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A pilot study investigating the effect of *Caralluma fimbriata* extract on the risk factors of metabolic syndrome in overweight and obese subjects: a randomised controlled clinical trial

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Appetite

Summary
Objectives: Central obesity is a key component of metabolic syndrome and it is often associated with other risk factors such as dyslipidemia, elevated plasma glucose levels and elevated blood pressure (BP). In this pilot study, the effect of *Caralluma fimbriata* (an edible succulent) extract in combination with controlled dietary intake and physical activity on these risk factors was assessed in overweight and obese Australian subjects.
Design: This was a randomised, double blind placebo controlled clinical trial. Forty-three adults aged 29-59 years were recruited. The eligibility criteria included a Body Mass Index (BMI) >25 kg/m^2, or a waist circumference >94 cm (male), >80 cm (female). Thirty-three participants completed the 12-week study at Victoria University Nutritional Therapy Clinic. Participants were randomly assigned into two groups. *C. fimbriata* extract and placebo were orally administered as 500 mg capsules twice daily (1 g/day) and dietary intake and exercise were monitored weekly.
Results: The results of thirty-three participants (experimental group, $n = 17$; placebo group $n = 16$) were analysed. The primary outcome measure was the decline in waist circumference. By week 9, the experimental group had lost 5.7 cm, compared to only 2.8 cm loss in the placebo group (Difference: −2.890; 95% CI; −5.802 to 0.023). Post intervention, the experimental group had lost 6.5 cm compared to 2.6 cm loss in the placebo group (Difference: −3.847; 95% CI; −7.466 to 0.228). Waist to hip ratio (WHR) also improved significantly after 12 weeks intervention in the experimental group, with a total reduction of 0.03 being recorded compared to 0.01 increase in the placebo group (Difference: −0.033; 95% CI; −0.064 to −0.002). There was also

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a significant decline in the palatability (visual appeal, smell, taste) of the test meal and sodium intake in the experimental group at week 12 ($p < 0.05$). In addition a significant reduction in body weight, BMI, hip circumference, systolic BP, HR, triglyceride levels, total fat and saturated fat intake within both groups was observed following the intervention period ($p < 0.05$).
Conclusion: Supplementation with *C. fimbriata* extract whilst controlling overall dietary intake and physical activity may potentially play a role in curbing central obesity, the key component of metabolic syndrome. Controlling dietary intake and exercise improved body weight and favourably influenced the metabolic risk profile.
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Introduction

Metabolic syndrome is a complex disorder characterised by a clustering of cardiovascular risk factors including abdominal/central obesity, dyslipidemia, elevated plasma glucose levels and elevated BP.[1] Central obesity is one of the major determinants of metabolic syndrome.[2] Pathological mechanisms involved in metabolic syndrome include ectopic lipid accumulation resulting in lipotoxicity and altered secretion of adipocytokines (adipocyte-derived hormones).[2] Visceral fat is metabolically active as a source of adipocytokines chiefly leptin,[3] adiponectin,[4] plasminogen activator inhibitor type 1,[5] tumour necrosis factor alpha[6] and non-esterified fatty acids.[7]

The majority of individuals affected by metabolic syndrome are overweight or obese, thus dietary treatment is focused on weight reduction.[8] Strategies for body fat reduction typically involve a combination of lifestyle changes such as limiting calorie intake, increasing physical activity, behavioural therapy, pharmacotherapy, and surgery.[9] The availability and popularity of natural dietary supplements for weight loss has risen dramatically in recent years.

Among potential natural supplements for weight reduction are the appetite suppressants. One such supplement is the extract of *Caralluma fimbriata*, an edible succulent plant, in the Asclepiadaceae family, native to India.[10] Indian tribal people have used the natural appetite suppressant for many centuries, and in times of famine it is a commonly used vegetable.[10] The appetite suppressing properties of *C. fimbriata* has been attributed to the active component, pregnane glycosides.[11] The mechanism of appetite suppression by pregnane glycosides is unclear, however one hypothesis is that *C. fimbriata* may down-regulate ghrelin synthesis in the stomach and neuropeptide-Y in the hypothalamus, resulting in appetite suppression.[12]

Preliminary human clinical trials have shown significant weight reductions in overweight Indian subjects with supplementation of *C. fimbriata* extract in addition to lifestyle modification.[13] A study by Kuriyan et al.[9] on the appetite suppressing effects of *C. fimbriata* in overweight Indian adults (25-60 yrs) showed a significant reduction in waist circumference after two months intervention. In addition the hunger level of participants reduced by 20% which may account for an 8% decline in energy intake of the experimental group.[10] However, Kuriyan et al. [9] did not identify a significant reduction in blood lipid profile in the subjects with or without *C. fimbriata* supplementation. Also, no human trials have reported the effect of *C. fimbriata* extract on other metabolic risk factors including plasma glucose levels, BP and adipocytokines such as leptin. The aim of this study was to determine whether *C. fimbriata* extract, in addition to a hypocalorie diet (deficit of 500 kcal/day of estimated energy requirements) and regular physical activity, can attenuate metabolic disturbances including central obesity, elevated BP, dyslipidemia and elevated blood glucose levels in generally healthy and obese Australian adults.

