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The Beneficial Effects of SesaVita™ on Lipid Profiles and Blood Glucose Levels in Subjects With Prediabetes and Mild-To-Moderate Hyperlipidemia in India

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Abstract

Individuals suffering from Type 2 diabetes develop prediabetes before progression of diabetes. In case of prediabetes people, the blood glucose levels are higher than normal but not sufficient to be diagnosed as diabetes. On the basis of existing reports on Sesame extract, SesaVita™ which is an herbal food supplement containing Sesame seeds (*Sesamum indicum* L.) extract may provide an option for management of prediabetes. The objective of this study was to determine the beneficial effects of SesaVita™ in prediabetes and mild to moderate hyperlipidemia subjects. This randomized, placebo-controlled, double-blind study comprised of 13 female and 07 male patients with prediabetes and mild to moderate hyperlipidemia, aged between 18 and 65 years. Twenty subjects were randomized to receive SesaVita™ (500 mg/day) or placebo along with therapeutic lifestyle changes for 6 weeks. The primary outcome was the measure of efficacy in terms of change in serum lipid profile and glycaemic levels on week 3 and 6. Secondary outcome measures include safety and tolerability evaluated by physical examination and clinical laboratory evaluations. Improvements in lipid profile and glycaemic levels were observed in SesaVita™ treated group when compared with placebo and baseline. A statistical significant reduction was observed in low density lipoprotein cholesterol (LDL-C), total cholesterol (TC), oral glucose tolerance test (OGTT) and fasting blood sugar (FBS) levels during week 3 and 6 when treated with SesaVita™ extract. No adverse events occurred and all safety parameters were within normal ranges during the study. This study revealed that the treatment with SesaVita™ was safe and well tolerated; may be beneficial in the management of prediabetes and mild-to-moderate hyperlipidemia.

Keywords: SesaVita™, prediabetes, hyperlipidemia, *Sesamum indicum*, lipid profile, glycaemic level

1. Introduction

Prediabetes, also known as intermediate hyperglycaemia, is a high-risk state for diabetes. It is defined as glycaemic variables that are higher than normal, but lower than the diabetes threshold (Tabák, Herder, Rathmann, Brunner, & Kivimäki, 2012). According to the American Diabetes Association (ADA), prediabetes is a fasting plasma glucose (FPG) of at least 100 mg/dL (5.6 mmol/liter) but less than 126 mg/dL (7.0 mmol/liter), which is frequently termed as impaired fasting glucose (IFG), or an abnormal 2-hours response to a 75-g oral glucose tolerance test (OGTT) of at least 140 mg/dL (7.8 mmol/liter) and less than 200 mg/dL (11.1 mmol/liter), which is often termed as impaired glucose tolerance (IGT) (Aroda & Ratner, 2008). About 5-10% of people per year with prediabetes will progress to diabetes, with the same proportion converting back to normoglycaemia. Experts have projected that by the year 2030, the prevalence of prediabetes will be more than 470 million people (Tabák, Herder, Rathmann, Brunner, & Kivimäki, 2012).

Prediabetes people may suffer from the factors such as hyperlipidemia, hypertension and insulin resistance-linked obesity which increase the risk of heart disease. Simultaneous presence of insulin resistance and β-cell dysfunction-abnormalities were found in prediabetes people that start before glucose changes are

detectable. The associations between prediabetes and early forms of nephropathy, chronic kidney disease, small fibre neuropathy, diabetic retinopathy and increased risk of macrovascular disease were evidenced by observational reports (Tabák, Herder, Rathmann, Brunner, & Kivimäki, 2012). Management of individuals suffering from prediabetes includes reduction of cardiovascular disease risk factors, specifically lipid and blood pressure abnormalities. Intensive lifestyle intervention is required to prevent progression from prediabetes to diabetes (Twigg, Kamp, Davis, Neylon, & Flack, 2007).

