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SHORT COMMUNICATION

Effect of Tulsi (*Ocimum sanctum* Linn.) Supplementation on Metabolic Parameters and Liver Enzymes in Young Overweight and Obese Subjects

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Abstract *Ocimum sanctum* Linn. (also known as Tulsi) is a sacred Indian plant, the beneficial role of which, in obesity and diabetes is described traditionally. This is a randomized, parallel group, open label pilot study to investigate the effect of *O. sanctum* on metabolic and biochemical parameters in thirty overweight/obese subjects, divided into two groups A and B. Group A (n = 16) received one 250 mg capsule of Tulsi (*O. sanctum*) extract twice daily in empty stomach for 8 weeks and group B (n = 14) received no intervention. Statistically significant improvements in the values of serum triglycerides ($p = 0.019$); low density lipoprotein ($p = 0.001$); high density lipoprotein ($p = 0.001$); very low density lipoprotein ($p = 0.019$); Body Mass Index, BMI ($p = 0.005$); plasma insulin ($p = 0.021$) and insulin resistance ($p = 0.049$) were observed after 8 weeks in the *O. sanctum* intervention group. The improvement in HDL-C in the intervention group when compared to the control group was also statistically significant ($p = 0.037$). There was no significant alteration of the liver enzymes SGOT and SGPT in both the intervention ($p = 0.141$; $p = 0.074$) and control arms ($p = 0.102$; $p = 0.055$) respectively. These observations clearly indicate the beneficial effects of O. sanctum on various biochemical parameters in young overweight/obese subjects.

Keywords *Ocimum sanctum* · Obesity · Serum lipid · Insulin resistance

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Introduction

Obesity, defined as an excess of adipose tissue, is a global epidemic today [1]. The Body Mass Index (BMI), calculated as weight in kilograms divided by the height in metres squared, closely correlates with excess adipose tissue and is therefore used for evaluation of obesity. On the basis of percentage body fat and morbidity data, limits of normal BMI are lower in Asian Indians (Normal BMI: 18.0–22.9 kg/m^2, Overweight: 23.0–24.9 kg/m^2, Obesity: $\geq$25 kg/m^2) [2]. Overweight and obese persons are at increased risk of type 2 diabetes mellitus, hypertension, hyperlipidemia and cardiovascular disease. Dietary modification and physical activity are considered the mainstay in the management of obesity and related complications with drug therapy remaining controversial and being associated with adverse effects [1].

Ocimum sanctum Linn. (also known as Tulsi), belonging to the family Lamiaceae, is a sacred Indian plant which has been traditionally used against multiple ailments and holds promise in the management of obesity and its co-morbidities. The beneficial role of Tulsi in obesity and diabetes is described in traditional Indian Ayurvedic literature. Further, the hypoglycemic and hypolipidemic effects of *Ocimum sanctum* have been shown by various workers on experimental animal models [3–6]. The supplementation of *Ocimum sanctum* also modulates insulin resistance in fructose fed rats [7] and diet-induced obese rats [8].

Supplementation with *Ocimum sanctum* has also been shown to improve lipid profile [9] and protect the organs and blood vessels from atherosclerosis [5, 10] in laboratory animals fed high fat diets.

Clinical trials using *Ocimum sanctum* in patients of Type 2 Diabetes Mellitus [11–14] and metabolic syndrome [15] have shown to decrease glucose levels, improve blood pressure and lipid profile. A polyherbal drug containing *Ocimum sanctum* (Cardipro+) when administered to patients with Coronary Artery Disease (CAD) has resulted in significant improvement in blood pressure, lipid profile, left ventricular ejection fraction (LVEF) and left ventricular mass (LVM) [16].

Other metabolic effects of *Ocimum sanctum* include protection of liver, heart [5] and pancreatic islet cells from free radical damage [17], enhancement of liver bile acid synthesis [5], reduction in liver lipid synthesis [9], lowering of cortisol levels [18] and reduction in inflammation [19]. Certain components of *Ocimum sanctum* viz. eugenol, thymol, carvacrol, and 4-allylphenol have shown strong antioxidant activities comparable to those of the known antioxidants, α-tocopherol and butylated hydroxy toluene [20, 21].