Methods

Participants

This study was a randomised, double blind, placebo controlled clinical trial. It was conducted at Victoria University, Nutritional Therapy Clinic, Melbourne, Australia. Potential volunteers were recruited through the general public and staff members at Victoria University. The recruitment period was approximately four months. Thirty-three volunteers (29-59 years), with a BMI greater than 25 kg/m^2 or a waist circumference >94 cm (male), >80 cm (female) were randomly assigned (Fig. 1) into either the placebo ($n = 16$; 14 females, 2 males) or the experimental group ($n = 17$; 12 females, 5 males).

For randomisation, participants were coded and allocated into two groups based on their physical characteristics including age, body weight, BMI, waist and hip circumference and WHR. Stratified randomisation was used to ensure all baseline variables associated with the outcome were evenly distributed. The method used to ensure allocation concealment was sequentially numbered containers. The containers were equal in weight, similar in appearance and tamper-proof. The principal investigator implemented the allocation sequence and assigned the participants into their groups. The capsules were opaque and indistinguishable in appearance, size, texture and smell. The taste of the capsules was identical provided that they were swallowed whole as instructed. Staff and participants involved in the intervention process of the trial were blinded to group assignment. The randomisation code was broken only after data collection was completed. Patient and staff blinding to treatment was monitored throughout the study. This was evaluated by asking participants whether they thought they were in the treatment or placebo group and staff were also asked if they knew whether their patient was in the treatment or placebo group. Inclusion criteria included: male or female aged between 29 and 59 years of age, BMI >25 kg/m^2 or a waist circumference >94 cm (male), >80 cm (female). Waist circumference is important as the majority of individuals with a larger waist circumference (central obesity) are at a higher risk of developing metabolic syndrome. Exclusion criteria included: cigarette smoker, heart, liver and

