestinal side effects; the remainder was due to issues unrelated to the

interventions. As a result, 58 participants were included in the final analysis. There was no difference in attrition between intervention arms. Most of participants who were taking anti-hyperglycemic medications were taking metformin with over 50% of which used the agent as monotherapy; of those who were taking additional anti-hyperglycemic agents, all other except 3 were taking two agents. There was no difference between test and control group with respect to anti-hyperglycemic medication, and the duration of diabetes was comparable (please see Table 1).

Weight and Body Fat

All outcomes measured are presented in **Table 2**. Salba-chia supplementation reduced weight over 6-months by 1.9±0.5kg ($P<0.05$), whereas no significant change was observed in the control (-0.3±0.5kg), resulting in a significant between intervention effect ($P=0.02$) favoring Salba-chia. At individual times, Salba-chia significantly reduced weight at 18 weeks (-1.4±0.4kg vs. 0.4±0.4kg, respectively; $P=0.045$) and 6-months (-1.8±0.5kg vs. -0.5±0.4kg, respectively; $P=0.039$) when compared to control **(Figure 1)**. This was accompanied by a greater reduction in waist circumferences between interventions ($P=0.027$) with 3.5±0.7cm on Salba-chia compared to 1.1±0.7cm on the control **(Figure 1)**. No significant differences were observed in mean hip circumference and percent body fat, measured using either DXA methods, between interventions. However, a within intervention reduction of android (3.7±2.8%, $P=0.031$) and gynoid fat (6.9±3.9%, $P=0.047$) was observed in Salba-chia, but not in control.

Other Outcomes

Measures of glycemic control (HbA_{1c} and fasting glucose), did not significantly differ between the interventions at 6-months. Salba-chia intervention resulted in a reduction in hs-CRP levels of -1.1±0.5mg/L (-39.3±17.1%) compared to -0.2±0.4mg/L (-6.5±19.7%) change in the control (P=0.045). Among satiety-related hormones, a significant change was observed in plasma adiponectin levels when comparing between interventions (P=0.022), with a 6.5±0.7% increase from baseline in Salba-chia compared to 0±0.6% in control. A within intervention effect was observed for ghrelin, where Salba-chia reduced ghrelin levels by 17% (P=0.039) from baseline with no reduction in control, but between group differences remained non-significant (P=0.094).

Safety Parameters

There were no major adverse events. Gastrointestinal adverse events were mild and transient, with comparable frequency in both groups. Changes from baseline in measures of renal and liver function and prothrombin time were similar within or between intervention groups **(Table 2)**.

Adherence

The mean daily consumption of the study supplement was 39.8g/day ground Salba-chia and 48.7g/day control. Based on weighing returned supplements, adherence for month 0-3 was 94±6% for the Salba-chia group and 84±6% for control. From months 3-6, supplement adherence declined to 85±5% on Salba-chia and 82±7% for control. Percent concentration of ALA was found to be nearly twice as high on Salba-chia versus the control group (P<0.0001) (**Table 2**).

Diet Analysis

At baseline, no differences were observed among the groups in calorie or macronutrient profile **(Table 3)**. Dietary fiber consumption increased over the study period by ≈10g/day on both interventions. As expected, estimated ALA intake was 4-fold higher in the Salba-chia group compared to control (P=0.028), resulting in the n-3:n-6 ratio of 1:1.5 on Salba-chia and 1:9 on control. No significant changes were seen between or within groups for any other nutrients. At 6-months, an estimated energy deficit of 64 kcal on control and 116kcal on Salba-chia arm from energy requirements was observed (P=0.77).

DISCUSSION

Therapies that promotes weight loss and reduce obesity-associated risk factors in T2DM are of great interest. Results from the present study revealed that a 6-month addition of Salba-chia to a calorie-restricted diet, in conjunction with the standard medical care, resulted in small, but significant, weight loss in overweight and obese participants with T2DM. Even modest weight loss, especially when accompanied with a reduction in visceral obesity, represents a clinically important achievement as weight management in this population is inherently challenging (16,17). In addition, Salba-chia improved obesity-related health outcomes, including reductions in hs-CRP and increased adiponectin concentrations.

