

Pterocarpus Marsupium and *Gymnema Sylvestre* Powder in Alleviation of Biochemical Abnormalities Associated with Human Type 2 Diabetes Mellitus



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Abstract

Objectives: This observational study investigated the antihyperglycemic, antihyperlipidemic and antioxidant potential of *Pterocarpus marsupium* (Vijaysaar) and *Gymnema sylvestre* (Gudmar) ("VG") Therapy in patients with type 2 diabetes mellitus.

Methods: Subjects with type 2 diabetes mellitus were administered a phytochemical formulation consisting 50 ml of aqueous extract derived from 3 gm "VG" powder was administered twice a day for six months. The blood glucose levels were monitored at monthly intervals; glycosylated hemoglobin, lipid profile and biomarkers of oxidative stress, liver and kidney functions were monitored at three monthly intervals.

Results: Daily administration of the "VG" Therapy regularly for 6 months resulted in significant reduction of blood glucose and glycosylated hemoglobin levels. There was also a significant increase in high-density lipoprotein cholesterol levels with concomitant decrease in total cholesterol, triglyceride, low-density lipoprotein cholesterol, and very-low-density lipoprotein levels. Significant improvement in the biochemical markers of oxidative stress was recorded.

Conclusion: The results suggest that herbal formulation "VG" is beneficial in improving glucose and lipid homeostasis in type 2 diabetics and may serve as an adjunct therapy.

Keywords: Hyperglycemia; Dyslipidemia; Oxidative stress; Type 2 diabetes mellitus; *Pterocarpus marsupium*; *Gymnema sylvestre*

Abbreviations: BMI: Body Mass Index; DBP: Diastolic Blood Pressure; FPG: Fasting Plasma Glucose; GSH: Reduced Glutathione; HbA1c: Glycosylated Haemoglobin; HDL: High-Density Lipoprotein Cholesterol; LDL: Low-Density Lipoprotein Cholesterol; PPG: Postprandial Glucose; SBP: Systolic Blood Pressure; SOD: Superoxide Dismutase; SGOT: Serum Glutamate Oxaloacetate Transaminase; SGPT: Serum Glutamate Pyruvate Transaminase; TBARS: Thiobarbituric Acid Reacting Substances; VLDL: Very low-density lipoprotein cholesterol; VG: Vijaysaar and Gurmar

Introduction

Type 2 diabetes mellitus is reaching epidemic proportions worldwide and is a complex metabolic disorder characterized by hyperglycemia and dysregulated lipid metabolism [1,2]. Abdominal obesity and dyslipidemia (increased triglycerides, high LDL-cholesterol and low HDL-cholesterol), and hypertension, as well as altered platelet function [3] are the major risk factors contributing to type 2 diabetes. The metabolic defects that underlie the development of type 2 diabetes may include islet β -cells dysfunction, hyperglucagonemia, elevated endogenous glucose production, development of peripheral insulin resistance, inflammation of adipose tissue, and dysregulation of adipokines production [4]. Chronic elevation of blood glucose which is a central factor in the production of

reactive oxygen species (ROS) [5] which in turn promote cellular damage and contribute to the development and progression of diabetic complications, such as cardiovascular disease, nephropathy, retinal blindness, neuropathy, and peripheral gangrene [6]. The conventional allopathic drugs, sulfonylureas, meglitinides, biguanides, metformin, thiazolidinediones, miglitol, acarbose, etc. although effective [7], are associated with minor or major side effects on long term use [8]. Statins used in the treatment of dyslipidemia have their own limitations [9].

Plant based Indian traditional medicines such as Ayurveda have been used since ancient times in the treatment of diabetes [10]. Ethnobotanical studies of traditional herbal medicine used for diabetes have identified more than 1,200 species of plants

with hypoglycemic activity [10]. Medicinal plants are frequently considered to be less toxic and free from side effects than synthetic ones. The antidiabetic effects of several plant extracts and herbal formulations and their bioactive compounds have been identified and characterized for the treatment of diabetes mellitus [11,12].

Polyherbal formulations [13], have been shown to exhibit antidiabetic, antihyperlipidemic and antioxidant potential in animal models as well as in diabetic patients [14]. The phytochemical based formulations consisting of multiple herbs are liable to produce a large number of metabolites that may act on multiple targets in the body and hence, polyherbal formulations (Which are used in traditional practice) are preferred over mono therapeutic ones. Although, phytochemical based formulations have extensively been used, studies on their proof of efficacy are limited [15].

