RESEARCH ARTICLE

A COMPARATIVE CLINICAL STUDY OF CHIRBILWA (*HOLOPTELEA INTEGRIFOLIA* PLANCH.) BARK GHANWATI AND NAVAK GUGGULU IN OVERWEIGHT

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ABSTRACT

A single blind clinical trial conducted for a period of 3 months to evaluate the effect of the bark of *Holoptelea integrifolia* (Family- Ulmaceae) on body weight and associated metabolic disorder in over weight human volunteers (BMI >25/m2). The trial and positive control groups received GHANAVATI (*Holoptelea integrifolia*) and NAVAKA GUGGULU (Standard Ayurvedic Preparation) respectively 30-60 minute before lunch and dinner. At baseline, after 3 months, significant improvement in body weight, BMI, chest, abdomen, waist, arm and thigh, biceps and triceps circumference, as well as haematological parameter (Hb, serum cholesterol, triglyceride, HDL, LDL, VLDL) were observed in the GHANAVATI group compared with NAVAKA GUGGULU. Bark extract of *Holoptelea integrifolia* may prove to be a useful tool in dealing with the emerging global epidemics of obesity, hyperlipedemia and cardio- metabolic disorders.

INTRODUCTION

Today it is estimated that there are more than 250 million obese people worldwide. Overweight and obesity are increasingly common health conditions globally. However, because fat mass is difficult to measure, the pragmatic definition of obesity is based upon body mass index (BMI). The World Health Organization guidelines define a BMI of 18.5 to 24.9 kg/m2 as normal, 25 to 29.9 kg/m2 as grade 1 overweight and greater than 30 kg/m2 as grade 2 overweight (World Health Organization, 1995). Overweight is increasingly prevalent in developed and developing populations (Flegal *et al*., 2002; National Audit Office, 2001) and is an important contributor to cardiovascular disease (Whitlock *et al*., 2002; Willett *et al*., 1995) operating in part through effects of weight gain on blood pressure,(Dyer *et al*., 1994) blood lipids,(Denke *et al*., 1993; Denke *et al*., 1994) blood glucose, (Grinker *et al*., 2000) type 2 diabetes mellitus, (Carey *et al*., 1997) osteoarthritis(Must *et al*., 1999) along with several common cancers, (Calle *et al*., 2003) and in addition, it impairs health-related quality of life. (Fontaine and Barofsky, 2001)

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The non-fatal health problems associated with overweight include skin problems (Dunn *et al*., 1997) and infertility. (Kirschner *et al*., 1982) Estimations of the burden of disease attributable to excess weight indicate that high body mass index (BMI) is a leading cause of loss of healthy life leading to 33 million disability adjusted life years (DALY) worldwide. (Ezzati *et al*., 2002). Traditional methods of weight reduction are limited (Douketis *et al*., 1999) with an overall pattern of moderate weight loss, followed by gradual weight regain. Numerous other weight management interventions are available, including surgery (for example liposuction, gastroplasty), vitamin and mineral supplements, meal replacements and pharmacological therapies. However, other than in the case of surgery (Sjostrom *et al*., 1999) the long term effectiveness of many of these interventions is unproven. Pharmacological therapies currently approved for weight loss such as sibutramine and orlistat. However, both medications are expensive, have side effects (for example, dry mouth, constipation, insomnia, and headaches with sibutramine, and faecal urgency, flatulence and reduced absorption of fat-soluble vitamins with orlistat) and are contraindicated in many people (Sjostrom *et al*., 1998; Yanovski *et al*., 2002). With the current "back to nature" thrust, many obese patients also look for some help from the alternative systems like Ayurveda. Bark of *Holoptelea integrifolia* or Chirbilva has been cited in Charaka,

Sushruta and is also reported to widely use as anti obesity drug. As per Indian traditional drug knowledge bark of *Holoptelea integrifolia* used for "lekhna kerma" mean scraping and stretching of excessive material. In another words we can say drug will absorb the excessive material and due to heat it will dissolve the fat. (Pandey *et al.*, 2007)

MATERIALS AND METHODS

Study design

This was an open label controlled clinical trial conducted in accordance with GCP Guidelines, the Declaration of Helsinki, (World Medical Association, 2008) The study was conducted at National Institute of Ayurveda Hospital (Jaipur, India), and included 2 weeks screening period followed by 3 months of treatment. Institutional Human ethical committee approved the protocol before initiation of the study and subjects provided written informed consent before any study procedure

Participants

Participants included generally healthy, normal, sedentary men and women aged 18 to 45 years old and BMI>25 kg/m2 were selected randomly in the Hospital of NIA. Pregnant or lactating woman (or those planning to become pregnant during the study), patient of hypertension, anemia, endocrinal diseases, women after menopause and patient aged more than 45 years were excluded from this study. Volunteers with BMI ≤25 kg/m2 or ≥ 40 kg/m2, recent use of any weight loss medication, supplements or programs, a history of weight reducing surgery, or an eating disorder were excluded from this study.

