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SHORT COMMUNICATION

Salacia reticulata Improves Serum Lipid Profiles and Glycemic Control in Patients with Prediabetes and Mild to Moderate Hyperlipidemia: A Double-Blind, Placebo-Controlled, Randomized Trial

H.N. Shivaprasad,[1] M. Bhanumathy,[1] G. Sushma,[1] T. Midhun,[1] K.R. Raveendra,[2] K.R. Sushma,[2] and K. Venkateshwarlu[2]

[1]*Research and Development Centre, Olive Lifesciences Pvt. Ltd., Sahakar Nagar, Bengaluru, India.*
[2]*Srinivasa Clinic and Diabetic Care Centre, Girinagar, Bengaluru, India.*

ABSTRACT The present randomized, double-blind, placebo-controlled study evaluated the efficacy and safety of *Salacia reticulata* leaves and root bark extracts in 29 patients with prediabetes and mild to moderate hyperlipidemia. Patients received either *Salacia* extracts (500 mg/day) or placebo along with therapeutic lifestyle changes for a period of 6 weeks. Efficacy was evaluated in terms of change in lipid profile and glycemic levels. The safety and tolerability was evaluated by a physical examination and clinical laboratory evaluations. Improvements in lipid profiles and glycemic levels were observed in *Salacia* extract-treated groups when compared to placebo at week 6. A statistical significant reduction was observed in low-density lipoprotein cholesterol and fasting blood sugar (FBS) levels at week 3 and 6 when treated with root bark extract. The leaves extract-treated group showed statistically significant reduction in FBS levels at week 6 only. No adverse events occurred and all safety parameters were within normal ranges during the study. This study revealed that treatment with *S. reticulata* was safe and well-tolerated and may be beneficial in the management of prediabetes and mild to moderate hyperlipidemia.

KEY WORDS: • ***hyperlipidemia*** • ***leaves*** • ***lipid profile*** • ***prediabetes*** • **Salacia reticulata** • ***root bark***

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Prediabetes, also known as intermediate hyperglycemia, is a high-risk state for diabetes. It is defined as glycemic variables that are higher than normal, but lower than the diabetes threshold. About 5–10% of people per year with prediabetes will progress to diabetes, with the same proportion converting back to normoglycemia. The worldwide prevalence of prediabetes is increasing and experts have projected that more than 470 million people will have prediabetes by the year 2030.[1] Prediabetes is associated with the simultaneous presence of insulin resistance and β-cell dysfunction—abnormalities that start before glucose changes are detectable. Those individuals suffering from prediabetes may often suffer from hyperlipidemia, hypertension, and insulin resistance-linked obesity—all factors that sharply increase the risk of heart disease.[1] Management includes reducing cardiovascular disease risk factors, specifically lipid and blood pressure abnormalities. Intensive lifestyle intervention is required to prevent progression of prediabetes to diabetes.[2]

Medicinal plants, since times immemorial, have been used in virtually all cultures for controlling and preventing diabetes. In Ayurvedic medicine, *Salacia* species (*e.g.*, *S. oblonga*, *S. prinoides*, and *S. reticulata*) known as Ponkoranti, have been used for thousands of years for the treatment of diabetes. *Salacia* extracts have been extensively consumed in Japan, the United States, and other countries as a food supplement for the prevention of obesity and diabetes.[3] Traditionally, *S. reticulata* is ingested as an herbal tea (Kothala Himbutu tea), in which, a tea bag of the herbal mixture is steeped in boiling water and ingested using a formula passed on in an oral tradition to members of the family of the ayurvedic physician.[4] The roots and stems of *S. reticulata* and the roots of *S. oblonga* have been extensively used for the treatment of rheumatism, gonorrhea, skin diseases, and particularly as a specific remedy for the initial stages of diabetes in the ayurvedic system of traditional medicine.[3] In several clinical studies, *Salacia* species have been reported for its hypoglycemic activity.[4–6] Thus, the present study aimed to investigate the efficacy and safety of *S. reticulata* leaves and root bark extracts in the management of patients with prediabetes and mild to moderate hyperlipidemia.