Gymnema sylvestre (Gudmar) is a climber grown in tropical forests of South-East and belongs to the family Asclepiadaceae. *G. sylvestre* is considered to have a great anti-diabetic potential and used in several anti-diabetic formulations. There are several reports in animal models as well as in diabetic patients which shows that extract of *G. Sylvestre* leaves have anti-diabetic potential [16,17], and these effects are attributes due to increase

in insulin secretion [18]. *Pterocarpus marsupium* (Vijaysaar) is the most versatile plant with a wide spectrum of biological activities and belongs to the family Fabaceae. The *P. marsupium* is reported to be anti-diabetic and associated with anti-obesity, anti-hyperlipidemic, antiinflammatory, anti-oxidative, anti-tumorigenic functions [19-21]. The aim of this study is to explore the therapeutic potential of combined effects of the regular consumption of *Pterocarpus marsupium* and *Gymnema sylvestre* in human subjects with type 2 diabetes mellitus.

Materials and Methods

Study sample

A total of 45 type 2 diabetic patients attending the weekend diabetes clinic run by the Centre for Translational Research, School of Studies in Biochemistry, Jiwaji University, India expressed their willingness to participate in the study. Of these, 35 subjects met the inclusion criteria who were then explained the necessity of maintaining defined lifestyle pattern during the course of the study. Out of 35 subjects, 8 subjects were eliminated during the course of the study due to non-compliance. The remaining 27 subjects took the drug regimen regularly as per the experimental design. Figure 1 shows the number of subjects enrolled and drop outs during the course of study. The patients' baseline characteristics are summarized in (Table 1).