Plant material

Stem bark of *Holoptelea integrifolia* was collected from Ayurvedic garden of National Institute of Ayurveda, Jaipur in the month of September. Because as per quality standards of Ayurveda; Bark, bulb and milk should be collected in autumn (Sharad). The plant and collected material was authenticated by Ms. Divya, Pharmacognocist, Department of Dravya Guna Vigyan, National Institute of Ayurveda, Jaipur. Collected bark was checked for foreign material and shade dried.

Preparation of Chirbilva Ghanavati

Collected Bark of Holoptelea integrifolia (Chirbilva) was broken into small pieces by multi mill. It was mixed with 16 times water and kept for 12 hours. Then it was heated at low temperature until it became its 25 percent. Remaining water extract was filtered by vacuum pump. Filtered water was placed on heat. When it became concentrated, it was removed from furnace. This material was placed for drying. When the material completely dried, medicine was moulded into "vati" form with a weight of 150 mg.

Group design

Eligible participants were randomly assigned to receive either Chirbilva Ghanvati (150 mg, BID) or Navak Guggulu (250 mg, BID).

Change in food and lifestyle was not being prescribed to any patient. Study drugs were packaged in identical, single serving containers. The study products were labeled and coded in such a manner that subjects were unaware of which product each participant was receiving.

Table No. 1 Age and sex wise distribution of 20 patients in two groups

S.No.	Age	Group I (Chirbilva Ghanwati)	Group II (Navak Gugglu)	Total	%
1.	18-25	01	00	01	5 %
2.	25-35	07	08	15	75%
3.	35-45	02	02	04	20%
Total		10	10	20	100%
		Male 05	Male 04		
		Female 05	Female 06		

Physical and Hematological parameters: All the patients were investigated before and after the study period for their physical parameters (anthropometric) like Body weight, BMI, Chest, Abdomen, Waist, Arm, Thigh, Biceps, Triceps Circumferences and Hematological parameters like Haemoglobin, Serum Cholesterol, Serum Triglycerides, HDL, VLDL, LDL. All anthropometric parameter were measured at each study visit by using a non stretch anthropometric tape at the end of normal expiration. (Adult Treatment Panel, 2002)

Hematological parameters were measured by pathological lab of NIA on blood samples. Serum total cholesterol was measured on the basis of Chod- PAP method by measuring absorbance at 505 nm due to formation of Red quinoneimine complex. (Allian *et al.*, 1974) Triglycerides were quantified on the basis of GPO- PAP method (Schettler, 1975; Trinder, 1969). The serum LDL- Cholesterol concentration was calculated according to the Friedewald equation (Friedewald, 1972); LDL-C ¼ total-C – HDL-C – TG/2.2*LDL-C was not calculated when the TG concentration was >4.5 mmol/L.

Statistical Analysis

To check the significance of results parametric Student's 't' test was performed by Graph pad InStat (DATASET 1.ISD) software.

RESULTS

Of the 53 participant screened 28 were randomly assigned to the two treatment groups. Only 20 participants completed the whole study. So we compare and analyse the data of 20 participants in the study. Results of Group I (Physical Tests) were tabulated in table No. 2. As per results of group I, the mean initial for body weight was 65.61 which reduced to 63.65 after treatment, therefore percentage reduction in body weight by 2.987%. Before treatment Mean BMI was 26.51 but after treatment it reduced to 25.67. Percentage reduction in BMI was 3.055%. After treatment through the bark of Holoptelea integrifolia chest circumference and abdomen circumference were reduced to 2.577% and 2.836%. Reduction in Waist circumference after treatment was 2.219%. By seeing these results we can say bark of Holoptelea integrifolia is an effective anti obesity drug. Values are expressed as Mean±SEM; n=10, *P<0.05, **P<0.01 significant difference before and after treatment by paired t test.