Medicinal plants, since times immemorial, have been used in virtually all cultures for controlling and preventing diabetes. In Asian countries, Sesame (*Sesamum indicum* L.) has been used to improve the nutritional status and prevent various diseases for thousands of years ago. Sesame is a traditional healthy food and it is not only rich in oil (about 50%) and protein (about 20%), but also rich in lignans including sesamin and sesaminol (up to 1.5%) (Chen et al., 2005). Modulation of fatty acid metabolism, inhibition of cholesterol absorption and biosynthesis, antioxidant and vitamin E-sparing effects, hypotensive effects, improvement of liver functions in connection with alcohol metabolism and antiaging effects are the pharmacological activities of sesame seed lignans (Kamal-Eldin, Moazzami, & Washi, 2011). The other activities of sesame lignans include acceleration of alcohol decomposition in the liver, immunoregulatory and anticarcinogenicity (Namiki, 2007).

In particular, the investigation of dietary substances to lower or regulate cholesterol and blood glucose levels is of special interest. A study reported that the sesamin isomers reduced blood cholesterol level in rats fed with cholesterol-enriched diet owing to increased faecal excretion of cholesterol and inhibition of the activity of liver microsomal 3-hydroxy-3-methyl-glutaryl CoA reductase (Namiki, 2007). In another study, dietary sesame appeared to exert beneficial effects on serum lipids and to improve antioxidant capacity in hypercholesterolemic patients (Chen et al., 2005). Therefore, the aim of the current study was to evaluate the beneficial effects of SesaVita™, an herbal food supplement containing Sesame seeds (*Sesamum indicum* L.) extract in the management of healthy lipid profile and blood glucose level in prediabetic and mild to moderate hyperlipidemic subjects.

2. Methods

2.1 Study Design

This study was a 6-week, randomized, double-blind, placebo-controlled experimental trial to determine the efficacy and safety of SesaVita™ as a dietary supplement for lowering lipids and blood sugar levels.

2.2 Study Site

The study was conducted between April 2012 and June 2012; and carried out in Srinivasa clinic and diabetic care center, Bangalore, India.

2.3 Ethics Approval

The study protocol was reviewed and approved by the Institutional Ethics Committee, Bangalore; and all enrolled subjects provided their consent before the start of the study. The trial was conducted in accordance with the principles of Good Clinical Practice and the Declaration of Helsinki.

2.4 Recruitment of Target Participants

Only participants who fulfilled the inclusion criteria for this current study were recruited. For example, age: 18-65 years old, and some hyperlipidemia as well as prediabetes conditions. Participants suffering from mild to moderate hyperlipidemia should have low density lipoprotein-cholesterol (LDL-C) range 160-189 mg/dL [considered high as per Adult Treatment Panel (ATP) III guidelines, but used in this study as baseline values], TC > 200 mg/dL and with none or one of the risk factors such as current cigarette smoking, family history of premature coronary heart disease (CHD) [CHD in male first degree relative <55 years; in female first degree relative < 65 years], hypertension (BP > 140/90 mmHg or on antihypertensive medication), and with low high-density lipoprotein cholesterol (HDL-C < 40 mg/dL). Participants suffering from prediabetes should have impaired glucose tolerance [2-hours post 75-g OGTT levels in the range of ≥ 140 to ≤ 200 mg/dL] or impaired fasting blood sugar (FBS levels in the range of ≥ 110 to ≤ 125 mg/dL). Along with these criteria, participants should be mentally competent and able to understand all study requirements and sign the informed consent form.

Some volunteers, though interested in this study were excluded from participation according to the following exclusion criteria: If their age was < 18 or > 65 years; if they were suffering from advanced chronic illness that would impair follow-up or monitoring; women who were pregnant or breastfeeding and women of childbearing age; those participants who were unable to complete follow up and were on any medication that would affect evaluation like statins and; patients with mental illness or dementia, with a history of drug and/or alcohol abuse,

subjects allergic to any medication. Twenty subjects who fulfilled the inclusion criteria such as suffering from prediabetes and mild to moderate hyperlipidemia were recruited in this study.

2.5 Sample Preparation

The investigational substance (SesaVita™) is developed by M/s. Olive Lifesciences Pvt. Ltd., Bangalore, India. Sesame seeds were washed and dried, and sesame oil was extracted using organic solvent at room temperature for 4-hours. Thereafter, the miscella was filtered, and the product was concentrated and crystallized using organic solvent at room temperature. Crystals were filtered out and dried under vacuum. The dried material was re-dissolved in an organic solvent and refluxed with activated charcoal for 2-hours. The material was passed through hyflo bed and concentrated the clear filtrate to thick paste. Organic solvent washings were given to thick paste at room temperature to get the pure crystals. Crystals (SesaVita™) were filtered out, pulverized and dried under vacuum at 70 ºC.