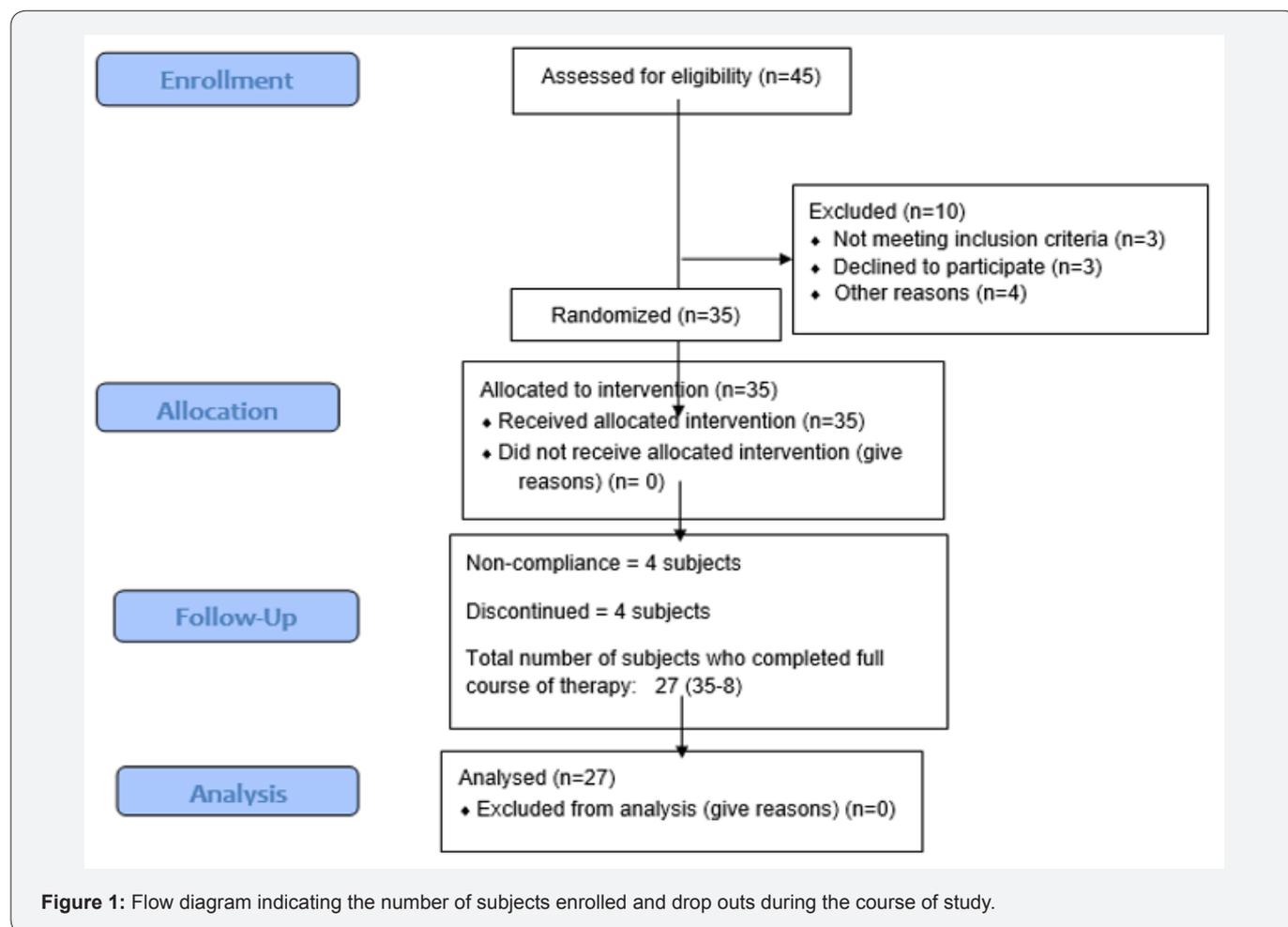


Figure 1: Flow diagram indicating the number of subjects enrolled and drop outs during the course of study.

Table 1: Baseline characteristics of study population.

Measure	n=27
Sex (n), (Male/Female)	22/5
Age (years)	53.11±1.56
Duration of disease (years)	5.42±1.16
Weight (kg)	69.98±1.95
Height (cm)	166.67±1.52
BMI (kg/m ²)	25.21±0.64
SBP (mm Hg)	133.70±2.59
DBP (mm Hg)	81.70±0.97
FBG (mg/dl)	168.75±8.44
PPBG (mg/dl)	256.03±10.22
HbA1c (%) (mmol/mol)	7.68±0.21 (60.4)

Data are expressed as Mean ± SEM;

BMI-Body mass index; SBP- Systolic blood pressure; DBP- Diastolic blood pressure; FBG-Fasting blood glucose; PPBG-Post prandial blood glucose; HbA1c: Glycosylated Haemoglobin.

Study design

The study design included following steps:

- Selection of patients meeting inclusion criteria and those consented to participate in the study.
- Measurement of anthropometric and biochemical parameters once before and at selected intervals during the course of the study.
- Administration of “VG” Therapy in defined dose daily for a period of 6 months.
- Measurement of parameters at the end of the study.
- Analysis of the data.

Inclusion criteria

- Non-insulin dependent diabetes diagnosed, as per the criteria of the World Health Organization;
- Both genders between the ages of 30-65 years;
- Body Mass Index in the range of 18.5 to 40;
- Participants who understood the benefits of the study and signed a written informed consent;

Exclusion criteria

- Presently using other blood glucose regulating agents;
- Daily intake of alcoholic beverages;
- Smokers consuming more than 1 pack/day;
- Patients diagnosed as type I and insulin dependent type II diabetics;
- Patients with hepatic or renal disease, pancreatitis, cardiac problems, uncontrolled hypertension, malnutrition and severe immune deficiency.
- Non-compliance during the course of study.

Before starting the study all participating subjects were given a verbal explanation about the objectives of the study, nature of drug formulation (Kwath) to be consumed daily, (“VG” Therapy) rationale and duration of therapy in local language. They were asked to avoid a carbohydrate rich diet and advised regular walking for about 4-5 km during the course of study. The patients who consented to participate in the study were registered, anthropometric measurements; weight, height and waist were recorded at the beginning and at selected intervals during the study period. The patients were kept exclusively on “VG” therapy.

Composition of drug (VG) formulation

The “VG” formulation consisted of a mixture of *Pterocarpus marsupium* (Vijaysaar), and *Gymnema sylvestre* (Gurmar) (Table 2) and was provided by the M/S Dindayal Industries Ltd. India. The individual plants were identified by Prof. A.K. Jain, School of Studies Botany, Institute of Ethnobiology Jiwaji University Gwalior. Voucher specimens were prepared and deposited at the Centre (IOE-501 and IOE-505).

