To evaluate efficacy and safety of *Caralluma fimbriata* in overweight and obese patients: A randomized, single blinded, placebo control trial

**INTRODUCTION**

Obesity epidemic is a leading cause of morbidity and mortality in developing as well as developed countries. World Health Organization’s projects alarming data by 2015, projecting 23 billion adults population to be overweight and more than 700 million to be obese. Obesity and body mass index (BMI) correlate with an increased risk of cardiovascular diseases (CVD) and related morbidity and mortality. Reduction in weight leads to decrease in disease risk factors. It has been found that modest weight loss of ≤10% in obese patients with related complications is associated with better health outcomes as there is improvements in glycemic control, reduction in blood pressure (BP) and reduction in cholesterol levels.

**Aim:** The aim of the following study is to evaluate the efficacy and safety of *Caralluma fimbriata* extract (CFE) in overweight and obese individuals in a prospective, randomized, placebo controlled trial. **Materials and Methods:** Commercially available CFE was assessed in overweight and obese individuals. A total of 89 patients were randomized into a treatment group (*n* = 47) and placebo group (*n* = 42) to receive either CFE in the form capsules/oral 500 mg *b.d.* for 12 weeks or matching placebo in similar way. Patients were evaluated clinically and biochemically at 4, 8 and 12 weeks for anthropometric measurements, appetite, biochemical investigations and other safety parameters. **Results:** At the end of study period both CFE and placebo for 12 weeks caused only numerical reduction in weight, body mass index, waist circumference, hip circumference and waist hip ratio in overweight and obese individuals. However, these parameters failed to attain significant statistical levels (*P* ≥ 0.05). CFE and placebo both failed to elucidate any modification of the appetite. There were no significant changes in the biochemical and clinical parameters in both the test and placebo group. However, CFE was well-tolerated and adverse events noted were mild and transient in nature. **Conclusion:** A commercially available extract of CFE in an oral dose of 1 g/day claimed to have anti-obesity effect failed to yield any positive results on anthropometry and appetite in overweight and obese individuals beyond placebo. There were also no significant differences in the clinical and biochemical parameters. However, CFE was well tolerated. Thereby, underscoring the need to carry more research before CFE is recommended as an anti-obesity drug.

**Key words:** Anti-obesity drugs, appetite, *Caralluma fimbriata*, herbal, obesity
The strategies to treat obesity involve life-style interventions and pharmacological therapies. Many medications were introduced in for obesity management in past and were withdrawn from the market subsequently.[8-10] Rimonabant, a selective antagonist of cannabinoid type 1 receptor due to safety concerns (psychiatric effects)[11,13] and sibutramine, due to it associated potentials to increases BP and pulse rate were withdrawn from the market recently.[14] Currently, orlistat which is a pancreatic and gastrointestinal tract lipase inhibitor is the only agent approved by Food and Drug Administration for long-term use in obesity. However, it is also associated with gastrointestinal side-effects and questionable efficacy.[15]

Thus, the focus of anti-obesity treatment has shifted toward herbal drugs. However, there are few concerns about the safety and efficacy of even herbal supplements as well.[16] Adverse events including hepatic injury, psychiatric, autonomic, gastrointestinal and palpitations have been reported with the use of some herbal supplements.[17] These reports contradict the myth regarding the safety of herbs and calls for detailed scientific evaluation of herbal supplements before they are recommended.

*Caralluma fimbriata* is one such Indian herb widely used for obesity in traditional medicine. It is an edible succulent cacti, which belongs to the family Asclepiadaceae. It is well-known as a famine food, appetite suppressant and grows wild all over India.[18] The scan of literature reveals few studies regarding the efficacy and safety of *C. fimbriata* in humans for the management of obesity and whatever data is available is equivocal. Hence, the current study was undertaken to evaluate efficacy and safety of *C. fimbriata* with respect to anthropometric parameters and appetite suppression in overweight and obese individuals to supplement the earlier work to arrive at conclusive result before it is advocated as anti-obesity drug.

**MATERIALS AND METHODS**

A prospective, randomized, placebo controlled trial was conducted in Post Graduate Department of Pharmacology and Therapeutics in collaboration with the Department of Internal Medicine at Tertiary Care Teaching Hospital. The study protocol was approved by the institutional ethics committee under number Pharma/IEC/2010/328 dated 27.10.2010. Written informed consent was obtained from all the subjects after explaining them the nature and purpose of study. All principles of Bioethics were followed. All patients received herbal drug under supervision of AYUSH out-patient department (OPD) of the hospital.