2.6 Procedure

Twenty subjects were randomized to receive SesaVita™ or placebo (microcrystalline cellulose) along with therapeutic lifestyle changes (TLC) for 6 weeks (Figure 1). SesaVita™ (n = 11) or placebo (n = 9) were orally administered twice a day (500 mg/day in two divided doses) 20 minutes before breakfast and dinner. The dosing schedule was maintained for the duration of the study.

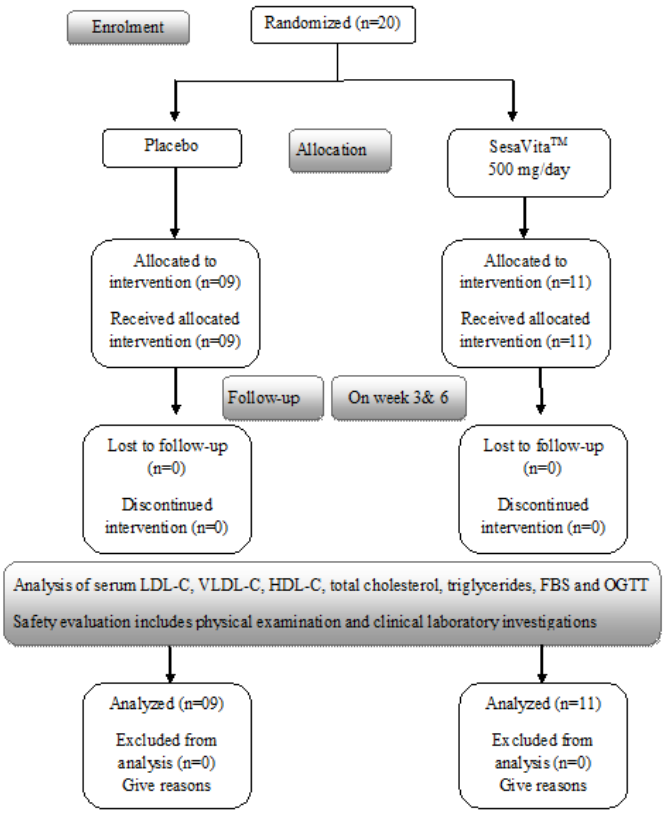

Figure 1. Study flow chart

FBS: Fasting blood sugar, HDL-C: High density lipoprotein cholesterol, LDL-C: Low density lipoprotein cholesterol, OGTT: Oral glucose tolerance test, VLDL-C: Very low density lipoprotein cholesterol.

2.7 Follow-Up

The subjects were followed-up for six weeks.

Initial visit (Day 0): The participants were randomized to one of the two groups (Placebo and SesaVita™). Their medical history was recorded using questionnaires and their physical examination was performed. The

corresponding test substance was dispensed and recommended to follow therapeutic lifestyle changes which includes low fat diet, weight management and increased physical activity to all the participants.

Follow-up visits: During week 3 and 6, the changes in serum lipid profile and glycaemic levels were measured. The physical examination and clinical laboratory evaluations [Electrocardiogram (ECG), haematology, biochemical tests, liver function tests and urine analysis] were carried out on week 6.

2.8 Assessment of Efficacy

The efficacy was assessed by measuring serum lipid profile (LDL-C, total cholesterol, very low-density lipoprotein cholesterol, HDL-C and triglycerides) and glucose levels (FBS and OGTT) on week 3 and 6 in patients with prediabetes and mild to moderate hyperlipidemia. Serum lipid profile was measured using commercially available kit of metro lab auto analyzer. Glucose levels were measured using glucometer (Accu-chek active glucose monitor).

2.9 Assessment of Safety

On completion of 6-weeks treatment, each subject was specifically questioned about the presence or absence of any side effects which the patient or the physician may attribute to the drug treatment. Along with this, physical examination and clinical laboratory evaluations such as ECG, haematology, biochemical tests, liver function test and urine analysis were carried out during initial and final visits.