Additionally, the ethanolic extract of leaves of *Ocimum sanctum* has been shown to exert hepatoprotective effect in experimental rat models wherein liver damage was induced by atorvastatin, hydrogen peroxide or carbon tetrachloride [22, 23]. The safety margin of the Tulsi extract has also been reported to be very high by various toxicity studies [24–27]. A decrease in sperm count has been reported in experimental animal models supplemented with a very high dose of *Ocimum sanctum* but was found to be reversible after its cessation [24–27].

Despite availability of extensive evidence outlined above, no study has yet been conducted evaluating the role of *Ocimum sanctum* in obese subjects, especially the young obese. Therefore, the present study intends to evaluate the role of Tulsi i.e. *Ocimum sanctum* in obesity as the use of Tulsi may be an easily available, cost-effective and safe way of achieving control of plasma glucose, insulin resistance and serum lipid profile in over-weight and obese persons.

Materials and Methods

This is a randomized, parallel group, open label pilot study which was conducted in the Departments of Physiology and Biochemistry, All India Institute of Medical Sciences, Bhubaneswar.

The study followed guidelines enshrined in the Declaration of Helsinki and Tokyo and was duly granted ethical clearance by the Institute Ethics Committee, AIIMS, Bhubaneswar. The trial was registered on the ClinicalTrials.gov website (NCT02681939).

Thirty overweight/obese subjects (selected on the basis of Body Mass Index greater than or equal to 23 kg/m^2) of both sexes within the age group 17–30 years were included in the study on a voluntary basis. Subjects found addicted to alcohol and tobacco products; suffering from liver disease, malabsorption, nephrotic syndrome, thyroid disorder, allergy or any other chronic disease; on drugs like fluoroquinolones, anticonvulsants, antihypertensives, corticosteroids, hormonal contraceptives, hypolipidemic agents, anti-psychotics, protease inhibitors and isotretinoin were excluded from the study.

A subject information sheet was developed, to inform the participants about the purpose of the study, procedures, potential benefits and risks involved. They were also informed about their ability/right to withdraw from the study at any point of time even after consenting, without assigning any reason. After obtaining informed consent from the subjects, they were randomly assigned to one of two groups A and B. Random allocation of participants into either group was accomplished using a computer generated randomization sequence. Participants belonging to group A (n = 16) received one 250 mg capsule of Tulsi (*Ocimum sanctum*) extract twice daily in empty stomach for 8 weeks and group B (n = 14) received no intervention. The Tulsi (*Ocimum sanctum*) capsules were procured from The Himalaya Drug Company, India, of batch number 22500096, dated April 2015, manufacturing License number L-AUS-133.

The subjects were advised to be on a normal routine diet, not to skip any meal and not to change their exercise pattern (if any) during the study period. The compliance of the intervention was monitored by providing the required number of capsules for one week and asking the subjects to return for refilling every week. Periodic visits and telephonic enquiries were also made. For each subject, a count of unused capsules (if any) was kept. A compliance rate of more than 80 % was considered as adequate.

All the subjects were asked to report after an overnight fasting of 12 h on two occasions i.e. at the start of the study and after 8 weeks of allocation of intervention. After measurement of body weight and height, 5 mL of early morning fasting venous blood sample was collected under aseptic measures on each occasion. Each blood sample was collected in plain vacutainer and an EDTA-Sodium fluoride vial. The sample in plain vacutainer was allowed to clot for collection of serum which was then used for analysis of Lipid Profile [Triglycerides, Total Cholesterol, Low Density Lipoproteins (LDL-C), High Density Lipoproteins (HDL-C), and Very Low Density Lipoproteins (VLDL-C)] and Liver Enzymes [Aspartate aminotransferase, SGOT and Alanine aminotransferase, SGPT]

in fully automated Beckman Coulter AU5800 Biochemistry analyser. The sample collected in EDTA-Sodium Fluoride vials were centrifuged at 5000 rpm for 10 min and the plasma obtained was used for analysis of Glucose (by Hexokinase method in fully automated Beckman Coulter AU5800 biochemistry analyser). Approximately 500 micro litre of plasma was collected in a micro centrifuge tube and was stored at −80 °C. Once all samples were collected (i.e. after 8 weeks), the stored plasma was used for analysis of Insulin by sandwich ELISA supplied by Diametra©. Insulin resistance was calculated using Homeostasis Model Assessment HOMA-2 calculator version 2.2.3© Diabetes Trials Unit, University of Oxford.