A total of 106 patients attending Medicine OPD were enrolled for the study. Out of these 106 patients, 89 patients fulfilled the eligibility criteria and were subsequently included in the study. Figure 1 depicts the algorithm of the study.

The overweight (BMI ≥25.0-29.9 Kg/m²) and obese (BMI ≥30 Kg/m²)[19] patients of either sex in the age group of 18-50 years with or without truncal obesity and abdominal obesity were included in the study.[20] The exclusion criteria included pregnant and lactating women, patient currently on other anti-obesity medications or medications known to affect body weight, history of recent weight loss (>3 kg in the previous 3 months), history of eating or psychiatric disorders, current/past history of any drug/alcohol abuse or dependence, any serious illness or history of hospitalization in the previous 3 months. Clinical evaluation with complete medical history, general physical examination and systemic examination was done. After enrollment the subjects underwent standardization and stabilization for a period of 2 weeks: Overweight and obese patients without existing co-morbid conditions were stabilized on diet and physical activity. Overweight and obese patients with existing co-morbid conditions were standardized according to the recommended guidelines of treatment in addition to diet and physical activity. The patients were then randomized by a table of random numbers into two groups, to receive either *Caralluma fimbriata* extract (CFE) or matching placebo. CFE available commercially (Cap S 500 mg) of the same batch of manufacturing (1 g daily)/oral for 12 weeks in the test group was used. Dose selection of the test drug was made from the available clinical study.[21] The placebo group was similarly administered placebo in the form of 2 identical capsules to CFE: twice a day/oral for 12 weeks. All subjects were also provided with the same standard advice regarding diet and physical activity.

Patients were evaluated clinically and biochemically in current single blind study where patients were blind to treatment for a period of 3 months at 4, 8 and 12 weeks for anthropometric measurements (weight, waist circumference [WC], hip circumference [HC], waist hip ratio [WHR], BMI); appetite assessment using visual analog scales (VAS) for “hunger”, “thoughts of food”, “urge to eat” and “fullness of stomach”.[22] Biochemical investigations like lipid profile (Total cholesterol, low-density lipoprotein cholesterol [LDL-c], high-density lipoprotein cholesterol [HDL-c], very-low-density lipoprotein cholesterol [VLDL], total triglycerides), blood glucose (fasting/postprandial), liver function tests (Total protein, Serum Bilirubin, aspartate aminotransferase [AST], alanine aminotransferase [ALT] and alkaline phosphatase), renal function tests (serum creatinine and serum urea), complete blood counts (hemoglobin [Hb], total leukocyte count [TLC], platelet count) were undertaken. Other parameters evaluated include BP, pulse rate, electrocardiography (ECG) and recording of any
adriamycin (ADR) during the study period. Compliance was assessed on basis of number of drop outs and capsule counts done 4 weekly.

**Statistical analysis**

The changes from the baseline scores by the test herbal and placebo are analyzed by Student’s t test for paired data whereas inter group comparisons are carried out by ANOVA and $P < 0.05$ was considered to be statistically significant.

**RESULTS**

A total of 106 patients were enrolled for the study. Out of these 106 patients, 89 patients fulfilled the eligibility criteria and were subsequently included in the study. Table 1 shows that baseline characteristics, which were similar in both groups. On comparative analysis of test group ($n = 47$) and placebo ($n = 42$) on weight, BMI, WC, HC and WHR no significant differences ($P > 0.05$) were observed in regards to the change of body weight, BMI, WC, HC and WHR over 12 weeks [Table 2]. The data on comparative analysis of test drug and placebo on appetite assessment from the VAS is presented in Table 3. There were no significant differences ($P > 0.05$) observed in the change of “hunger”, “thoughts of food”, “urge to eat” and “fullness of stomach” in both groups over the study period i.e. (4, 8 and 12 weeks).