Table 2: Details of herbs used in “VG” herbal formulation.

Botanical name	General Indian name	Family	Part used	Harberium
			Accession No.	
<i>Gymnema sylvestre</i> (Retz.) R.Br.	Gurmar	Asclepiadaceae	Leaves	IOE-501
<i>Pterocarpus marsupium</i> Roxb.	Vijaysaar	Fabaceae	Heart wood	IOE-505

Composition of VG formulation: 1:1.

Preparation of VG kwath

3 gm of VG powder was suspended in 100 ml drinking water, kept overnight, boiled till 50% water is evaporated, cooled to room temperature and consumed on an empty stomach twice a day for six months under the supervision of an Ayurvedic Physician.

Biochemical parameters

The fasting and postprandial plasma glucose levels were monitored at monthly intervals, while the glycosylated hemoglobin (HbA1c), biomarkers of oxidative stress viz., Superoxide dismutase (SOD), catalase, reduced glutathione (GSH), Thiobarbituric Acid Reactive Substances (TBARS) and lipid profile, biochemical markers of kidney and liver functions were monitored at baseline, at the middle (3 month) and at the end (6 month) of the therapy.

Fasting and postprandial plasma glucose was estimated by the Glucose oxidase/Peroxidase method [22]. Glycosylated hemoglobin (HbA1c) was estimated by the ion exchange resin method [23]. Estimation of plasma total cholesterol by the Cholesterol oxidase Phenolaminophenazone CHOD-PAP

method [24], triglyceride by GPO-PAP method [25], High density lipoprotein cholesterol (HDL) by Polyethylene glycol/CHOD-PAP method [26], Low-density lipoprotein cholesterol (LDL) and Very-low density lipoprotein cholesterol (VLDL) were calculated by the Friedewald formula, urea by the modified Berthelot method [27], uric acid by uricase/PAP method [28], creatinine by modified Jaffe's kinetic method [29], Alanine transaminase (SGPT or ALT) and serum Aspartate transaminase (SGOT or AST) by the modified International Federation of Clinical Chemistry method [30], and bilirubin by method of L. Jendrassik [31] was assayed using standard kits from Crest Biosystems, Goa (India). Markers of oxidative stress such as super oxide dismutase (SOD) Winterbourn et al. [32], catalase by Sinha, [33], glutathione (GSH) Ellman et al. [34], and Thiobarbituric Acid Reactive Substances (TBARS) Ohkawa et al. [35] were checked.

Ethical clearance

The study protocol was duly approved by the Institutional Human Ethics Committee (JU/IHEC/2013-A/13).

Statistical analysis

Statistical analysis was carried out using a paired t test (Sigma stat 3.5). A p-value *p<0.05, **p<0.001 was considered statistically significant.

Results

Effect of VG therapy on hyper-glycemia

Table 3 shows the fasting and postprandial blood glucose levels at monthly intervals in subjects on "VG" therapy. A significant decrease was recorded for fasting (13.5% P<0.05), postprandial (15.0%, <0.001) glucose levels and glycosylated hemoglobin (9.8%) at the end of six months therapy.

Table 3: Effect of "VG" administration on hyperglycemia in type 2 diabetics.

Duration	Variations in Biochemical Markers of Hyperglycemia During the Course of Therapy		
	FPG (mg/dl)	PPBG (mg/dl)	HbA1c (%) (mmol/mol)
Base line values	168.75±8.44	256.03±10.22	7.68±0.21 (60.4)
1 month	157.98±7.63*	245.59±10.20*	
2 month	151.45±7.82*	237.41±10.84*	
3 month	150.04±7.78*	228.97±10.95**	7.25±0.23* (55.7)
4 month	148.43±7.71*	226.44±11.52**	
5 month	146.58±5.92*	219.92±10.17**	
6 month	145.85±8.03*	217.47±10.34**	6.93±0.19** (52.2)
Mean (%) change	(↓13.5%)	(↓15.0%)	(↓9.8%)

Data are expressed as Mean ± SEM; *p<0.05; **p<0.001 compared to Base line values

HDL-High-density lipoprotein cholesterol; LDL-Low-density lipoprotein cholesterol; VLDL- Very- low density lipoprotein cholesterol; TC-Total cholesterol

Effect of VG therapy on lipidemia

Table 4 shows the results of the lipid profile of patients on "VG" therapy. Total cholesterol, triglycerides, LDL and VLDL were

significantly decreased after six months therapy by 9.6%, 14.4%, 15.7%, and 14.4% respectively (P<0.05). HDL cholesterol was elevated from 32.50±1.11 to 35.69 ± 1.02 (P<0.001).