Table No. 2 Effects of Holoptelea integrifolia Ghanvati on Measurement of 10 patients in Group I

Measurement	Mean± SEM		Percentage Change	Difference (Mean± SEM)
	Before Treatment	After Treatment		
Body weight (Kg)	65.61± 2.048	63.65± 2.011	2.987	1.96± 0.087**
BMI (Kg/Meter2)	26.51± 0.532	25.67± 0.529	3.055	0.81± 0.356**
Chest Circumference (Inch)	37.25± 0.889	36.29± 0.837	2.577	0.96± 0.154**
Abdomen Circumference (Inch)	34.55± 1.079	33.57± 1.071	2.836	0.98± 0.174**
Waist Circumference (Inch)	40.55± 1.363	39.65± 1.274	2.219	0.90± 0.163**
Arm Circumference (Inch)	11.40± 0.332	11.10± 0.303	2.631	0.3± 0103*
Thigh Circumference (Inch)	20.25± 0.724	19.80± 0.663	2.32	0.47± 0.133**
Biceps (Inch)	2.16± 0.114	2.10± 0.102	2.777	0.06±0.022*
Triceps (Inch)	2.32± 0.646	2.26±0.581	2.586	0.06± 0.022*

Table No. 3 Effects of Navak Guggulu on Measurement of 10 patients in Group II

Measurement	Mean± SEM		Percentage Change	Difference (Mean± SEM)
	Before Treatment	After Treatment		
Body weight (Kg)	70.10± 2.541	68.45±2.53	2.35	1.65± 0.15**
BMI (Kg/Meter2)	26.61± 1	25.87± 0.937	2.78	0.74± 0.084**
Chest Circumference (Inch)	39.38± 1.18	39.05± 1.127	0.84	0.33± 0.153
Abdomen Circumference (Inch)	33.35± 1.10	32.55± 1.10	2.40	0.80± 1.03**
Waist Circumference (Inch)	35.40± 1.59	35.10± 1.50	0.85	0.30± 0.213**
Arm Circumference (Inch)	11.70± 0.37	11.65± 0.37	0.43	0.05± 0.05
Thigh Circumference (Inch)	20.10± 0.21	19.70± 0.32	1.99	0.40± 0.07*
Biceps (Inch)	2.43± 0.12	2.34± 0.20	3.70	0.09± 0.09*
Triceps (Inch)	2.40± 0.26	2.37± 0.29	1.25	0.03± 0.26

Table No. 4 Effect on Haematological & Biochemical parameters in Group I

Haematological parameters	Mean± SEM		Percentage Change	Difference (Mean± SEM)
	Before Treatment	After Treatment		
Haemoglobin	12.31± 0.317	12.77±2.53	+3.73	0.46± 0.274
Serum Cholesterol	177.36± 6.768	165.93± 7.877	-6.44	11.43± 2.247**
Serum Triglycerides	131.19± 9.303	123.1± 7.295	-6.16	8.09± 4
HDL	58.13± 2.719	61.08± 2.52	+5.07	2.95± 1.11*
VLDL	27.83± 1.82	25.33± 1.82	-5.31	1.48± 0.796
LDL	91.80± 7.88	89.91± 8.42	-2.05	1.89± 1.24

Table No. 5 Effect on Haematological & Biochemical parameters in Group II

Haematological parameters	Mean± SEM		Percentage Change	Difference (Mean± SEM)
	Before Treatment	After Treatment		
Haemoglobin	11.53± 0.216	11.8±0.213	+2.34	0. 27± 0.176
Serum Cholesterol	164.33± 5.849	160.74± 4.908	-2.13	3.49± 2.127
Serum Triglycerides	119.83± 5.68	106.47± 4.609	-11.15	13.36± 3.976**
HDL	55.99± 1.666	56.13± 1.502	+0.25	0.14± 0.954
VLDL	25.17± 1.215	24.13± 1.312	-4.13	1.04± 1.34
LDL	87.99± 6.668	83.86± 6.462	-4.69	4.13± 2.584

Table No. 6 Comparison of Both physical and Haematological parameters in Group I and Group II