2.10 Statistical Analysis

The data presented here are given as mean values with standard error of the mean (SEM). Statistical analysis was performed using unpaired t test and one-way ANOVA followed by Dunnett's t test. The statistical significance was set at (^{a}), (*) $p < 0.05$ and (^{b}), (**) $p < 0.01$. The above statistical applications were performed using Instat ver. 5.00, GraphPad Software Inc., San Diego, CA, USA.

3. Results

A total of 20 patients who fulfilled the selection criteria and voluntarily consented were enrolled in the current study and randomly assigned into two groups (Placebo and SesaVita^{TM}). The characteristics of the patients including age, weight, height, pulse rate, blood pressure (diastolic and systolic), serum lipid profile and glycaemic levels of all groups at baseline are summarized in Table 1.

Table 1. Characteristics of the patients at baseline

	Placebo (n=9)	SesaVita^{TM} (n=11)
Age (years)	49.11±2.73	50.09±3.71
Weight (kgs)	66.14±3.14	64.04±1.50
Height (cms)	163.00±2.59	162.27±2.29
Pulse rate/min	88.22±2.54	77.72±2.24
BP systolic (mmHg)	126.88±1.37	127.27±3.35
BP diastolic (mmHg)	82.22±1.22	81.36±1.62
Lipid profile (mg/dL)		
LDL-C	165.04±1.19	167.59±1.45
TC	237.77±4.17	235.81±5.08
VLDL-C	28.15±1.79	24.13±2.67
HDL-C	43.21±2.39	45.10±1.76
TG	147.77±7.31	112.27±15.38
Glycaemic values (mg/dL)		
FBS	116.11±1.76	110.45±6.20
OGTT	170.55±6.93	167.90±4.28

Data is presented as mean ± SEM.

BP: Blood pressure, LDL-C: Low density lipoprotein cholesterol, TC: Total cholesterol, VLDL-C: Very low density lipoprotein cholesterol, HDL-C: High density lipoprotein cholesterol, TG: Triglycerides, FBS: Fasting blood sugar, OGTT: Oral glucose tolerance test.

Changes in serum lipid profile and glycaemic levels of the treated group are summarized in Table 2. In comparison with the placebo group, SesaVita™ treated group showed a significant decrease ($p < 0.01$) in LDL-C level at week 3 and 6. No significant differences were found in other serum lipids among the groups; however, a non-significant decreasing tendency was observed in total cholesterol and TG levels at week 3 and 6. In addition, SesaVita™ showed a significant decrease ($p < 0.05$, $p < 0.01$) in FBS level at week 3 and 6, respectively when compared to placebo. No significant differences were found in OGTT level between the groups; however, a decreasing tendency was observed at week 3 and 6.

When compared to baseline SesaVita™ group showed a significant decrease ($p < 0.01$) in LDL-C level at week 3 and 6. In addition, during week 6 it also showed a significant decrease ($p < 0.01$, $p < 0.05$) in total cholesterol and FBS level respectively. It also showed a significant decrease ($p < 0.05$, $p < 0.01$) in OGTT level at week 3 and 6, respectively. The physical examination and clinical laboratory investigations performed on day 0 and week 6 in placebo and treated groups were found to be within normal limits. No adverse events were reported in patients treated with SesaVita™. Thus, the treatment with SesaVita™ was found to be safe and well tolerated by all patients during the complete intervention period.

Table 2. Effect of SesaVita™ on serum lipid profile and glycaemic levels in patients with prediabetes and mild to moderate hyperlipidemia

Variables		Placebo	SesaVita™
Lipid profile (mg/dL)			
LDL-C	Baseline	165.04±1.19	167.59±1.45
	Week 3	158.55±1.18	144.36±3.03**[b]
	Week 6	153.55±1.59	135.81±4.02**[b]
TC	Baseline	237.77±4.17	235.81±5.08
	Week 3	229.66±3.75	220.90±5.79
	Week 6	225.33±3.89	210.36±4.85[b]
VLDL-C	Baseline	28.15±1.79	24.13±2.67
	Week 3	24.22±1.94	31.81±3.77
	Week 6	23.66±2.38	29.09±3.22
HDL-C	Baseline	43.21±2.39	45.10±1.76
	Week 3	46.88±1.64	45.00±1.85
	Week 6	48.11±1.96	45.81±1.63
TG	Baseline	147.77±7.31	112.27±15.38
	Week 3	145.44±7.05	120.22±12.14
	Week 6	143.55±6.58	118.54±9.26
Glycaemic levels (mg/dL)			
FBS	Baseline	116.11±1.76	110.45±6.20
	Week 3	111.11±1.86	102.00±1.35*
	Week 6	109.22±1.54	97.45±1.69**[a]
OGTT	Baseline	170.55±6.93	167.90±4.28
	Week 3	162.00±6.57	148.36±5.73[a]
	Week 6	158.00±5.66	146.36±4.53[b]