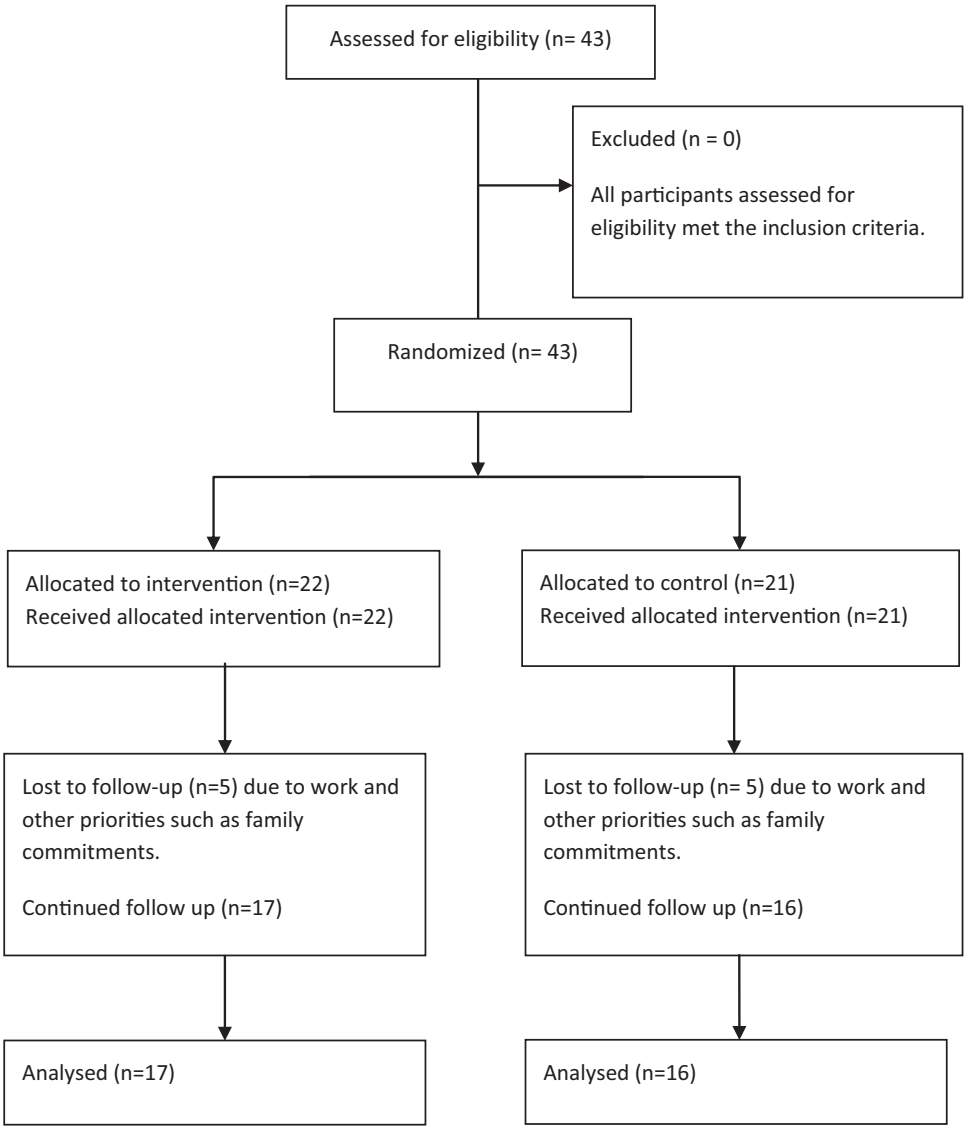

Figure 1 The study flow chart.

kidney disease, pregnancy, type 1 diabetes and individuals on weight loss medication.

The study was approved by the Human Research Ethics Committee of Victoria University, Australia (HRETH 10/22) and registered by ANZCTR. At the beginning of the study all eligible volunteers were informed about the details of the study including that they would be randomly assigned into one of the two groups (experimental or placebo) prior to signing the consent form.

Outcome measures

Prior to intervention, the participants completed a medical and a health and wellbeing questionnaire (Your Health and Wellbeing; SF-36v2 Health Survey). The baseline assessment included anthropometry, metabolic parameters, dietary intake, appetite, BP and heart rate (HR). The control capsule was a 500 mg capsule containing 100% maltodextrin. The *C. fimbriata* extract and placebo capsules were provided in a 2-piece hard shell capsule form and delivered in blindly labelled sealed bags as 500 mg capsules twice daily (1 g/day) before meals for 12 weeks. This dosage was determined based on the previous study by Kuriyan et al. (2007).[10] Both capsules were supplied by AZPA Pharmaceuticals Pty Ltd, Melbourne, Australia. The ingestion of the capsules was monitored weekly during the nutrition consultations and a capsule calendar was also administered at the beginning of the trial and submitted at the completion of the 12 weeks.

During the intervention period dietary intake and exercise were controlled. Both groups received consistent dietary and exercise advice once per week. In order to obtain optimal compliance among participants, it was deemed helpful to provide and control participant's dietary and physical activity level. The dietary intake was monitored through 3-day food diaries fortnightly and participation in physical activity was also noted on the food diary submitted. The participants followed a hypocaloric diet (deficit of approximately 500 kcal/day of estimated energy requirements) based on the Adult Weight Management

Evidence-Based Nutrition Practice Guidelines.[14] In addition the lifestyle recommendations provided were in accordance with the Dietary Guidelines for Australian Adults.[15] Anthropometric measurements and BP were taken during each consultation. Appetite sensations were assessed in week 6 and three-day food diaries were collected fortnightly to monitor dietary intake.

After the 12 weeks intervention, anthropometry, BP, HR, appetite, dietary assessment including a 3-day food diaries, and biochemical analyses of metabolic parameters were conducted. The food diaries were analysed using Food Works Professional 2009, version 6 (Xyris Software, QLD, Australia Pty Ltd).[16]

Anthropometric measurements

Anthropometric measures were taken in accordance with standard equipment and technique.[17] Measurements were taken twice with the mean of the measurements used as the final reading. Height was measured after the removal of shoes using a stadiometer to the nearest millimetre. Body weight was taken using digital scales (Tanita Inner Scan, BC-545, Cloverdale, WA, Australia) when heavy clothing was removed. BMI was calculated using the following formula: BMI = weight (kg)/height (m).[2] Waist circumference was measured to the nearest 0.1 cm at the midway point between the lowest costal border and the iliac crest in a horizontal plane (above the umbilicus). Hip circumference was measured in a horizontal plane at the maximum posterior protuberance of the buttocks. Waist to hip ratio (WHR) was calculated using the following formula: WHR = Waist circumference (cm)/hip circumference (cm).

BP measurements

BP was measured in a seated position using an automated digital BP monitor (UA-767 Plus, A & D Medical), where the inflatable cuff of the sphygmomanometer was positioned at the brachial artery in the right upper extremity of each subject. BP was measured twice with the final BP reading obtained by calculating the mean of the two readings. HR was also recorded using the automated digital BP monitor.

Biochemical analyses of metabolic parameters

Following an overnight fast of at least 8 h, 10 ml of forearm venous blood was collected using the Vacutainer System at baseline and post intervention (BD vacutainer tubes, Becton, Dickinson and Company). A glucometer (MediSense, Precision Plus, Abbott Diabetes Care Inc.) was used to determine fasting glucose levels. The blood samples were transported to the laboratory on ice packs immediately after collection. Blood was then centrifuged for 13 min at 3000 g at 4 °C. Plasma was collected into aliquots and frozen at −80 °C for further analysis of triglycerides, total cholesterol, high density lipoprotein (HDL) cholesterol and leptin. Triglycerides, total cholesterol and HDL cholesterol were analysed following the manufacturer's instructions of the assay kit (Thermo Fisher Scientific Inc, Middletown, USA) using a spectrophotometer. LDL cholesterol was calculated using the Friedewald equation.[18] The leptin (human) Enzyme Immunometric Assay Kit was used to analyse leptin in plasma according to the manufacturer's instructions (Assay Designs Stressgen 2008).