A randomized, double-blind, placebo-controlled experimental trial was designed to determine the efficacy and safety of *Salacia* extracts as a dietary supplement for

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Address correspondence to: M. Bhanumathy, MPharm, Research and Development Centre, Olive Lifesciences Pvt. Ltd., Sahakar Nagar, Bengaluru 560 092, India, E-mail: bhanumathy@olivelifesciences.com

lowering lipids and blood sugar levels. The study protocol was reviewed and approved by the Institutional Ethics Committee (Bangalore, India). The trial was conducted in accordance with the principles of Good Clinical Practice and the Declaration of Helsinki. Patients were eligible for enrolment according to the following selection criteria:

- Age between 18 and 65 years old.
- As per Adult Treatment Panel III guidelines: Baseline low-density lipoprotein cholesterol (LDL-C) ranging 160–189 mg/dL, total cholesterol >200 mg/dL, and with no or one of the below risk factors
  - Current cigarette smoking
  - Family history of premature coronary heart disease
  - Hypertension (blood pressure >140/90 mmHg or on antihypertensive medication)
  - Low high-density lipoprotein cholesterol (HDL-C <40 mg/dL)
  - Age (men >40 years; women >40 years)
- Patients with impaired glucose tolerance or impaired fasting blood sugar (FBS).
- Patients being mentally competent and able to understand all study requirements and sign the informed consent form.

Patients were excluded from participation according to the following criteria:

- Age less than 18 years or over 65 years.
- Suffering from advanced chronic illness that would impair follow-up or monitoring.
- Women who were pregnant or breastfeeding and women of childbearing age.

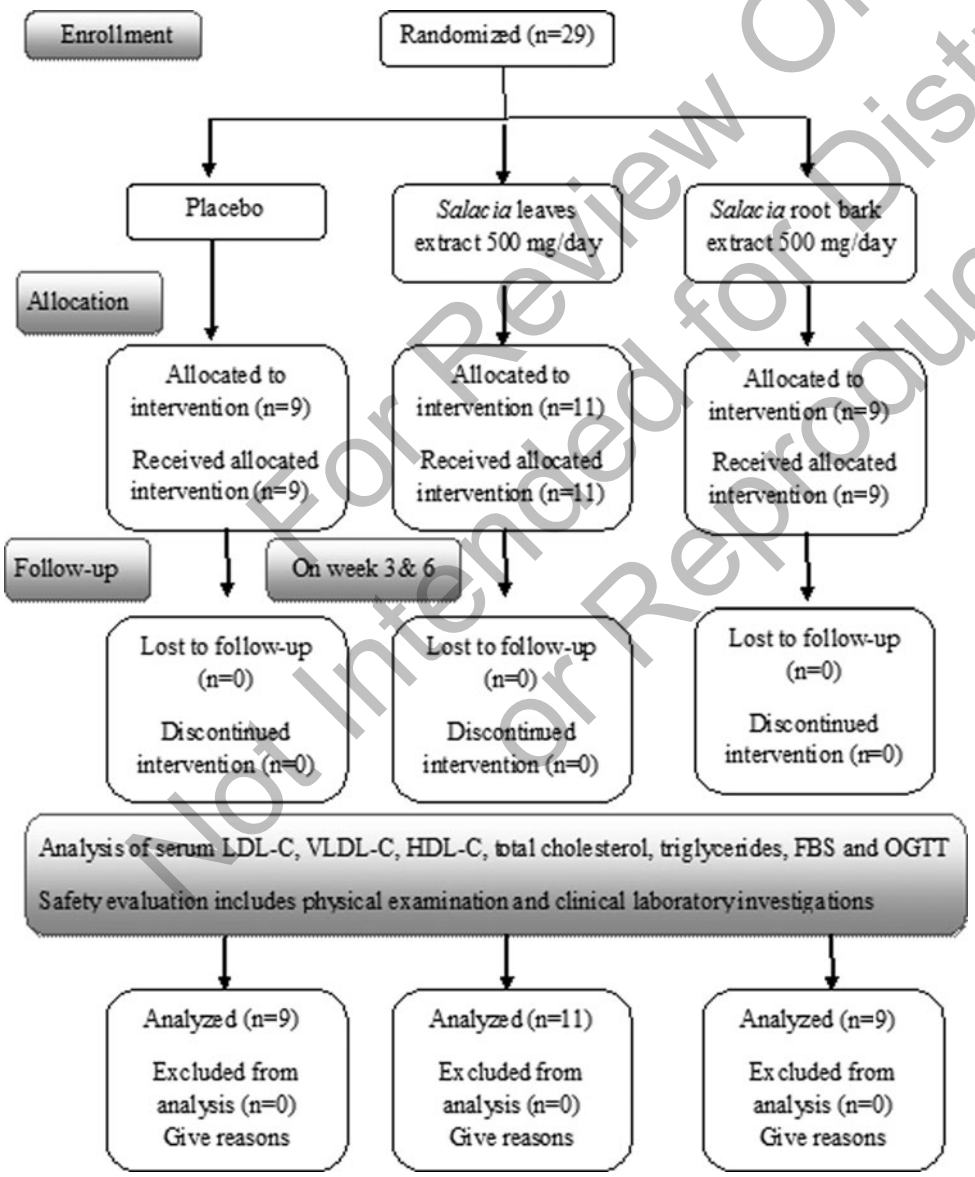

FIG. 1. Study flowchart.