Measurement	n	Percentage Difference before treatment and after treatment	
		Group I	Group II
Body weight (Kg)	10	-2.987	-2.35
BMI (Kg/Meter2)	10	-3.055	-2.78
Chest Circumference (Inch)	10	-2.577	-0.84
Abdomen Circumference (Inch)	10	-2.836	-2.40
Waist Circumference (Inch)	10	-2.219	-0.85
Arm Circumference (Inch)	10	-2.631	-0.43
Thigh Circumference (Inch)	10	-2.32	-1.99
Biceps (Inch)	10	-2.777	-3.70
Triceps (Inch)	10	-2.586	-1.25
Hb%	10	+3.73	+2.34
Serum Cholesterol	10	-6.44	-2.13
Serum Triglycerides	10	-6.16	-11.15
HDL	10	+5.07	+0.25
VLDL	10	-5.31	-4.13
LDL	10	-2.05	-4.69

Results of Group II (Physical Tests) were tabulated in table No. 3. As per results of group II, The mean initial for body weight was 70.10 after treatment it reduced to 68.45. Percentage reduction in body weight after with Navak Guggulu was 2.35%. In group II Percentage reduction in BMI and abdomen circumference was 2.76 and 2.40 %. Values are expressed as Mean±SEM; n=10, *P<0.05, **P<0.01 significant difference before and after treatment by paired t test.

Results of Group I (Haematological & Biochemical Tests) were tabulated in table No. 4. As per Haematological results of group I, Haemoglobin was increased to 3.73%. Serum cholesterol was reduced to 11.43%. Values are expressed as Mean±SEM; n=10, *P<0.05, **P<0.01 significant difference before and after treatment by paired t test. Values are expressed as Mean±SEM; n=10, *P<0.05, **P<0.01 significant difference before and after treatment by paired t test. Results of Group I and Group II were compared in Table No 6

Figure No. 2

Percent changes from baseline in Body weight (Kg), BMI (Kg/Meter2), Chest Circumference (Inch), Abdomen Circumference (Inch), Waist Circumference (Inch), Arm Circumference (Inch), Biceps (Inch), Triceps (Inch), Triceps (Inch), Hb%, Serum Cholesterol, HDL, VLDL, and LDL before and after treatment in both group I and Group II.
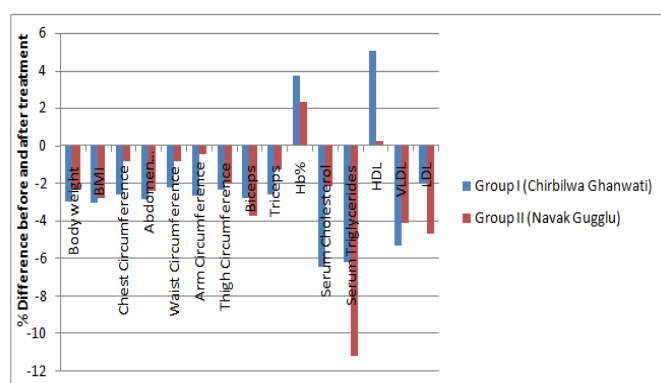
By comparing these results we can say that bark of *Holoptelea integrifolia* was an effective anti obesity drug. During this study, there was not any allergic condition or side effect was being reported by volunteers.

DISCUSSION

In this study, our aim was to evaluate the anti obesity effect of the bark of *Holoptelea integrifolia* on body composition in overweight men and women without advise to change in any lifestyle. The group receiving the Chirvilba Ghanvati made up from bark of *Holoptelea integrifolia* tended to have greater weight loss, significant reductions in abdomen, waist, arm, thigh, biceps and triceps circumference. In hematological study Chirvilba Ghanvati prescribed group was having significant reduction in serum cholesterol, serum triglycerides, VLDL and LDL. To our knowledge, only previous study has evaluated the influence of the whole *Holoptelea integrifolia* plant extract with or without combinations of various biological acceptable excipients against diet induced obesity.

But in our study we used pure bark as a whole not any extract because this way of medication was prescribed in great indian ayurvedic texts. There was also an interesting point that blood haemoglobin level was increased in all volunteers. So bark of *Holoptelea integrifolia* can be assessed as a haematinic drug for anaemic patients.

Conclusion

Therefore we can say that the anti adipogenic and prolipolytic composition comprising bark of *Holoptelea integrifolia* of the present invention is effective for inhibition, amelioration or prevention of various diseases caused by uncontrolled adiposeness and lipolysis thereof, for example, obesity, overweight, lipid storage disease, hyperlipedemia, atherosclerosis, thrombosis and hypercholesterolemia. Additional research is warranted to further clarify the mechanisms responsible for these effects.

Acknowledgement

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