To our knowledge, no previous study has demonstrated the weight-reducing properties of seeds, and/or reduction of the particular obesity related factors. However, despite the reduction in weight, there was no significant change in metabolic parameters such as HbA_{1c} or fasting blood glucose. A positive control used in the present trial may have lessened the ability of detecting an improvement in metabolic parameters. Additionally, the lack of change should be taken in the context of modest weight loss and well-maintained baseline values. This is consistent with other study findings that failed to document a significant decrease in HbA_{1c} in obese and overweight type 2 diabetic patients who lost between 2-5% of the baseline weight (18). Interestingly, as the

current findings and those from our previous study showed a reduction in hs-CRP by an equal margin, these reproducible findings may be considered as a significant effect of Salba-chia (11). Nevertheless, the magnitude of weight change observed after Salba-chia administration is clinically significant and resembles the effect of liraglutide added to metformin therapy, which compared with metformin monotherapy lowered body weight by 1.8 kg in T2DM patients over 2 years (19).

An earlier study using the common black chia variety (also *Salvia hispanica* L.) published by Nieman et al. did not report weight loss (20). Differences in findings may be attributed to methodological variances, such as study design, non-diabetic population selection, and study material standardization. Whereas Salba-chia in our study was consumed in conjunction with a calorie-restricted diet, chia was provided on top of a normocaloric diet, generating an excess of >200kcal daily, which precluded weight loss. Moreover, different varieties of chia and growing conditions yield variable nutrient compositions, with protein, total fat, ALA, and fiber content ranging from 16-24%, 26-34%, 57-65% of fat, and 22-38%, respectively (20-22). In contrast, Salba-chia is a variety of *Salvia hispanica* L. that is selectively bred into a single genotype to yield a highly standardized composition (11,23). Additionally, the black chia was provided as whole seeds twice daily in 25g portions after soaking for 10min in water. The bioavailability of nutrients, which may have contributed to the weight change and metabolic benefits seen in our study using ground seeds, may be impeded by consuming chia in the whole form, as was later corroborated by the same authors (24).

Weight loss in the Salba-chia group was accompanied by reductions of 3.5cm in waist circumference, which is greater than that seen with different types of GLP-1 receptor agonists of -1.85cm in comparison with placebo or insulin treatment (17). Although there was no difference

between interventions, there was a significant reduction of android (3.7±2.8%, P=0.031) and gynoid fat (6.9±3.9%, P=0.047) from baseline in the Salba-chia group, but not in control, supporting the assumption that there was an attenuation in visceral fat. According to a recent study, increased visceral fat was associated with a greater mortality for any given BMI category (25). Decline in visceral adiposity induces adipokine secretion, such as adiponectin, and reduces inflammatory factors like hs-CRP, which are both suggested as surrogate cardiovascular markers in overweight and obese individuals. The reductions on the current study would be in line with a 37% decrease in hs-CRP observed in the JUPITER trial, where benefits on major cardiovascular end-points were clearly demonstrated (26). The absence of reduction in circulating lipids with Salba-chia as previously observed in our 2007 study may suggest an independent, non-LDL effect of Salba-chia on hs-CRP (11,27).

The comparator intervention of oat bran and inulin was intended to serve as a positive control. Despite the fact that participants received 3g of beta-glucan from oat bran per day, as per the Food and Drug Administration recommendations, there was no reduction of serum cholesterol (28). The amount of inulin in the control supplement was ~12g/day. Inulin is a soluble non-viscous fermentable fiber that has been suggested to play a role in body weight regulation, abdominal obesity and satiety hormone stimulation (29). However, these effects were not revealed in the current study.

Finally, adiponectin was increased on the Salba-chia intervention, which may be partially explained by the reduction in visceral obesity, as measured by waist circumference seen in the study. In overweight and obese subjects, adiponectin inversely correlates with obesity indicators and negatively regulates hs-CRP expression. The route through which Salba-chia increases

adiponectin levels is unclear, but some evidence suggests that the high level of ALA and high antioxidant capacity could potentially be involved (30,31).