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Table 1. Characteristics of the Patients at Baseline

	Placebo (n = *9*)	Salacia *leaves extract* (n = *11*)	Salacia *root bark extract* (n = *9*)
Age (years)	49.11 ± 2.73	43.00 ± 1.53	51.66 ± 3.56
Weight (kg)	66.14 ± 3.14	73.11 ± 2.47	70.56 ± 1.84
Height (cm)	163.00 ± 2.59	166.45 ± 1.94	169.44 ± 2.68
Pulse rate (beats/min)	88.22 ± 2.54	77.27 ± 3.33	82.22 ± 3.15
BP systolic (mmHg)	126.88 ± 1.379	125.45 ± 2.61	138.00 ± 10.34
BP diastolic (mmHg)	82.22 ± 1.22	79.45 ± 1.75	85.22 ± 1.10
Lipid profile (mg/dL)			
LDL-C	165.04 ± 1.19	164.00 ± 1.10	165.68 ± 3.32
TC	237.77 ± 4.17	236.27 ± 3.40	233.00 ± 6.28
VLDL-C	28.15 ± 1.79	28.74 ± 2.31	22.40 ± 1.62
HDL-C	43.21 ± 2.39	43.72 ± 1.90	44.00 ± 2.67
TG	147.77 ± 7.31	153.36 ± 15.57	114.88 ± 9.34
Glycemic values (mg/dL)			
FBS	116.11 ± 1.76	115.54 ± 1.43	115.22 ± 1.35
OGTT	170.55 ± 6.93	170.09 ± 4.95	165.00 ± 5.29

Data are expressed as mean ± SEM.

BP, blood pressure; 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; SEM, standard error of the mean.

- Those subjects unable to complete follow-up and subjects on any medication that would affect evaluation of *Salacia* drug.
- Patients with mental illness or dementia, with a history of drug and/or alcohol abuse, subjects allergic to any medication.

Subjects were randomly assigned to the treated groups or the placebo group by an automated randomization system.

The investigational substance (*Salacia* leaves and root bark extracts) were developed by M/s. Olive Lifesciences Pvt. Ltd. (Bangalore, India). Subjects were randomized to receive *Salacia* extracts (leaves [$n = 11$] and root bark [$n = 9$]) 500 mg/day or placebo 500 mg/day ($n = 9$) along with therapeutic lifestyle changes for 6 weeks (Fig. 1). *Salacia* extracts or placebo were orally administered twice a day (500 mg/day in two divided doses) 20 min before breakfast and dinner. The dosing schedule was maintained for the duration of the study. The subjects were followed up for 6 weeks. At week 3 and 6, the changes in serum lipid profile and glycemic levels were measured. The physical examination and clinical laboratory evaluations were carried out on week 6.

Efficacy was assessed by measuring the serum lipid profile (LDL-C, total cholesterol, very low-density lipoprotein cholesterol, HDL-C, and triglycerides) and glucose levels (FBS and oral glucose tolerance test [OGTT]) on week 3 and 6 in patients with prediabetes and mild to moderate hyperlipidemia. On completion of the 6-week treatment, each subject was specifically questioned about the presence or absence of any side effects, which the patient

Table 2. Effect of *Salacia* Extracts on Serum Lipid Profile in Patients with Prediabetes and Mild to Moderate Hyperlipidemia

Lipid profile (mg/dL)		*Placebo*	Salacia *leaves extract*	Salacia *root bark extract*
LDL-C	Week 3	158.55 ± 1.18	154.45 ± 1.71	144.66 ± 3.00**
	Week 6	153.55 ± 1.59	144.90 ± 1.81	138.11 ± 2.90**
TC	Week 3	229.66 ± 3.75	224.18 ± 5.32	215.44 ± 6.80
	Week 6	225.33 ± 3.89	217.72 ± 5.30	209.00 ± 5.26
VLDL-C	Week 3	24.22 ± 1.94	24.27 ± 3.43	24.33 ± 2.97
	Week 6	23.66 ± 2.38	25.00 ± 3.43	24.44 ± 2.81
HDL-C	Week 3	46.88 ± 1.64	45.45 ± 2.18	47.55 ± 2.07
	Week 6	48.11 ± 1.96	47.81 ± 1.48	48.66 ± 1.89
TG	Week 3	145.44 ± 7.05	144.81 ± 12.50	109.22 ± 8.11
	Week 6	143.55 ± 6.58	133.54 ± 11.54	111.88 ± 7.54

Data are expressed as mean ± SEM.