Appetite assessment

The appetite of participants was assessed at baseline, weeks 6 and 12 using the visual analogue scales method (VAS).[19] A breakfast test meal was provided for subjects following an overnight fast (8 h) and a standard meal the night before the test was also required. The maximum amount of time given for subjects to consume the test breakfast meal was 30 min. Before and immediately after the test meal, participants were required to record their appetite sensations for 'hunger', 'desire to eat', and 'fullness of stomach (satiety)' on a scale of 0—100 mm.

Participants were asked to circle the line on a scale of 0—100 mm that best matched how they felt at the time on each 100-mm line: How hungry do you feel? (not hungry at all-very hungry); How strong is your desire to eat? (very weak-very strong); How full do you feel? (not full at all-very full) and also rated the palatability (visual appeal, taste, smell, aftertaste) of the breakfast. Appetite sensations were assessed both in a fasted state and in response to the meal.

Statistical analysis

The sample size for the trial (a minimum of 13) was determined by statistical power analysis, two tailed *t*-test at the 0.05 significance level for the power of 90% of expected differences in the major measured variable of the experiment i.e. appetite.[10] A 10% reduction in appetite was considered significant, based on the previous study conducted by Kuriyan et al. (2007).[10] All data were expressed as mean ± standard deviation. Changes in waist circumference between the two groups at various time points are also expressed as magnitudes (delta). The *t* test was performed to assess whether significant differences existed between the experimental and placebo groups at baseline, weeks 6 and 12. A one-way ANOVA and multiple comparisons using a Tukey HSD post hoc analysis were performed to assess the change in the parameters over time within the group. *P* values of less than 0.05 ($p < 0.05$) were considered statistically different. Statistical analysis was performed and 95% confidence intervals (CI) was calculated using the SPSS package, version 19 (SPSS, Chicago, IL, USA).

Results

All screened volunteers met the inclusion criteria ($n = 43$). Ten participants (five in the experimental and five in the placebo group) did not complete the trial due to work and family commitments. These participants were excluded from the study (Fig. 1). In addition, there was no breach of the blinding process identified throughout the intervention period.

The physical characteristics of the participants including age, body weight, BMI, waist and hip circumference and

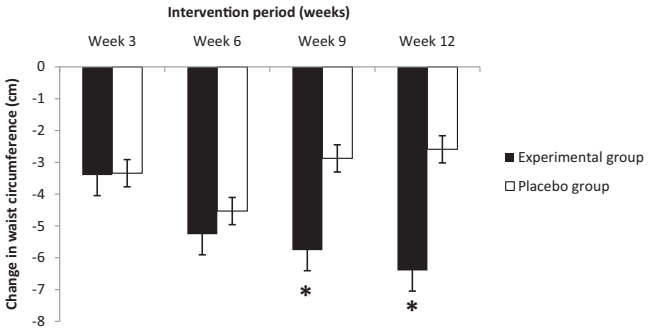

Figure 2 Change in waist circumference over the intervention period. *Significant difference between the two groups at week 9 (Difference: −2.890; 95% CI; −5.802 to 0.023) and week 12 (Difference: −3.847; 95% CI; −7.466 to 0.228).

WHR were not significantly different between the two groups at baseline (Table 1).

The primary outcome measure of this study was the decline in waist circumference. By week 9, the experimental group had lost 5.7 cm, compared to only 2.8 cm loss in the placebo group (Difference: −2.890; 95% CI; −5.802 to 0.023). Post intervention, the experimental group had lost 6.5 cm compared to 2.6 cm loss in the placebo group (Difference: −3.847; 95% CI; −7.466 to 0.228) (Fig. 2). WHR also improved significantly after 12 weeks intervention in the experimental group, with a total reduction of 0.03 being recorded compared to 0.01 increase in the placebo group (Difference: −0.033; 95% CI; −0.064 to −0.002). There were no significant differences between the experimental and placebo group for anthropometry and blood pressure over the intervention period (Table 2). However there were significant within group changes observed compared to baseline data. Both groups showed a significant reduction in body weight, BMI and hip circumference after 12 weeks intervention ($p < 0.05$). Furthermore a significant reduction in systolic blood pressure and heart rate was also recorded in both groups ($p < 0.05$) (Table 2).