The precise mechanism of action by which Salba-chia promotes weight loss and improves obesity-related risk factors is unknown. Its rich nutrient composition, including fiber, ALA, protein, minerals, and level of antioxidants may act individually or collectively to demonstrate benefits. Numerous studies have shown that ingestion of fiber can mitigate hunger, reduce postprandial glycemia, and promote short-term weight loss (32,33). Furthermore, dietary fiber has been linked to reducing chronic inflammation, producing small but significant reductions in hs-CRP of 0.37mg/L in obese populations (34). The 1.1mg/L reduction of hs-CRP presently shown may be considered clinically meaningful if sustained over an extended period of time.

A limitation of our study is the relatively short duration, especially in the context of the achieved results. Namely, the reduction in weight and waist circumference in the Salba-chia group started near the beginning of the intervention and was sustained until the end of the 6-month follow-up, suggesting that further reduction in anthropometric parameters might have occurred if the study duration was longer. The attrition rate of 33% and 26% for the test and control interventions, respectively, appears modest although this is not different from many other dietary weight loss studies (35,36). Other outpatient weight loss programs have shown as little as 50% adherence to the study at the 6-month time point (5).

Strengths of the study include the utilization of a double-blind protocol, which is rarely achievable during dietary trials and is a strong advantage in controlling research bias. Furthermore, both Salba-chia, with its favorable nutrient composition, and oat bran/inulin control, with well-recognized health benefits, were attractive to apply in this population that

300 encompassed a broad BMI and age range. This preserved a relatively high rate of adherence, and
301 is suggestive of high translational potential for use in the general public.
302 In summary, the present study suggests the potential benefits of Salba-chia consumption in
303 T2DM patients treated with a calorie-restricted diet and pharmacological standard of care, by
304 promoting weight loss, reducing visceral obesity, improving low grade body inflammation, and
305 increasing adiponectin secretion.
306 Future studies for Salba-chia should evaluate the clinical applicability and cardiovascular
307 benefits that extend beyond T2DM.

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Pulse Canada, Canadian Sugar Institute, Dr. Pepper Snapple Group, The Coca-Cola Company, Corn Refiners Association, World Sugar Research Organization, Dairy Farmers of Canada, Società Italiana di Nutrizione Umana (SINU), III World Congress of Public Health Nutrition, C3 Collaborating for Health, White Wave Foods, Rippe Lifestyle, mdBriefcase. He has ad hoc consulting arrangements with Winston & Strawn LLP, Perkins Coie LLP, and Tate & Lyle. He is on the Clinical Practice Guidelines Expert Committee for Nutrition Therapy of both the Canadian Diabetes Association (CDA) European Association for the study of Diabetes (EASD), and Canadian Cardiovascular Society (CCS), as well as being on an American Society for Nutrition (ASN) writing panel for a scientific statement on sugars. He is a member of the International Carbohydrate Quality Consortium (ICQC) and Board Member of the Diabetes and Nutrition Study Group (DNSG) of the EASD. He serves an unpaid scientific advisor for the Food, Nutrition, and Safety Program (FNSP) and the Technical Committee on Carbohydrates of the International Life Science Institute (ILSI) North America. His wife is an employee of Unilever Canada. All other authors have no conflicts of interest related to the study to declare.

VV conceived and designed the study, analyzed and interpreted the data, supervised the study, and drafted the manuscript. ALJ conceived and designed the study, analyzed and interpreted the data, supervised the study, and critically revised the manuscript for intellectual content. CB, LC, and EJ contributed to the collection, analysis, and interpretation of the data and critically revised the manuscript for intellectual content. ALG contributed to protocol design, statistical analysis, and critically revised the manuscript for intellectual content. RPB contributed to protocol design, fatty acid and lipid analysis, and critically revised the manuscript for intellectual content. FA, AZ, and HVTH. contributed to data collection and analysis. LD, JLS, RGJ, and AH contributed to protocol design, study supervision, and critically revised the manuscript for intellectual

content. All authors reviewed the manuscript and provided administrative, technical, or material support. VV is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Table 1. Baseline characteristics and disposition of participants.