All the biochemical investigations like lipid profile (total cholesterol, LDL-c, HDL-c, VLDL, total triglycerides), blood glucose (fasting/postprandial), liver function tests (total protein, serum bilirubin, AST, ALT and alkaline phosphatase), renal function tests (serum creatinine and serum urea), complete blood counts (Hb, TLC, platelet count) and other parameters like BP, pulse rate, ECG showed no statistical variation ($P > 0.5$) between two arms. Thereby, indicating test drug to be safe.
Most adverse events reported by patients receiving test drug or placebo were mild in severity and transient in nature [Table 4]. The incidence of nausea was 8.5% in the test group versus 11.9% in the placebo group, palpitation was 4.2% in the test group versus 2.4% in the placebo group, glossitis was 4.2% in the test group versus 4.8% in the placebo group, generalized weakness was 10.6% in the test group versus 7.1% in placebo group, constipation was 2.1% in test group versus 4.8% in placebo group and 2.1% showed exacerbation of BP in the test group. However, no patient dropped from study due to ADR.

### Table 1: Baseline physical characteristics of the subjects

| Parameter       | Test group (n=47) (%) | Placebo group (n=42) (%) |
|-----------------|-----------------------|--------------------------|
| Age (years)     | Mean±SD               |                          |
|                 | 38.82±6.25            | 38.09±7.63               |
| Sex             | Male:Female           |                          |
|                 | 19 (40.43):           | 15 (35.71):              |
|                 | 28 (59.57):           | 27 (64.28):              |
| Weight (kg)     | Mean±SD               |                          |
|                 | 88.62±12.66           | 88.33±12.7               |
| Height (m)      | Mean±SD               |                          |
|                 | 1.62±0.06             | 1.62±0.06                |
| BMI (kg/m²)     | Mean±SD               |                          |
|                 | 33.52±3.78            | 33.27±3.78               |
| WC (cm)         | Mean±SD               |                          |
|                 | 108.1±10.18           | 105.58±11.94             |
| HC (cm)         | Mean±SD               |                          |
|                 | 112.28±10.94          | 108.52±13.11             |
| WHR             | Mean±SD               |                          |
|                 | 0.97±0.08             | 0.98±0.08                |

SD=Standard deviation, BMI=Body mass index, WC=Waist circumference, HC=Hip circumference, WHR=Waist hip ratio

### Table 2: Comparative analysis of test group (n=47) and placebo group (n=42) on weight, BMI (mean±SD), WC, HC and WHR (mean±SD)

| Time (weeks) | Group (mean±SD) |
|--------------|------------------|
|              | Weight (kg)      | BMI (kg/m²)   | WC in cm | HC in cm | WHR       |
|              | Test Placebo     | Test Placebo  | Test Placebo | Test Placebo | Test Placebo |
| 0            | 88.62±12.66      | 88.33±12.7   | 33.52±3.78  | 33.27±3.78  | 108.1±10.18 |
|              | 108.11±10.19     | 105.58±11.94| 112.28±10.94| 108.52±13.11| 0.97±0.08   |
| 4            | 88.40±12.53      | 88.26±12.58  | 33.44±3.72  | 33.18±3.74  | 107.83±9.92 |
|              | 105.39±12.10     | 108.48±13.10| 111.96±10.53| 112.26±10.66| 0.96±0.08   |
| 8            | 88.23±12.52      | 88.04±12.84  | 33.38±3.72  | 33.09±3.79  | 107.70±9.84 |
|              | 105.40±12.21     | 111.96±10.53| 108.51±13.06| 108.48±13.10| 0.97±0.08   |
| 12           | 88.19±12.62      | 88.00±12.92  | 33.36±3.80  | 33.07±3.82  | 107.51±9.80 |
|              | 105.42±12.24     | 111.94±10.63| 108.47±13.19| 108.04±13.09| 0.98±0.08   |

*n=Number of subjects; *P>0.05 (NS). SD=Standard deviation, WC=Waist circumference, HC=Hip circumference, WHR=Waist hip ratio

### Table 3: Comparative analysis of test drug (n=47) and placebo(n=42) on appetite (mean±SD)

| Time (weeks) | Hunger | Thoughts of food | Urge to eat | Fullness of stomach |
|--------------|--------|------------------|-------------|---------------------|
|              | Test drug | Placebo | Test drug | Placebo | Test drug | Placebo | Test drug | Placebo |
| 0            | 74.89±14.26 | 77.50±14.26 | 67.98±13.1 | 66.76±16.33 | 65.36±15.66 | 64.83±19.4 | 49.98±13.29 | 51.62±13.89 |
| 4            | 74.55±14.19 | 77.23±13.83 | 67.59±12.64 | 66.69±15.52 | 65.02±15.51 | 64.67±19.56 | 50.51±13.13 | 51.93±13.89 |
| 8            | 74.06±14.03 | 76.83±13.31 | 67.15±12.49 | 66.07±15.66 | 64.64±15.2 | 64.62±19.43 | 50.68±13.35 | 52.02±13.93 |
| 12           | 74.00±14.00 | 76.52±13.12 | 67.11±12.66 | 65.93±15.64 | 64.62±15.27 | 64.33±19.32 | 51.00±13.41 | 52.14±14.21 |