The metabolic parameters of the two groups are shown in Table 3. There were no significant differences in metabolic parameters between the two groups over the intervention period. However, there was a significant reduction in triglyceride levels after 12 weeks intervention in both groups compared to baseline data ($p < 0.001$). The health and well-being survey results showed an overall improvement in general health in both groups. The 3-day food diary analysis (Table 4) showed a significant decline in total fat and saturated fat intake in both the experimental and placebo groups ($p < 0.05$). In addition, sodium intake in the experimental group was significantly reduced from 3.4 g to 2.2 g after 12 weeks intervention ($p < 0.05$).

The data on appetite assessment using the VAS method (Table 5) showed a significant reduction in the palatability (visual appeal, smell, taste) of the test meal in the experimental group compared to baseline data ($p < 0.05$). Although the placebo group showed a reduction in desire to eat at week 6 (Difference: 0.625; 95% CI; −1.45 to 2.70) (post ingestion) and week 12 (Difference: 0.856; 95% CI; −1.56 to 3.27) (before ingestion), and hunger (before ingestion) (0.777; 95% CI; −1.55 to 3.10) at week 12 there was no significant change observed in total energy intake between the two groups at any time point.

In general, the *C. fimbriata* and placebo capsule preparations in our study were well tolerated. There were few adverse events and these were considered mild. Two participants in the experimental group experienced minor side effects in the first few weeks of the intervention period which included a skin rash and constipation. These symptoms subsided within two weeks following cessation of the intervention.

Discussion

The present study demonstrated that supplementation with *C. fimbriata* extract in combination with a hypocalorie diet was associated with a clinically significant reduction in central adiposity, a major component of metabolic syndrome. The primary finding was a decline in waist circumference following 12 weeks supplementation in the experimental group. The observed treatment effect (treatment minus placebo) is markedly stronger in this study compared to that reported in the study by Kuriyan et al. (2007),[10] with an intervention period of two months.

Obesity is considered a major health problem, increasing the risk of metabolic syndrome,[10] CVD, type 2 diabetes and other lifestyle related diseases.[20] Obesity and its associated co-morbidities continue to present an escalating challenge to contemporary medicine. Waist circumference is a useful and convenient measure of central obesity. Therefore the decline in waist circumference following *C. fimbriata* supplementation is vital as it implicates the potential role of this plant extract in the treatment of central obesity and the prevention of metabolic syndrome and other lifestyle related diseases.

Table 1 Physical characteristics of the subjects at baseline.

Parameter	Experimental group ($n = 17$)	Placebo group ($n = 16$)
Age (yrs)	46.7 ± 9.7	46.4 ± 10.4
Body weight (kg)	93.0 ± 16.5	91.8 ± 15.3
Body mass index (kg/m^2)	32.5 ± 6.4	31.8 ± 4.1
Waist circumference (cm)	102.1 ± 11.2	100.3 ± 12.1
Hip circumference (cm)	117.6 ± 12.8	116.1 ± 6.9
Waist to hip ratio	0.87 ± 0.06	0.86 ± 0.08

Values are expressed as means ± standard deviation (SD), n = number of subjects.

Table 2 Anthropometry, BP & HR at baseline, week 6 and week 12.

Parameter	Experimental	Placebo	Difference[a] (95% CI)
Body weight (kg)			
Baseline	93.0 ± 16.5	91.8 ± 15.3	
Week 6	91.1 ± 16.3	89.8 ± 16.1	0.191 (−1.18 to 1.56)
Week 12	91.0 ± 16.6[b]	89.0 ± 16.1[b]	0.787 (−1.85 to 3.42)
BMI (kg/m^2)			
Baseline	32.5 ± 6.4	31.8 ± 4.1	
Week 6	32.1 ± 6.5	31.2 ± 4.2	0.213 (−0.41 to 0.84)
Week 12	31.9 ± 6.2[b]	30.9 ± 4.2[b]	0.349 (−0.41 to 1.10)
Waist circumference (cm)			
Baseline	102.1 ± 11.2	100.3 ± 12.1	
Week 6	96.8 ± 9.7	95.8 ± 12.6	0.733 (−4.00 to 2.53)
Week 12	95.6 ± 10.1[b]	97.7 ± 12.7[b,c]	−3.847 (−7.47 to 0.23)
Hip circumference (cm)			
Baseline	117.6 ± 12.8	116.1 ± 6.9	
Week 6	114.6 ± 13	113.6 ± 5.7	0.498 (−2.53 to 1.53)
Week 12	114.1 ± 12.7[b]	112.1 ± 6.1[b]	0.561 (−2.18 to 3.33)
WHR			
Baseline	0.87 ± 0.1	0.86 ± 0.1	
Week 6	0.85 ± 0.1	0.84 ± 0.1	0.004 (−0.029 to 0.04)
Week 12	0.84 ± 0.1[b]	0.87 ± 0.1[b,c]	−0.033 (−0.06 to −0.00)
Systolic blood pressure (mm Hg)			
Baseline	126.4 ± 11.4	135.3 ± 26	
Week 6	120.6 ± 15.8	125.2 ± 19.5	4.421 (−3.10 to 11.95)
Week 12	120.1 ± 15.4[b]	122.1 ± 14[b]	7.015 (−4.39 to 18.42)
Diastolic blood pressure (mm Hg)			
Baseline	86.6 ± 9.8	88.9 ± 15.9	
Week 6	84.9 ± 12.2	86.5 ± 12.3	0.640 (−5.02 to 6.30)
Week 12	84.1 ± 15.5	84.4 ± 8.6	2.031 (−5.22 to 9.28)
Heart rate (Beats/min)			
Baseline	69.8 ± 10.4	76.9 ± 16.1	
Week 6	68.5 ± 10.2	68.4 ± 10.2[c]	7.175 (1.56 to 12.78)
Week 12	65.3 ± 8.9[b]	70.1 ± 11.3[b]	2.309 (−3.25 to 7.87)