**$P < .01$.

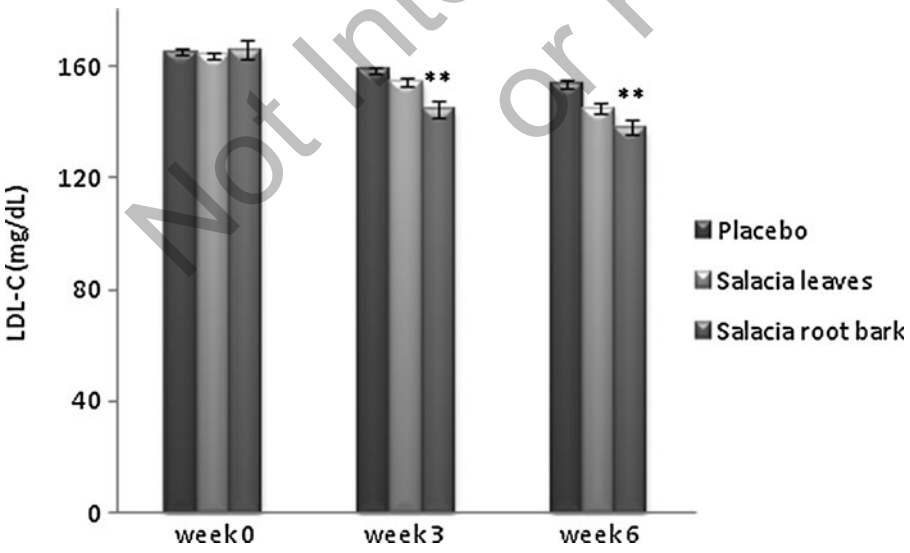

FIG. 2. The effect of *Salacia* extracts on the low-density lipoprotein cholesterol (LDL-C) level in patients with prediabetes and mild to moderate hyperlipidemia. **$P < .01$.

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Table 3. Effect of *Salacia* Extracts on Glycemic Levels in Patients with Prediabetes and Mild to Moderate Hyperlipidemia

Variables		*Placebo*	Salacia *leaves extract*	Salacia *root bark extract*
Glycemic levels (mg/dL)				
FBS	Week 3	111.11 ± 1.86	105.81 ± 2.56	98.44 ± 2.96**
	Week 6	109.22 ± 1.54	100.81 ± 2.30*	95.88 ± 2.47**
OGTT	Week 3	162.00 ± 6.57	159.09 ± 5.01	143.00 ± 5.68
	Week 6	158.00 ± 5.66	149.45 ± 5.39	142.55 ± 4.97

Data are expressed as mean ± SEM.
*$P < .05$, **$P < .01$.

or the physician may attribute to the drug treatment. Along with this, a physical examination and clinical laboratory evaluations such as electrocardiogram, hematology, biochemical tests, liver function test, and urine analysis were carried out during the initial and final visits.

Data were presented as a mean value and a standard error of the mean. Statistical analysis was performed using one-way analysis of variance followed by the Dunnett's *t* test. The statistical significance was set at $P < .05$ and $P < .01$. The above statistical applications were performed using Instat ver. 5.00 (GraphPad Software, Inc., San Diego, CA, USA).

A total of 29 patients who fulfilled the selection criteria and willing to give informed consent were enrolled in the study and randomly assigned into three groups (placebo, *Salacia* leaf extract, and *Salacia* root bark extract). The characteristics of the patients like age, weight, height, pulse rate, blood pressure (diastolic and systolic), serum lipid profile, and glycemic levels of all groups at baseline are summarized in Table 1. Changes in serum lipid profile of treated groups are summarized in Table 2. In comparison with the placebo group, the *Salacia* root bark extract-treated group showed a significant decrease ($P < .01$) in LDL-C levels at week 3 and 6 (Fig. 2). No significant differences were found in other serum lipids among the groups; however, a nonsignificant decreasing tendency was observed in total cholesterol and TG levels at week 3 and 6. The change in glycemic levels of treated groups is summarized in Table 3. In comparison with the placebo group, the *Salacia* root bark extract-treated group showed a significant decrease ($P < .01$) in the FBS level at week 3 and 6. The *Salacia* leaf extract-treated group showed a statistical significant decrease ($P < .05$) in the FBS level only at week 6 (Fig. 3). No significant differences were found in the OGTT level between the groups; however, a nonsignificant decreasing tendency was observed at week 3 and 6.