	Salba-chia (n=27)	Control (n=31)
Participant disposition		
Screened (n = 357)		
Randomized	39	38
Withdrawn	13	10
Schedule conflict	5	4
Adverse effects*	2	1
Unrelated reasons	6	5
Completed	26	28
Included in primary analysis**	27	31
Baseline characteristics		
Age (years)	60 ± 2	60 ± 2
Diabetes duration (years)	6.8 ± 10	6.7 ± 8
Sex		
Male	7 (26)	11 (35)
Female	20 (74)	20 (65)
Body mass index (kg/m^2)	31.0 ± 0.9	30.7 ± 0.7
Body weight (kg)	84.1 ± 2.6	84.2 ± 2.7
Waist circumference (cm)		
Male	103.5 ± 3.5	104.6 ± 3.0
Female	104.9 ± 2.5	102.2 ± 1.9

Blood pressure (mmHg)		
Systolic	122.0 ± 2.4	124.0 ± 2.3
Diastolic	72.7 ± 1.6	73.1 ± 1.9
Blood biomarkers		
HbA_{1c} (%)	6.8 ± 1.2	7.0 ± 1.0
Fasting blood glucose (mmol/L)	7.4 ± 1.9	7.4 ± 1.7
C-reactive protein (mg/L)	2.8 ± 0.6	3.1 ± 0.6
Diabetes treatment and medication use		
Diet only	7 (26%)	6 (20%)
Anti-hyperglycemic medications	20 (74%)	25 (80%)
MET only	14	14
MET + SU	2	3
MET + TZD	0	1
MET + DPP4	2	4
MET +SU + TZD	2	1
SU + DPP-4	0	1
MIG + TZD	0	1
Lipid-lowering medications	6 (22%)	8 (26%)
Anti-hypertensive medications	15 (56%)	19 (61%)

Data are means ± SD or *n* (%). MET -Metformin; SU -Sulphonylurea; TZD -Thiazolidinedione; DPP-4 -Dipeptidyl peptidase 4 inhibitors; MIG –Meglitinides; *The adverse events withdrawals

are due to transient gastrointestinal side effects such as increased flatulence and soft stool.

**participants who completed more than 18 weeks of the intervention

Table 2. Mean (± SEM) changes in outcome measures after 6-month administration of Salba-chia or control in 58 individuals with type 2 diabetes.

	Salba-chia			Control			*P* value
Measurement	n	Baseline	6-Month	n	Baseline	6-Month	between-treatment
Anthropomorphic measurements							
Body weight (kg)	27	84.1 ± 2.8	82.2 ± 0.5*	31	83.8 ± 2.6	83.5 ± 0.5	0.020
Waist circumference (cm)	27	104.6 ± 1.9	100.2 ± 0.8*	31	104.3 ± 1.8	103.2 ± 0.8	0.027
Body Composition (DXA)							
Body fat (%)	24	44.0 ± 1.7	41.9 ± 0.4	27	41.2 ± 1.6	42.0 ± 0.4	0.854
Android fat (%)	24	48.8 ± 1.3	47.0 ± 0.5*	27	47.8 ± 1.2	47.8 ± 0.5	0.218
Gynoid fat (%)	24	47.8 ± 2.0	44.5 ± 0.3*	27	43.1 ± 1.9	45.0 ± 0.3	0.385
Glycemic control (plasma)							
HbA_{1c} (%)	27	6.6 ± 0.2	6.5 ± 0.1	31	7.0 ± 0.2	6.7 ± 0.1	0.231
Fasting glucose (mmol/L)	27	7.4 ± 1.9	7.4 ± 1.4	31	7.5 ± 0.3	7.3 ± 0.3	0.351
Fatty Acids (% composition) [1]							