Table 4: Effect of "VG" administration on lipidemia in type 2 diabetics

Biochemical Parameter	Variation in Lipid Profile at 3 Month Intervals During the Course of Therapy			
	Base line value	3 Month	6 Month	Mean (%) change
Total cholesterol (mg/dl)	143.26±4.14	134.59±2.79*	129.42±3.02*	(↓9.6%)
Triglyceride (mg/dl)	147.64±14.16	128.07±11.75*	126.33±7.04*	(↓14.4%)
HDL- cholesterol (mg/dl)	32.50±1.11	34.59±0.84**	35.69±1.02**	(↑9.8%)
LDL-cholesterol (mg/dl)	81.22±3.30	74.39±3.04*	68.47±2.61*	(↓15.7%)
VLDL (mg/dl)	29.53±2.83	25.61±2.35*	25.27±1.41*	(↓14.4%)
TC/HDL Ratio	4.58±0.26	3.96±0.15**	3.71±0.15**	(↓18.9%)
LDL/HDL Ratio	2.59±0.15	2.21±0.13**	1.98±0.11**	(↓23.4%)

Data are expressed as Mean ± SEM; *p<0.05; **p<0.001 compared to Base line values

HDL-High-density lipoprotein cholesterol; LDL-Low-density lipoprotein cholesterol; VLDL- Very- low density lipoprotein cholesterol; TC-Total cholesterol

Effect of VG therapy on biomarkers of oxidative stress

Significant (P<0.05, P<0.001), improvements in GSH level (from 1.98±0.17 to 2.59±0.21 mg/dl), SOD activity (from

0.63±0.05 to 0.94±0.08 μM/min/mg protein), catalase activity (from 7.64±0.24 to 9.44±0.23 μM/min/mg protein) were recorded. A significant decrease (P<0.001) in TBARS (from

457.19±8.09 to 415.15±7.47 (moles of Malondialdehyde/ml of blood) were recorded at the end of six months therapy.

Effect of VG therapy on markers of toxicity

The effect of “VG” therapy on kidney function was monitored by estimating urea, uric acid and creatinine levels in plasma

at specified intervals during the course of therapy. The data presented in Table 5 showed significant (P<0.05), reductions in Urea (from 29.97±1.20 to 27.10±0.88mg/dl) and uric acid (from 5.08±0.20 to 4.67±0.20 mg/dl) and notable reduction in creatinine (from 0.78±0.06 to 0.73±0.05) at the end of six months therapy.

Table 5: Effect of “VG” administration on biomarkers of oxidative stress in type 2 diabetics.

Biochemical Parameter	Variation in Biomarkers of Oxidative Stress at 3 Month Intervals During the Course of Therapy			
	Baseline values	3 Months	6 Months	Mean (%) change
GSH:(mg/ml)	1.98±0.17	2.40±0.28	2.59±0.21*	(↑30.5%)
SOD:(µM/min/mg protein)	0.63±0.05	0.80±0.05	0.94±0.08**	(↑48.4%)
Catalase:(µM/min/mg protein)	7.64±0.24	8.46±0.29	9.44±0.23**	(↑23.5%)
TBARS:(n moles of MDA/ml of blood)	457.19±8.09	430.53±6.52*	415.15±7.47**	(↓9.1%)

Data are expressed as Mean ± SEM; *p<0.05; **p<0.001 compared to Base line values

GSH: Reduced glutathione; SOD-Superoxide dismutase; TBARS- Thiobarbituric acid reacting substances.

Table 6: Effect of “VG” administration on biochemical markers of toxicity.