Values are expressed as means ± SD.
[a] Treatment minus Placebo.
[b] A significant difference was observed at week 12 compared to baseline data ($p < 0.05$).
[c] There was a significant change between groups. Exclusion of the value zero of the 95% CI implies statistical significance at the 5% level.

The waist circumference significantly declined independent of body weight in the experimental group after 12 weeks intervention. A similar result was reported by Kuriyan et al. (2007).[10] This may be due to different rates of lipolysis in different depots of body fat during negative energy balance.[10] Another possibility may be an increase in lean muscle tissue parallel to fat loss with the increase in energy expenditure. Furthermore it may be attributed to the role of the pregnane glycosides, the main chemical component of *C. fimbriata*. Studies have shown that pregnane glycosides are involved in the inhibition of adipocyte proliferation, differentiation and maturation. A previous study has shown that *C. fimbriata* has the potential to prevent hyperplastic obesity in mice 3T3-L1 pre-adipocyte cell line samples.[21] It has also been demonstrated that *C. fimbriata* extract is capable of inhibiting adipocyte maturation.[21] Pregnane glycosides have been reported to inhibit pre-adipocyte cell division in the early phase of adipogenesis by either down-regulation of cyclin-dependent kinase (CDK) or inhibition of import cyclin D1-CDK/6 complex into the nucleus.[21] Several other studies also found that adipocyte proliferation and differentiation in adipose tissue were inhibited by pregnane glycosides.[22–24]

Further research into the underlying mechanisms of *C. fimbriata* extract on central obesity reduction is needed. Measurement of body composition using Dual Energy X-ray Absorptiometry (DXA) and/or three dimensional whole body laser scanning would be able to provide information on muscle mass, segmental body fat content and distribution. In addition animal studies focusing on the expression of genes and enzymes associated with lipogensis and lipolysis would be useful in elucidating the particular role of *C. fimbriata* extract in central obesity reduction.

A waist circumference indicative of central obesity is linked with a chronic inflammatory state, promoted by low-grade plasma increases in the adipocytokines including circulating leptin, tumour necrosis factor alpha,

Table 3 Metabolic parameters at baseline and week 12.

Parameter	Experimental	Placebo	Difference[a] (95% CI)
Fasting blood glucose (mmol/L)			
Baseline	5.6 ± 0.6	6.6 ± 1.5	
Week 12	5.6 ± 1.1	6.6 ± 1.7	0.038 (−0.62 to 0.69)
Triglycerides (mmol/L)			
Baseline	2.12 ± 1.4	2.6 ± 1.8	
Week 12	0.6 ± 0.2[b]	0.8 ± 0.3[b]	0.271 (−1.19 to 1.24)
Total cholesterol (mmol/L)			
Baseline	4.3 ± 1.4	4.3 ± 1.4	
Week 12	3.7 ± 0.8	4.0 ± 1.1	0.449 (−1.60 to 0.69)
HDL cholesterol (mmol/L)			
Baseline	0.9 ± 0.2	0.7 ± 0.3	
Week 12	1.0 ± 0.4	0.9 ± 0.6	−0.091 (−0.50 to 0.32)
LDL cholesterol (mmol/L)			
Baseline	3.0 ± 1.3	3.0 ± 1.1	
Week 12	2.5 ± 1.0	2.9 ± 1.3	0.389 (−1.49 to 0.72)
HDL: LDL ratio (mmol/L)			
Baseline	0.4 ± 0.4	0.3 ± 0.1	
Week 12	0.4 ± 0.3	0.3 ± 0.1	0.022 (−0.27 to 0.31)
Leptin ng/ml			
Baseline	25.1 ± 18.3	26.1 ± 16.8	
Week 12	28.8 ± 20.3	24.9 ± 8.8	4.884 (−14.07 to 23.84)

Values are expressed as means ± SD.
[a] Treatment minus Placebo.
[b] A significant difference was observed at week 12 compared to baseline data ($p < 0.05$). Exclusion of the value zero of the 95% CI implies statistical significance at the 5% level.

Table 4 Food intake assessment at baseline, week 6 and week 12.