*n=Number of subjects; #P>0.05 (NS). SD=Standard deviation

### Discussion

Obesity is implicated for approximately 300,000 deaths in the USA/year.[23] The general public use various methods for weight loss including herbs, vitamins, nutritional supplements and meal replacement preparations. Complementary and alternative therapies have long been used in the Eastern world but recently these therapies are being used increasingly world-wide. When conventional medicine fails to treat chronic diseases and conditions such as obesity efficaciously and without adverse events, many people seek unconventional therapies including herbal medicine.

Evaluation of the data generated from the current study revealed that CFE did not lead to any significant reduction in weight and BMI (P > 0.05) during the 12 weeks of the study. When compared with the placebo group no significant difference (P > 0.05) was observed at any time point during the study period. Our study results are in accordance with the study conducted by Kuriyan et al., 2007.[21]
period of the study. When compared with the placebo group no significant difference \( (P > 0.05) \) was observed at any time point during the study period. Our results are however in accordance with the study conducted by Kuriyan et al.\[21\] which also reported non-significant decline.

Appetite assessment based on VAS in the current study failed to yield any positive results with CFE. No significant differences \( (P > 0.05) \) were observed in the change of “hunger”, “thoughts of food”, “urge to eat” and “fullness of stomach” over a period of 12 weeks when compared to baseline both in the test and placebo group, however, a numerical improvement in all the parameters could be appreciated in both the groups. Furthermore, there were no significant differences \( (P > 0.05) \) observed in the change of appetite on comparative analysis between the test and placebo group. Kuriyan et al.\[21\] however, in their study reported a significant decline in the hunger levels in the experimental group when compared to the placebo group. A small sample size in their study could have led to disparity with our results.

Our study explored product safety in the form of clinical evaluations and reported adverse events. The biochemical and clinical parameters of the subjects belonging to both the experimental and placebo group showed no alterations at different assessment points of the study. Furthermore, no significant differences were observed on comparative analysis between the test and placebo group. Most adverse events reported by patients in our study were mild in severity and transient in nature. The observed adverse events in the present study were nausea, palpitation, glossitis, insomnia, generalized weakness and constipation. No significant differences were observed between placebo and treatment groups in number of reported adverse events and no subjects were removed from the study for a treatment-related adverse event. However, strangely one known case of hypertension presented with exacerbation of BP which was transient in nature and was controlled. The patient continued with CFE with no recurrence of the adverse event during the entire period of the study. In a similar way studies by Kuriyan et al. and Lawrence and Choudhary also reported no serious adverse event with the use of CFE.\[21,24\].

The foregoing discussion brings forth that a commercially available extract of \( C. \) fimbriata in an oral dose of 1 g/day for 12 weeks has failed to yield any positive results on anthropometry and appetite in overweight and obese patients. The current study underscores the need to carry more research before CFE is recommended as an anti-obesity drug in the clinical practice. The negative anti-obesity results seen with CFE in the current study open up a new debate about method of issuing regulatory approval to manufacture and sale any product without much of the existing scientific evidence in its favor.

There are some limitations in the present study such as short duration, single blind design and inadequate sample size. In future, studies of longer duration are further needed to substantiate the much hyped health claims of CFE. An important concern in all pharmacological trials, particularly those in which herbal products are evaluated, is the amount and bioavailability of the active agent. As a standard procedure, we took commercially available standardized extract of CF in the form of capsules. However, we did not measure the active ingredient (pregnane glycosides) blood levels or evaluate its tissue or cytosolic activity which was not in the purview of our study.

### CONCLUSION

A commercially available extract of \( C. \) fimbriata in an oral dose of 1 g/day claimed to have anti-obesity effect failed to yield any positive results on anthropometry and appetite in overweight and obese individuals beyond placebo.