The results of all the parameters evaluated were recorded in the subject's Data Collection Form. The results were analyzed using SPSS version 20. All the variables were assessed for normal distribution by Shapiro–Wilk method.

The variables found to be normally distributed were expressed as mean ± standard deviation. The mean values before and after the trial were compared within groups using the two-tailed paired *t* test. For inter-group comparison, two-tailed independent t-test was used.

The variables which were not normally distributed were expressed as median and inter-quartile (Q1–Q3). Non parametric tests: Mann–Whitney *U* test and Wilcoxon Signed Rank test were used for testing significance between the two groups and within a group respectively. A two-tailed *p* value less than 0.05 was considered to be statistically significant.

Results

In Table 1, the baseline parameters of the intervention and control groups have been outlined. There was no statistical difference in any of the anthropometric parameters.

Lipid Profile

As shown in Table 2, a significant improvement was seen in the following lipid parameters in the intervention group: Triglycerides, LDL-C, VLDL-C, LDL/HDL and Total Cholesterol/HDL decreased (12.14 %; $p = 0.019$, 11.73 %; $p = 0.001$, 12.14 %; $p = 0.019$, 29.08 %; $p = 0.000$, 21.26 %; $p = 0.000$ respectively) and HDL-C increased (21.74 %; $p = 0.001$). Inter-group significance was found in the intervention group as compared to the control for HDL-C ($p = 0.037$) which was not present for other parameters. Total cholesterol did not change significantly in either group. No significant change was found for any other parameter in the control group with the exception of HDL-C ($p = 0.025$).

Plasma Glucose, Insulin, HOMA-IR and BMI

Table 3 shows that there has been significant decrease in the plasma insulin, HOMA-IR (Homeostasis Model Assessment for Insulin Resistance) and BMI (Body Mass Index) (28.49 %; $p = 0.021$, 24.79 %; $p = 0.049$, 1.98 %; $p = 0.005$ respectively) in the intervention group but no inter-group significance could be found. Plasma glucose values increased significantly in the control group (10.25 %; $p = 0.012$) while no significant change was found in the intervention group ($p = 0.070$).

Liver Enzymes

There was no significant alteration of the liver enzymes SGOT and SGPT in both the intervention ($p = 0.141$; $p = 0.074$) and control arms ($p = 0.102$; $p = 0.055$) respectively. The results are shown in Table 4.

Discussion

Ocimum sanctum, i.e. Tulsi, as a plant has been used in Indian culture since antiquity for a number of medical conditions. Our study has for the first time demonstrated the beneficial effect of *O. sanctum*in young overweight/obese subjects. Supplementation with *O. sanctum* capsules twice daily for 8 weeks resulted in significant improvement in body weight, BMI, serum lipid profile (except serum total cholesterol), plasma insulin and insulin resistance (IR) in the intervention group. Furthermore, the increase in

Table 1 Baseline characteristics of study groups

Characteristics	*O. sanctum* intervention group (n = 16)	Control group (n = 14)	*p*
Age (years)	21.06 ± 1.39	20.86 ± 0.66	0.660
Body weight (kg)	76.06 ± 12.97	76.29 ± 9.30	0.958
Height (m)	1.70 ± 0.07	1.71 ± 0.65	0.701
BMI (kg/m^2)[a]	25.21 (24.03–28.35)	26.25 (24.49–27.70)	0.608

Results are expressed as mean ± standard deviation except BMI

[a] BMI is expressed as median (Q1–Q3), where *Q1* 1st quartile and *Q3* 3rd quartile

Table 2 Levels of total cholesterol, Triglycerides, LDL-C, HDL-C, VLDL-C, LDL/HDL and TC/HDL