Parameter	Experimental	Placebo	Difference[a] (95% CI)
Carbohydrate intake (g)			
Baseline	226.5 ± 70.3	230.2 ± 75.3	
Week 6	201.8 ± 93.5	193.7 ± 37.3	11.833 (−56.66 to 80.33)
Week 12	183.5 ± 99.6	209.5 ± 92.4	−22.381 (−106.74 to 61.98)
Fat intake (g)			
Baseline	101.8 ± 40	83.8 ± 44.9	
Week 6	66.9 ± 37.6	69.9 ± 21.9	−21.030 (−56.89 to 14.83)
Week 12	54.9 ± 21.5[b]	52.2 ± 22.1[b]	−15.328 (−51.49 to 20.84)
Saturated fat intake (g)			
Baseline	41 ± 15.9	33.6 ± 20.8	
Week 6	26.8 ± 17	26.1 ± 7.8	−6.771 (−22.79 to 9.25)
Week 12	18.4 ± 6.9[b]	18 ± 8.2[b]	−6.976 (−21.74 to 7.79)
Protein intake (g)			
Baseline	98.6 ± 44.8	100.8 ± 31	
Week 6	95.2 ± 47.1	92.4 ± 28.3	4.993 (−34.40 to 44.39)
Week 12	92.9 ± 40.2	84.2 ± 29.1	10.974 (−19.36 to 41.31)
Sodium intake (mg)			
Baseline	3405.8 ± 1679.3	2807.0 ± 1129.1	
Week 6	2518.5 ± 1048	3067.8 ± 3594.6	−1148.143 (−3048.08 to 751.80)
Week 12	2156.2 ± 885[b]	1968.9 ± 913	−411.575 (−1651.21 to 828.06)
Energy intake (kJ)			
Baseline	9105 ± 3473	8805 ± 3330	
Week 6	8386 ± 3431	7438 ± 1522	647.960 (−2096.84 to 3392.76)
Week 12	7552 ± 2527	7484 ± 2385	−231.919 (−2879.56 to 2415.72)

Values are expressed as means ± SD.
[a] Treatment minus Placebo.
[b] A significant difference was observed at week 12 compared to baseline data ($p < 0.05$). Exclusion of the value zero of the 95% CI implies statistical significance at the 5% level.

Table 5 Appetite sensations at baseline, week 6 and week 12.

Parameter	Experimental	Placebo	Difference[a] (95% CI)
Before ingestion			
Hunger			
Baseline	4.7 ± 2.5	3.4 ± 2.4	
Week 6	5.6 ± 2.2	5.5 ± 2.8	0.768 (−3.27 to 1.73)
Week 12	6.4 ± 2.2	4.5 ± 2.3[c]	0.777 (−1.55 to 3.10)
Desire to eat			
Baseline	5.2 ± 2.5	3.9 ± 2.6	
Week 6	5.8 ± 2.0	5.1 ± 2.8	0.339 (−2.75 to 2.07)
Week 12	6.2 ± 2.2	4.4 ± 2.4[c]	0.856 (−1.56 to 3.27)
Post ingestion			
Hunger			
Baseline	0.7 ± 1.8	0.4 ± 0.8	
Week 6	2.0 ± 2.8	1.1 ± 1.5	0.750 (−1.47 to 2.97)
Week 12	1.9 ± 2.6	1.9 ± 2.4	0.134 (−2.46 to 2.19)
Desire to eat			
Baseline	1.6 ± 2.0	0.9 ± 1.5	
Week 6	1.9 ± 2.1	0.5 ± 0.9[c]	0.625 (−1.45 to 2.70)
Week 12	1.9 ± 2.5	1.9 ± 2.2	0.344 (−2.52 to 1.83)
Fullness			
Baseline	8.4 ± 1.9	7.3 ± 2.5	
Week 6	8.6 ± 1.5	8.2 ± 2.0[c]	−1.649 (−2.72 to 0.58)
Week 12	8.3 ± 1.9	8.7 ± 1.4[c]	−2.029 (−3.56 to 0.50)
Palatability			
Baseline	6.4 ± 2.8	5.8 ± 3.0	
Week 6	5.9 ± 2.7	6.0 ± 3.2	−1.732 (−3.67 to 0.21)
Week 12	6.1 ± 2.5[b]	6.5 ± 2.8	−1.577 (−3.33 to 0.18)
Meal weight (g)			
Baseline	277.6 ± 101.2	232.6 ± 102.4	
Week 6	261.9 ± 120.4	238.4 ± 70.5	−24.060 (−129.71 to 81.59)
Week 12	248.8 ± 136.9	287.6 ± 95.4	−92.583 (−200.69 to 15.52)

Appetite assessment was performed using the visual analogue scales (VAS) method. Values are expressed as mean ± SD.
[a] Treatment minus Placebo.
[b] A significant difference was observed at week 12 compared to baseline data ($p < 0.05$).
[c] There was a significant change between groups. Exclusion of the value zero of the 95% CI implies statistical significance at the 5% level.

plasminogen activator inhibitor type 1 and a reduction in adiponectin.[2] *C. fimbriata* extract has been shown to significantly reduce leptin levels and inhibit leptin resistance in rat studies.[25] However, the present study did not show a significant reduction in leptin levels following 12-week *C. fimbriata* administration. Further human trials of a longer intervention period investigating the effect of *C. fimbriata* supplementation on adipocytokines is warranted considering the promising results reported in rat models.