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### REFERENCES

1. Srivastava N, Lakhan R, Mittal B. Pathophysiology and genetics of obesity. Indian J Exp Biol 2007;45:929-36.
2. WHO Fact Sheet 311. 2006. Available from: http://www.who.int/mediacentre/factsheets/fs311/en/index.html. [Last accessed on 2013 Aug 15].
3. Mertens IL, Van Gaal LF. Overweight, obesity, and blood pressure: The effects of modest weight reduction. Obes Res 2000;8:270-8.
4. Wilson PW, D’Agostino RB, Sullivan L, Parise H, Kannel WB. Overweight and obesity as determinants of cardiovascular risk: The Framingham experience. Arch Intern Med 2002;162:1867-72.
5. Thompson D, Edelsberg J, Colditz GA, Bird AP, Oster G. Lifetime health and economic consequences of obesity. Arch Intern Med 1999;159:2177-83.
6. Goldstein DJ. Beneficial health effects of modest weight loss. Int J Obes Relat Metab Disord 1992;16:397-415.
7. Sharma S, Bakshi R, Tandon VR, Mahajan A. Postmenopausal obesity. JK Sci 2008;10:105-6.
8. Lessof MH, Myerson A. Benzedrine sulfate as an aid to be the treatment of obesity. N Engl J Med 1938;218:119-205.
9. Connolly HM, Crary JL, McGoon MD, Hensrud DD, Edwards BS, Edwards WD, et al. Valvular heart disease associated with fenfluramine-phentermine. N Engl J Med 1997;337:581-8.
10. Haddock CK, Poston WS, Dill PL, Foreyt JP, Ericsson M. Pharmacotherapy for obesity: A quantitative analysis of four decades of published randomized clinical trials. Int J Obes Relat Metab Disord 2002;26:262-73.
11. Van Gaal LF, Rissanen AM, Scheen AJ, Ziegler O, Rössner S, RIO-Europe Study Group. Effects of the cannabinoid-1 receptor blocker rimonabant on weight reduction and cardiovascular risk factors in overweight patients: 1-year experience from the RIO-Europe study. Lancet 2005;365:1389-97.
12. Pi-Sunyer FX, Aronne LJ, Heshmati HM, Devin J, Rosenstock J, RIO-North America Study Group. Effect of rimonabant, a cannabinoid-1 receptor blocker, on weight and cardiometabolic risk factors in overweight or obese patients: RIO-North America: A randomized controlled trial. JAMA 2006;295:761-75.
13. Leite CE, Mocelin CA, Petersen GO, Leal MB, Thiesen FV, Rimonabant: An antagonist drug of the endocannabinoid system for the treatment of obesity. Pharmacol Rep 2009;61:217-24.
14. Williams G. Withdrawal of sibutramine in Europe. BMJ 2010;340:c324.
15. Padwal R, Li SK, Lau DC. Long-term pharmacotherapy for overweight and obesity: A systematic review and meta-analysis of randomized controlled trials. Int J Obes Relat Metab Disord 2003;27:1437-46.
16. Alraei RG. Herbal and dietary supplements for weight loss. Top Clin Nutr 2010;25:136-50.
17. Pittler MH, Schmidt K, Ernst E. Adverse events of herbal food supplements for body weight reduction: Systematic review. Obes Rev 2005;6:93-111.
18. Caralluma fimbriata – Caralluma-Flowers of India. Available from: http://www.flowersofindia.net/catalog/slides/Caralluma.html. [Last assessed on 2013 Oct 12].
19. Obesity: Preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser 2000;894:i-xii, 1-253.
20. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002;106:3143-421.
21. Kuriyan R, Raj T, Srinivas SK, Vaz M, Rajendran R, Kurpad AV. Effect of Caralluma fimbriata extract on appetite, food intake and anthropometry in adult Indian men and women. Appetite 2007;48:338-44.
22. Silverstone T. Techniques for evaluating antiobesity drugs in man. In: Bjorntorp P, Cairella M, Howard AN, editors. Recent Advances Obesity Research. 1981. p. 173-9.
23. Weisberg SP. Societal change to prevent obesity. JAMA 2002;288:2176.
24. Lawrence RM, Choudhary S. Caralluma fimbriata in the treatment of obesity. 12th Annual World Congress of Anti-Aging Medicine, Las Vegas, 2-5 December, 2004.

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