Biochemical Parameter	Variation in Biomarker of Toxicity at 3 Month Intervals During the Course of Therapy			
	Base line values	3 Month	6 Month	Mean (%) Change
Urea (mg/dl)	29.97±1.20	28.21±0.97*	27.10±0.88*	(↓9.5%)
Uric acid (mg/dl)	5.08±0.20	4.88±0.22*	4.67±0.20*	(↓8.0%)
Creatinine (mg/dl)	0.78±0.06	0.73±0.06	0.73±0.05	(↓5.9%)
Total Billurubin (mg/dl)	0.83±0.06	0.74±0.05	0.70±0.04*	(↓16.3%)
SGOT (IU/L)	22.47±1.61	20.30±1.47	18.00±1.04*	(↓19.9%)
SGPT (IU/L)	23.60±2.32	21.55±2.29	19.26±1.38	(↓18.3%)
LDL/HDL Ratio	2.59±0.15	2.21±0.13**	1.98±0.11**	(↓23.4%)

Data are expressed as Mean ± SEM; *p<0.05; **p<0.001 compared to Base line values.

SGOT- Serum Glutamate Oxaloacetate Transaminase; SGPT- Serum Glutamate Pyruvate Transaminase.

Significant (P< 0.05), variations in biochemical markers of liver functions, namely bilirubin (from 0.83±0.06 to 0.70±0.04 mg/ml) and SGOT (from 22.47±1.61 to 18.00±1.04 IU/L) as well

as SGPT (from 23.60±2.32 to 19.26±1.38 IU/L), at the end of six months was observed (Table 6).

Effect of VG therapy on hypertension and body mass index

Table 7: Effect of “VG” therapy on Hypertension & Body Mass Index.

	Variations at 3 Month Intervals During the Course of Therapy			
	Base line values	3 Months	6 Months	Mean (%) Change
SBP (mm Hg)	133.70±2.59	130.52±2.45	129.22±2.39*	(↓3.3%)
DBP (mm Hg)	81.70±0.97	80.15±1.02	79.56±0.93*	(↓2.6%)
BMI (kg/m2)	25.21±0.64	24.56±0.62**	24.22±0.60**	(↓3.9%)

Data are expressed as Mean ± SEM; *p<0.05; **p<0.001 compared to Base line values

SBP- Systolic blood pressure; DBP- Diastolic blood pressure; BMI-Body mass index.

Table 7 shows variations in systolic blood pressure (from 133.70±2.59 to 129.22±2.39 mmHg), diastolic blood pressure (from 81.70±0.97 to 79.56±0.93 mmHg) and body mass index (from 25.21±0.64 to 24.22±0.60 kg/m2) at the end of the six months therapy.

In India, the indigenous systems of medicine viz., Ayurveda, Siddha & Unani employ plant based extracts for treatment of diabetes (Premeha in Ayurveda). Most of the Ayurveda based formulations depend on plants/herbs based decoctions, and powders. In the present study, administration of the aqueous extract of VG that consisted of equal amounts of the ingredients for over a period of 6 months to type 2 diabetic subjects resulted in significant improvements of altered biochemical markers.

Discussion

Currently, plant based therapies (main or supplementary) are being used globally for the management of type 2 diabetes.

Significant alleviation in glucose homeostasis, as marked by noticeable changes in glycosylated hemoglobin, blood glucose levels, and lipid profile were observed. The *G. sylvestre* leaf extracts are reported to reduce hyperglycaemia in experimental animals [16], and human type II diabetics [17]. The *G. Sylvestre* is reported to promote insulin secretion, probably by regeneration of pancreatic beta cells [17,18]. The gymnemagenin and gymnemic acids in *G. sylvestre*, showed to exhibit potent antioxidant, and hepatoprotective activities [36]. Ethanolic extract of *G. sylvestre* was reported to possess anti-apoptotic potential in STZ-induced diabetic cardiomyopathy, and affected the levels of leptin, insulin, dyslipidemia, apolipoproteins, lipids, LDH (serum lactate dehydrogenase) in experimental models [37]. Administration of deacylgymnemic acid DAGA (200mg/kg), a derivative of gymnemic acid reduced Systolic blood pressure and significantly improved the fasting plasma glucose and HOMA-IR (homeostatis model assessment insulin resistance) with marginal improvement in lipid profile [38]. The *G. sylvestre* is also reported to inhibit absorption of glucose from intestine. The atomic arrangement of gymnemic acid molecules is similar to that of glucose molecules and they reduce the blood glucose level by preventing the absorption of sugar molecule in the intestine. It is attributed by filling the receptor location in the absorptive external layer of the intestine by gymnemic acid molecules [39].