Variables		*O. sanctum* intervention group (n = 16)	Control group (n = 14)	p^b
Total Cholesterol (mg/dL)	Baseline	189.00 ± 41.72	164.86 ± 36.16	0.104
	After 8 weeks	183.63 ± 36.11	164.86 ± 23.32	0.107
	p^a	0.243	1.000	
Triglycerides (mg/dL)	Baseline	100.94 ± 32.22	92.79 ± 28.73	0.473
	After 8 weeks	88.69 ± 35.29	87.71 ± 39.35	0.944
	p^a	0.019	0.578	
LDL-C (mg/dL)	Baseline	123.69 ± 29.61	104.73 ± 26.53	0.077
	After 8 weeks	109.18 ± 26.68	101.81 ± 18.18	0.392
	p^a	0.001	0.415	
HDL-C (mg/dL)	Baseline	45.13 ± 11.34	41.57 ± 13.17	0.434
	After 8 weeks	54.94 ± 8.45	46.29 ± 13.02	0.037
	p^a	0.001	0.025	
VLDL-C (mg/dL)	Baseline	20.19 ± 6.44	18.56 ± 5.75	0.473
	After 8 weeks	17.74 ± 7.06	17.54 ± 7.87	0.944
	p^a	0.019	0.578	
LDL/HDL	Baseline	2.82 ± 0.66	2.63 ± 0.73	0.458
	After 8 weeks	2.00 ± 0.49	2.34 ± 0.71	0.150
	p^a	0.000	0.055	
TC/HDL	Baseline	4.28 ± 0.80	4.11 ± 0.82	0.560
	After 8 weeks	3.37 ± 0.59	3.75 ± 0.87	0.170
	p^a	0.000	0.090	

Results are expressed as mean ± standard deviation

[a] *p* value was calculated using paired *t* tests

[b] *p* value was calculated using student's *t* test

HDL-C in the intervention group when compared to the control group was found to be statistically significant. However, no inter-group significance was seen for other parameters.

Our results for serum lipid profile correlated well with studies wherein *O. sanctum* was supplemented in patients of type 2 diabetes mellitus [11–14] and metabolic syndrome [15]. However, the percentage change reported in our study differed from other studies. Also the study in patients of metabolic syndrome had reported inter-group significance for all parameters [15] while in this study it was true for HDL-C alone. This can be accounted for by the fact that the current study was conducted on a small number of relatively young, obese/overweight and otherwise healthy population over a short period of 8 weeks. This was quite in contrast to previous studies which were conducted on a relatively older population with overt Type 2 Diabetes/Metabolic Syndrome. While the studies in type 2 diabetes had used a similar sample size and duration of intervention, the study in metabolic syndrome had been conducted on a bigger sample over a longer period of 3 months. Fasting glucose levels did not change significantly with *O. sanctum* supplementation in our present study while all previous studies had shown a hypoglycemic effect [11–15]. It is important to note that the subjects participating in this study had normal fasting plasma glucose levels to start with and *O. sanctum* supplementation resulted in no further significant change. However, there was a significant increase in the fasting glucose levels in the control group. This was found to be in agreement with the proposed concept of *O. sanctum* as an 'adaptogen' by virtue of which it helps in adaptation to stress and promotion of homeostasis [28]. Plasma insulin and insulin resistance had not been measured in any of the previous studies though one study in type 2 diabetic patients had explored the possibility of *O. sanctum* leaves in improving β-cell function and enhancing insulin secretion [12]. The current study has for the first time shown improvement in plasma insulin and insulin resistance in humanswith *O. sanctum* supplementation.

Our results were also consistent with several studies using *O. sanctum* conducted on experimental obese/dyslipidemic/diabetic animal models [3–8]. Various mechanisms of action for *O. sanctum* had been suggested in these studies viz. downregulation of mRNA levels of hepatic lipogenesis genes-sterol regulatory element binding protein

Table 3 Levels of plasma glucose, plasma insulin, HOMA-IR, BMI and body weight in *O. sanctum* intervention and control groups at baseline and 8th week of study

Variables		*O. sanctum* intervention group (n = 16)	Control group (n = 14)	p^c
Plasma glucose (mg/dL)	Baseline	87.06 ± 5.45	85.07 ± 6.69	0.377
	After 8 weeks	92.25 ± 11.08	93.79 ± 9.13	0.684
	p^a	0.070	0.012	
Plasma insulin (μU/mL)*	Baseline	5.79 (3.20–12.97)	4.15 (3.25–10.09)	0.759
	After 8 weeks	4.14 (3.11–5.92)	5.73 (4.26–9.00)	0.179
	p^b	0.021	0.861	
HOMA-IR*	Baseline	0.85 (0.48–1.89)	0.60 (0.48–1.43)	0.728
	After 8 weeks	0.64 (0.45–1.00)	0.86 (0.63–1.34)	0.313
	p^b	0.049	0.638	
BMI (kg/m^2)*	Baseline	25.21 (24.03–28.35)	26.25 (24.49–27.70)	0.608
	After 8 weeks	24.70 (23.55–27.82)	25.54 (23.97–27.61)	0.822
	p^b	0.005	0.075	
Body weight (kg)	Baseline	76.06 ± 12.97	76.29 ± 9.30	0.958
	After 8 weeks	74.78 ± 12.57	75.43 ± 10.32	0.880
	p^a	0.004	0.068	