In our study, WHR was significantly reduced following supplementation of the *C. fimbriata* extract with a balanced dietary intake and physical activity level in the experimental group. Previous studies have shown that a smaller WHR is associated with a reduced risk of developing impaired glucose metabolism, type two diabetes mellitus, CVD[26] and also an improvement in blood lipid profile.[27] In addition a smaller WHR is associated with a lower risk of metabolic syndrome disturbances, including lower triglyceride and glucose levels, increased HDL-cholesterol[28,29] and lower BP.[29]

The improvement in triglyceride levels and systolic BP, and the reduction in anthropometric parameters including, body weight and BMI in both experimental and placebo groups in the present study could possibly be attributed to a combination of controlled dietary intake, healthy dietary choices and exercise. Previous studies have shown that participation in structured exercise programmes reduces the prevalence of metabolic syndrome.[30] Moderate exercise is beneficial in modifying components of metabolic syndrome, including promoting loss of central fat accumulation, increasing muscle mass,[30] improved insulin sensitivity,[31] reduced BP,[32] increased HDL cholesterol and lower triglyceride levels,[33,34,37] It should be noted that all data on physical activity in the current study were based on self-reported information. Lack of monitoring on this was considered a limitation.

Both placebo and experimental groups showed a significant reduction in the intake of total fat and saturated fat after 12 weeks intervention. In addition we also observed an increasing trend in the consumption of whole grains, fruit and vegetables. Healthy dietary patterns high in whole grains, fruit, vegetables and low in saturated fat are fundamental recommendations for metabolic syndrome.[33] The

increase in the consumption of whole grains in this study may have contributed to the significant reduction in systolic BP, BMI and triglyceride levels in both groups.[33]

Whole grain, fruit and vegetable intake is linked with a decline in hunger and an increase in satiation, which may in turn cause a voluntary reduction in energy intake.[10] The human trial investigating the effect of *C. fimbriata* extract on obese Indians observed a significant decline in hunger, energy intake and less desirable foods including refined sugars, saturated fat, cholesterol and sweets after two months intervention.[10] In the present study no significant change in energy intake between the two groups was recorded over the intervention period although the placebo group showed a reduction in hunger and desire to eat at week 12. For the experimental group no marked change in all elements of appetite sensations except palatability was observed. The reduction in the consumption of less desirable foods indicates that the reward circuitry in the brain may be interrupted by supplementation, therefore affecting feeding behaviour.[34] This has been reported in other studies with medicinal plant supplementation, such as the alkaloid-rich *Mitragyna speciosa*.[35] More investigations are needed to elucidate the underlying mechanisms of pregnane glycosides on feeding behaviour and appetite regulation.

In the current study sodium intake in the experimental group was reduced after 12 weeks intervention. The significant reduction in the palatability of the test meal in this group could be associated with the decline in sodium intake. There may have been a change in taste sensation in the experimental group, which possibly led to a decreasing trend in food consumption and a reduction in the desire of consuming salty food in the experimental group. It is well known that sodium intake is strongly linked to BP regulation with reductions in sodium intake being strongly associated with reductions in systolic BP.[36] Clinical trials have demonstrated that reduced salt intake lowers BP in participants at risk of metabolic syndrome.[37] The significant reduction in sodium intake and palatability of meal in the experimental group could have possibly contributed to the reduction in systolic BP. However, more investigations are needed to elucidate these effects of *C. fimbriata* extract on taste sensation, salt intake and BP.

Further research into the underlying mechanisms of *C. fimbriata* extract on central obesity reduction is needed. In addition to what has been proposed in the previous paragraphs, further investigations on the effects of this supplement on inflammatory biomarkers in obese adults will also add to the understanding of the mechanisms behind the reduction in intra-abdominal fat mass. Moreover, double blind randomised controlled clinical trials of a longer duration and of a larger sample size would also be useful to understand the efficacy of *C. fimbriata* extract on the long-term treatment of obesity and associated lifestyle related diseases.

Conclusion

The present study suggests that supplementation with *C. fimbriata* extract was associated with a clinically meaningful reduction in central adiposity. The controlled exercise recommendations and modifications to dietary intake were linked with favourable changes of metabolic risk factors and an improvement in general health and wellbeing in overweight and obese Australian adults. This study may hold therapeutic promise as an approach for the treatment of obesity and associated lifestyle related risk factors.

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