ALA (18:3 n-3)	26	N/A	1.03 ± 0.11	28	N/A	0.5 ± 0.03	<0.001
LA (18:2 n-6)	26	N/A	21.1 ± 0.6	28	N/A	18.8 ± 0.5	0.006
Safety							
Urea (mmol/L)	27	6.0 ± 0.4	5.7 ± 0.2	31	5.2 ± 0.4	5.7 ± 0.2	0.953
Creatinine (μmol/L)	27	74.0 ± 3.3	74.0 ± 1.4	31	71.2 ± 3.1	72.6 ± 1.3	0.783
ALT (U/L)	27	25.6 ± 2.8	25.6 ± 1.6	31	32.5 ± 2.6	26.5 ± 1.5	0.167
Prothrombin time (s)	27	11.1 ± 0.1	10.9 ± 0.1	31	11.0 ± 0.1	11.1 ± 0.1	0.375
Other end points							
C-reactive protein (mg/L)	27	2.8 ± 0.6	1.7 ± 0.5*	31	3.1 ± 0.6	2.9 ± 0.4	0.045
Ghrelin (pg/mL)	26	676.6 ± 63.4	561.1 ± 25.8*	28	483.7 ± 61.2	579.6 ± 24.9	0.638
Adiponectin (μg/mL)	26	7.7 ± 0.9	8.2 ± 0.5*	28	6.6 ± 0.8	6.6 ± 0.4	0.022

Data are means ± SEM. Between treatment values were assessed with repeated measures ANCOVA with time as the repeated factor. *Significantly different from baseline within intervention as assessed with ANCOVA, $p < 0.05$. [1]Fatty acid values were only measured at 6-months. Abbreviations: ALA – alpha linolenic acid, ALT – alanine aminotransferase, DXA – dual energy x-ray absorptiometry, LA – linoleic acid, N/A – not available.

Table 3. Comparison of the nutritional profile of participant diets, including study supplements, between intervention groups as reported by 3-day food records. For all parameters, n=58.

Nutrient	Salba-chia (n=27)			Control (n=31)		
	0-months	3-months	6-months	0-months	3-months	6-months
Total energy (kcal)	1751±98	1666±88	1783±126	1639±81	1747±130	1740±118
Carbohydrate (g)	198.7±10.2	171.8±11.3	203.6±17.0	189.4±12.0	213.3±17.2	213.7±10.9
(% of total kcal)	(46.8±1.9)	(45.0±1.8)	(45.5±1.4)	(46.1±1.6)	(49.9±2.2)	(48.5±1.8)
Total Fibre (g)	27.2±1.5[a]	38.9±2.7[b]	37.1±2.1[b]	26.1±2.1[a]	37.6±2.5[b]	35.0±1.7[b]
Protein (g)	78.6±5.3	76.8±5.0	78.4±5.6	87.7±5.9	87.7±6.4	91.0±7.6
(% of total kcal)	(18.1±0.7)	(20.2±0.8)	(18.2±1.0)	(21.7±1.1)	(20.3±0.8)	(19.9±1.0)
Fat (g)	71.3±6.6	60.0±5.2	72.8±5.7	58.9±4.2	60.3±6.8	62.5±7.2
(% of total kcal)	(35.1±1.7)	(34.8±1.6)	(36.3±1.6)	(32.3±1.5)	(29.8±1.7)	(31.6±1.4)
SFA (% total kcal)	10.3±0.9	9.4±1.0	9.5±0.9	9.5±0.6	8.1±0.6	8.2±0.5
MUFA (% total kcal)	9.5±0.8	7.2±0.7	9.4±0.7	9.8±0.7	8.0±0.9	8.8±0.6
PUFA (% kcal)	15.3±1.2	18.2±1.0	17.5±1.3	13.0±1.0	13.8±1.3	14.5±0.8
n-6 (g)	9.3±1.3[a]	9.1±1.0[a]	12.0±1.7[b]	7.2±0.6[a]	10.7±1.2[b]	12.6±1.2[b]

n-3 (g)	1.4±0.2[a]	9.0±0.3[b]	8.8±0.5[b]	1.4±0.2	1.6±0.2	1.2±0.1
n-3 to n-6 ratio	1:6[a]	1:1[b]	1:1.3[b]	1:5[a]	1:6.7[a,b]	1:10[b]
Calcium (mg)	609.9±46.4	656.0±89.5	689.8±86.2	619.1±53.2	640.1±60.9	698.1±83.4

Data are mean ± SEM. Values with different superscript letters indicate significance, $p<0.05$ by ANCOVA. Abbreviations: MUFA – monounsaturated fatty acids, n-3 – omega-3 PUFA, n-6 – omega-6 PUFA, PUFA – polyunsaturated fatty acids, SFA – saturated fatty acids.