In a controlled study, an aqueous extract of the leaves of *G. sylvestre*, (GS4) when administered at the dose of 400mg/day, to subjects with insulin-dependent diabetes mellitus (IDDM), the insulin requirement came down together with fasting blood glucose, HbA1c and serum lipid levels soon after therapy. However, the GS4 administration failed to check glycosylated haemoglobin and glycosylated plasma protein levels on long term follow up. The GS4 therapy is reported to enhance insulin secretion rate, either by regeneration or revitalisation of the beta cells [40].

The effectiveness of GS4, further investigated as a supplementary drug to conventional oral anti-hyperglycemic drugs. Administration of GS4 (400mg/day) to 22 Type 2 diabetic patients receiving conventional therapy resulted in significant reductions in blood glucose and, glycosylated hemoglobin level. In addition, five of the 22 diabetic patients showed improved glycemic control with GS4 alone and were discontinued their conventional drug [17].

In another study, supplementation of the diet with *G. sylvestre* at the dose of 500 mg per day for a period of 3 months reduced polyphagia, fatigue, blood glucose levels with concurrent reductions in HbA1c, lipid profile suggesting beneficial effect of *G. sylvestre* supplementation in the management of diabetes mellitus [41].

Pterocarpus marsupium is traditionally used in Indian ayurvedic medicine for the treatment of diabetes and has been shown to control diabetes in experimental animals [42]. The phenolic C-glycosides present in *P. marsupium* regulated glucose homeostasis and significantly decreased the TNF- α

level in experimental diabetes [43]. The phenolics, marsupsin, pterosupin, pterostilbene and (-)-epicatechin present in *P. marsupium* have been identified as the blood sugar lowering components [20,44].

The alcohol extract of the bark of *P. marsupium* Roxb shown to exhibit potent antidiabetic activity and corrected the metabolic alterations in diabetic rats [42]. Aqueous extracts of *P. marsupium* Linn significantly attenuated hyper insulinaemia as well as hypertriglyceridaemia and also prevented the alteration in metabolic patterns [45]. The Indian Council of Medical Research undertook an anti-diabetic phase II open trial at four centers across India using Vijaysar (*Pterocarpus marsupium*). Vijaysar was tested in newly-diagnosed or untreated non-insulin dependent diabetes mellitus (NIDDM) patients between 35 and 60 age for 12 weeks. Among the 93 patients who completed 12 wk of treatment, both the fasting and postprandial blood glucose levels fell significantly ($P < 0.001$), by 32 and 45mg/dl at 12 wk from the initial means of 151 and 216mg/dl respectively. Mean HbA1c Other laboratory parameters remained stable during the designated treatment period of 12 wk. Also, no side-effects were reported [46].

Our previous study done with the polyherbal formulation, "GSPF kwath" which contains Vijaysar and Gurmar as two of the ingredients has shown antidiabetic and antioxidative effects [13]. "GSPF kwath", showed 23.5%, 26.7% and 11.7% reductions in fasting, postprandial blood glucose and HbA1c respectively. In the present study "VG" containing only two of the components of GSPF proved highly beneficial in restoring not only hyperglycemia but also lipidemia and antioxidative potential. The changes observed on glycemic, lipidemic and oxidative stress. Oral administration of "VG" therapy for 6 months had no adverse effects, either on kidney or liver functions and in fact showed a significant improvement in the functioning of these vital organs.

Conclusion

In conclusion, the "VG" administration to type 2 diabetic patients with varying degrees of glycemia, lipidemia and oxidative stress provide an efficient alternative to conventional antidiabetic drugs when coupled with active lifestyle and dietary changes. Significant decrease in biochemical markers viz., blood glucose, HbA1c, total cholesterol, triglycerides, LDL-cholesterol, and VLDL-cholesterol and higher values of HDL, following VG therapy are testimony to the anti-diabetic efficacy of VG. Further, the formulation did not show any adverse effects on liver and kidney functions and may be a potential natural and safe therapy for treatment and prevention of diabetic complications but randomized controlled trials are required to confirm these findings.

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