The physical examination and clinical laboratory investigations performed on day 0 and week 6 in the placebo and treated groups were found to be within normal limits. No adverse events were reported in patients treated with *Salacia* extracts. Thus, the treatment with *Salacia* extracts was found to be safe and well-tolerated by all patients during the complete intervention period. The results of this study will provide valuable information on the efficacy and safety of *Salacia* extracts in managing prediabetes and mild to moderate hyperlipidemia by lowering plasma cholesterol levels and glycemic levels. *S. reticulata* contains kotalanol, an α-glucosidase inhibitor, which has an action similar to that of acarbose. Active ingredients of *Salacia* include salacinol, kotalanol, kotalagenin-16 acetate, and mangiferin. The active ingredients have a variety of actions, including postprandial glucose decrease by inhibiting α-glucosidases in the intestinal brush border, and thus slowing carbohydrate breakdown into absorbable monosaccharides. The mechanism of action is therefore similar to α-glucosidase inhibitors such as acarbose. The catechin and tannin content may contribute to weight loss properties.[7] Due to the presence of the α-glucosidase inhibitor ingredient in *Salacia*, patients with prediabetes and mild to moderate hyperlipidemia exhibited improvements in serum lipid profiles and glycemic levels when treated with *Salacia* extracts. Changes in lifestyle, including a balanced diet and regular physical exercise may

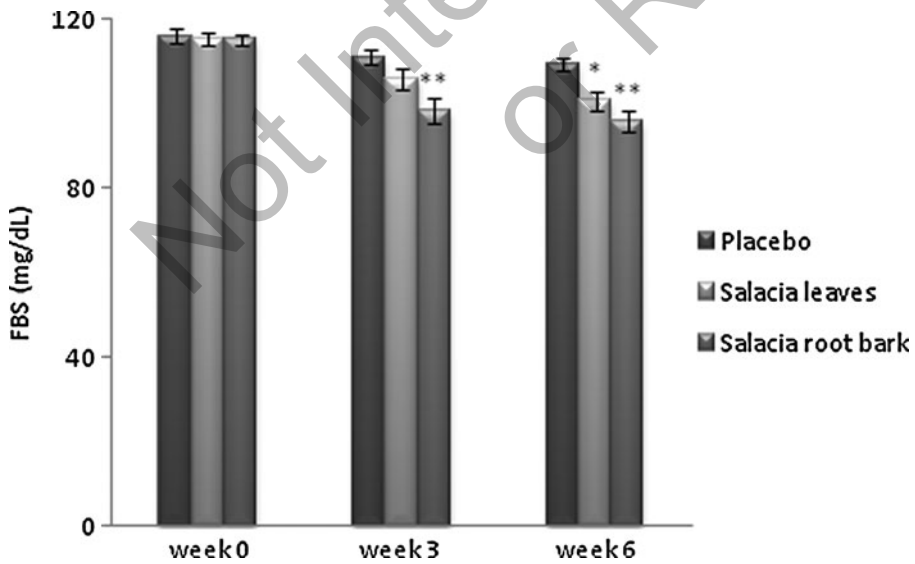

FIG. 3. The effect of *Salacia* extracts on the fasting blood sugar (FBS) level in patients with prediabetes and mild to moderate hyperlipidemia. *$P < .05$, **$P < .01$.

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serve as adjunct therapies for decreasing LDL-C and glycemia levels. Thus, *Salacia* extracts can be used as a dietary supplement in the management of patients with prediabetes and mild to moderate hyperlipidemia.

Based on the results obtained, it can be concluded that patients with prediabetes and mild to moderate hyperlipidemia treated with *Salacia* extracts for 6 weeks should realize positive changes in the lipid profile and blood glucose level. Thus, the herbal supplement (*Salacia* extracts) may be beneficial for maintaining lipids and glucose at normal levels in patients with prediabetes and mild to moderate hyperlipidemia.

AUTHOR DISCLOSURE STATEMENT

No competing financial interests exist.

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