Results are expressed as mean ± standard deviation

* Results are expressed as median (Q1–Q3), where *Q1* 1st quartile and *Q3* 3rd quartile

[a] *p* value was calculated using paired *t* tests

[b] *p* value was calculated using Wilcoxon Signed Ranks test

[c] *p* value was calculated using student's *t* test/Mann–Whitney U test

Table 4 Levels of SGOT, SGPT in *O. sanctum* intervention and control groups at baseline and 8th week of study

Variables		*O. sanctum* intervention group (n = 16)	Control group (n = 14)	p^b
SGOT (IU/L)	Baseline	27.00 (22.25–32.00)	26.00 (18.00–32.25)	0.667
	After 8 weeks	25.50 (19.25–28.75)	22.50 (16.00–29.00)	0.552
	p^a	0.141	0.102	
SGPT (IU/L)	Baseline	30.50 (25.25–41.50)	28.50 (21.50–38.00)	0.423
	After 8 weeks	23.50 (18.75–44.00)	19.00 (13.75–39.50)	0.448
	p^a	0.074	0.055	

Results are expressed as median (Q1–Q3), where *Q1* 1st quartile and *Q3* 3rd quartile

[a] *p* value was calculated using Wilcoxon Signed Ranks test

[b] *p* value was calculated using Mann–Whitney U test

1c (SREBP1c) and fatty acid synthase (FAS) [8]; stimulation of lipolytic activity; activation of lecithin cholesterol acyl transferase (LCAT) and hepatic lipoprotein lipase [6]; increase in bile acid synthesis using cholesterol as precursor [5]; protection of pancreatic islet cells from free radical damage [17] and improvement in antioxidant status [3, 5, 8] which can account for the improvement in serum lipid profile and insulin resistance.The tetracyclic triterpenoid [16-Hydroxy-4, 4, 10, 13-tetramethyl- 17-(4-methyl-pentyl)-hexadecahydro-cyclopenta[a]phenanthren-3-one] isolated from aerial part of *O. sanctum* could be the bioactive compound responsible for the improvement in these metabolic parameters [4].

Our study also showed no significant change in the values of liver enzymes due to *O. sanctum* supplementation. Barring occasional nausea, no other adverse effect was reported by our study participants. This was consistent with previous studies involving *O. sanctum* in humans [11–15] and experimental animals [24–27], thereby suggesting that its use is innocuous.

Due to ethical and monetary constraints, this study could be conducted only on a small number of subjects and for a

limited duration which might be responsible for the inter-group non-significance of most parameters. Also parameters such as post-prandial plasma glucose, HbA1c, serum adipokines and anti-oxidant parameters could not be assayed. Despite this, the current study has ascertained the beneficial effects of *O. sanctum* on various biochemical parameters while not being associated with any adverse effect(s). Though the improvement in insulin resistance with *O. sanctum* supplementation is a major highlight of this study, a larger study population and longer supplementation would bring out the effects of Tulsi extracts in a more observable manner.

With a high degree of safety margin, *O. sanctum* can therefore become an easily available and cost-effective way of improving insulin resistance and lipid profile in overweight and obese individuals. Further studies with a larger sample size and for comparison of *O. sanctum* with existing drugs for dyslipidemia and diabetes management need to be conducted to clearly evaluate its role in these metabolic disorders.

Conclusion

Our study has for the first time demonstrated the beneficial effect of *O. sanctum* in young overweight/obese subjects. Supplementation with *O. sanctum* capsules twice daily for 8 weeks resulted in significant improvement in body weight, BMI, serum lipid profile (except serum total cholesterol), plasma insulin and insulin resistance (IR) in the intervention group.

With a high degree of safety margin, *O. sanctum* can therefore become an easily available and cost-effective way of improving insulin resistance and lipid profile in over-weight and obese individuals.

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Compliance with Ethical Standards

Conflict of interest The authors do not have any financial/commercial conflict of interest in this work.

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