Data is presented as mean ± SEM. *Comparison with placebo; [a, b]Comparison with baseline; *$p < 0.05$, **$p < 0.01$; [a]$p < 0.05$, [b]$p < 0.01$

FBS: Fasting blood sugar, HDL-C: High density lipoprotein cholesterol, LDL-C: Low density lipoprotein cholesterol, OGTT: Oral glucose tolerance test, TC: Total cholesterol, TG: Triglycerides, VLDL-C: Very low density lipoprotein cholesterol.

4. Discussion

The findings from this investigation has provided valuable information on the probable efficacy and safety of SesaVita™ in managing prediabetes and mild to moderate hyperlipidemia by lowering serum cholesterol and glycaemic levels. Treatment with SesaVita™ in patients suffering from prediabetes and mild to moderate hyperlipidemia was found in this study to improve the lipid profile and glycaemic levels when compared to the placebo group and baseline. The high performance liquid chromatography (HPLC) characterization of SesaVita™ revealed the presence of 71.11% w/w total sesamin complex. Thus, the lowering plasma cholesterol and glycaemic levels might be related to the amounts of sesamin complex from sesame seeds.

The effects of sesamin, a lignan from sesame seeds, on various aspects of cholesterol metabolism were examined in rats maintained on various dietary regimens. It has been reported that, following administration of sesamin at dietary level of 0.5% for 4 weeks significantly reduced the concentration of serum and liver cholesterol with irrespective of the presence or absence of cholesterol in the diet. (Hirose et al., 1991). A clinical study in hypercholesterolemic patients reported that daily oral intake of sesamin for 4 weeks significantly decreased total and LDL cholesterol concentrations (Hirata et al., 1996). Sesamin as a dietary supplement administered in hyperlipidemic rats reduced plasma and liver total cholesterol and LDL cholesterol concentrations (Kamal-Eldin et al., 2000). The hypocholesterolemic effect of sesamin is probably through inhibition of intestinal absorption of cholesterol, increased excretion of cholesterol into bile and decreased activity of 3-hydroxy-3-methylglutaryl coenzyme A reductase (Hirose et al., 1991).

The earlier studies have reported that the serum lipids in hyperlipidemia can be improved by the dietary plant seeds or nuts, which have favorable fatty acid and nutrient profiles. A few functional components of sesame seeds shares with nuts are low levels of saturated fatty acids and high levels of monounsaturated and polyunsaturated fatty acids. In addition, to prevent hypercholesterolemia there are other bioactive molecules such as plant protein, dietary fiber, phytochemicals and lignans in nuts and sesame. (Iwamoto et al., 2000; Durak, et al., 1999; O'Byrne, Knauft, & Shireman, 1997; Chisholm et al., 1998; Curb et al., 2000; Zambón et al., 2000). Treatment with SesaVita™ in patients with prediabetes and mild to moderate hyperlipidemia which exhibited improvements in serum lipid profile and glycaemic levels may be due to presence of sesamin complex, lignans present in sesame seeds. Changes in lifestyle, including a balanced diet and regular physical exercise may serve as adjunct therapies for decreasing LDL cholesterol and glycemia levels. Thus, sesame extract can be used as dietary supplement in the management of healthy lipid and glucose levels in patients with prediabetes and mild to moderate hyperlipidemia.

5. Conclusion

Based on the results obtained in this study, it can be concluded that patients with prediabetes and mild to moderate hyperlipidemia treated with sesame extract for 6 weeks are likely to realize positive changes in their lipid profiles and blood glucose levels. Thus, the herbal supplement (SesaVita™) may be beneficial for maintaining healthy lipid and glucose levels in patients with prediabetes and mild to moderate hyperlipidemia.

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