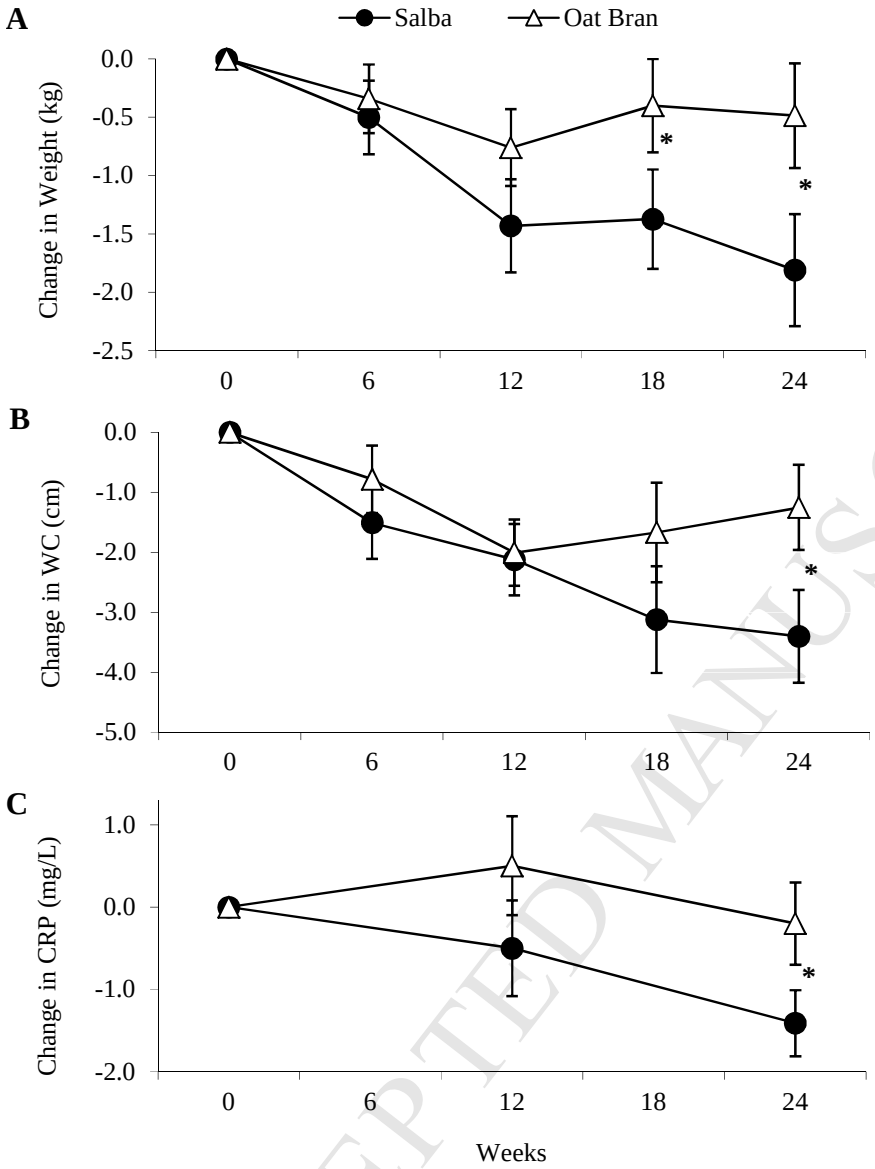

Figure 1 – *Change from baseline in body weight (kg) (A), waist circumference (cm) (B), and c-reactive protein (mg/L) (C) in 58 participants with type 2 diabetes. Black circles = Salba; white triangles = oat bran control. *Significantly different between interventions as assessed by analysis of variance ($p < 0.05$). WC denotes waist circumference and CRP denotes high sensitivity C-reactive protein.*

Research Highlights

- Salba-chia is one of the highest whole food sources of dietary fiber and α-linolenic fatty acids per total fat, minerals, and a good source of protein
- Isocaloric supplementation of Salba-chia for 6 months demonstrated greater body weight reduction compared to control
- Supplementation of Salba-chia may represent a promising addition to conventional therapy in the treatment of obesity in diabetes.