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Original article

Evaluation of "GSPF *kwath*": A *Gymnema sylvestre*-containing polyherbal formulation for the treatment of human type 2 diabetes mellitus

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Abstract

Introduction: Since ancient times, plant-based herbal formulations have been used in Indian traditional medicine to treat diabetes. This observational study investigated the antihyperglycemic, antihyperlipidemic, and antioxidant potential of a *Gymnema sylvestre* polyherbal formulation ("GSPF *kwath*") in patients with type 2 diabetes mellitus.

Methods: A before-and-after study of 32 human subjects with type 2 diabetes mellitus was carried out. Patients were administered "GSPF *kwath*" consisting of a mixture of 10 herbs: *G. sylvestre* (*gurmar*), *Syzygium cumini* (jamun seed), *Phyllanthus emblica* (*amla*), *Curcuma longa* (*haldi*), *Pterocarpus marsupium* (*vijaysaar*), *Terminalia chebula* (*harad*), *Cassia fistula* (*amaltas*), *Picrorhiza kurroa* (*kutki*), *Swertia chirata* (*chirayita*), and *Terminalia bellirica* (*behada*). Patients were administered 50 ml of aqueous extract derived from 10 g of "GSPF *kwath*" daily on an empty stomach for 6 months. The blood glucose levels were monitored monthly, and glycosylated hemoglobin, lipid profile and biomarkers of oxidative stress, and liver and kidney function markers were measured at 3-monthly intervals.

Results: Daily administration of "GSPF *kwath*" regularly for 6 months resulted in significant reductions of blood glucose and glycosylated hemoglobin levels. There was also a significant increase in high-density lipoprotein cholesterol levels and concomitant decreases in total cholesterol, triglyceride, low-density lipoprotein cholesterol, and very-low-density lipoprotein levels. Patients exhibited a significant improvement in the biochemical markers for oxidative stress.

Conclusions: The results suggest that the polyherbal formulation GSPF may have the potential to regulate both hyperglycemia and possibly hyperlipidemia. "GSPF *kwath*" may be a potentially safe and effective therapy for the treatment of type 2 diabetes mellitus.

Keywords: Antidiabetic; Antihyperlipidemic; Blood glucose; Oxidative stress; Polyherbal formulation; Type 2 diabetes mellitus

Introduction

Type 2 diabetes mellitus is a complex metabolic disorder characterized by hyperglycemia, hyperlipidemia, oxidative stress, and inflammatory responses. Hyperglycemia impairs both insulin action and insulin secretion, resulting in glucotoxicity and lipotoxicity, ultimately giving rise to diabetic complications, such as cardiovascular disease, nephropathy, retinal blindness, neuropathy, and peripheral gangrene [1]. Type 2 diabetes is a metabolic disorder that has reached epidemic proportions worldwide. Insulin resistance is a primary factor contributing to the development of type 2 diabetes. Peripheral insulin resistance contributes to reduced glycogen synthesis and failure to suppress glucose production [2]. Hepatic tissue,

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; FPG, fasting plasma glucose; GSH, reduced glutathione; GSPF, *Gymnema sylvestre* polyherbal formulation; HbA1c, glycosylated hemoglobin; 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-reactive substances; VLDL, very-low-density lipoprotein cholesterol.

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adipose tissue, and myocytes are major metabolic tissues that manage glucose and lipid homeostasis. Abdominal obesity and dyslipidemia (increased triglyceridemia, high low-density lipoprotein (LDL)-cholesterol, and low high-density lipoprotein (HDL)-cholesterol) [3] are the major risk factors contributing to type 2 diabetes. Although glucose-lowering drugs such as insulin secretagogues (sulfonylureas and meglitinides), insulin sensitizers (biguanides, metformin, and thiazolidinediones), and α-glucosidase inhibitors (miglitol and acarbose) are effective [4], they may be related to side effects, such as severe hypoglycemia, lactic acidosis, idiosyncratic liver cell injury, digestive discomfort, headache, and dizziness [5]. The use of statins in the treatment of dyslipidemia comes with its limitations [6].

Since ancient times, plant-based Indian traditional medicine has been used to treat diabetes. More than 1200 species of plants with hypoglycemic activity have been reported in the literature [7]. The antihyperglycemic effects of several plant extracts and herbal formulations and their bioactive compounds have been identified and characterized for the treatment of diabetes mellitus [8].

Polyherbal formulations [9] have been shown to exhibit antidiabetic, antihyperlipidemic, and antioxidant potential in animal models as well as in diabetic patients [9,10]. The phytochemical-based formulations containing 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 monotherapeutic ones. Phytochemical-based formulations have been used extensively, but proof of their efficacy is limited [11]. The aim of this study was to explore the therapeutic properties of the gurmar-containing polyherbal formulation "GSPF *kwath*" in human subjects with type 2 diabetes mellitus.

Methods

Study sample

A total of 44 patients with type 2 diabetes attending a weekend diabetes clinic run by the School of Studies in Biochemistry, Jiwaji University, India, were initially identified for the study. Of these, 38 subjects met the inclusion criteria and six subjects were eliminated during the course of the study due to noncompliance. The remaining 32 subjects underwent the drug regimen as per the study design. Fig. 1 shows the number of subjects enrolled and dropouts during the course of the study. The baseline characteristics of the patients are summarized in Table 1. The following criteria were employed for selection of subjects for the study.

Study design

The study design included the following steps:

(1) Patients meeting the inclusion criteria and consenting to participate in the study were selected.

Table 1
Baseline characteristics of participants in "GSPF *kwath*" polyherbal formulation.

Measure	$n = 32$
Sex (n) (male/female)	27/5
Age (years)	55.59 ± 1.47
Duration of disease (years)	6.05 ± 1.10
Weight (kg)	65.98 ± 2.88
Height (cm)	159.59 ± 5.44
BMI (kg/m^2)	25.18 ± 0.70
SBP (mmHg)	132.06 ± 3.81
DBP (mmHg)	81.50 ± 2.10
FBG (mg/dl)	168.23 ± 5.35
PPBG (mg/dl)	253.34 ± 7.12
HbA1c (%) (mmol/mol)	7.21 ± 0.12 (55.3)

Data are expressed as mean ± SEM.
BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; PPBG, postprandial blood glucose; HbA1c, glycosylated hemoglobin.

(2) Anthropometric and biochemical parameters were measured once prior to the study and at selected intervals during the course of the study.
(3) "GSPF *kwath*" was administered daily in defined doses for a period of 6 months.
(4) The parameters were measured at the end of the study.
(5) The data were analyzed.

Inclusion criteria

The following inclusion criteria were employed in the study:

(1) Diagnosis of non-insulin-dependent diabetes, as per the criteria of the World Health Organization;
(2) Both genders between the ages of 30 and 65 years;
(3) Body mass index (BMI) in the range of 18.5–40; and
(4) Participants who understood the benefits of the study and signed written informed consent forms.

Exclusion criteria

The following exclusion criteria were employed in the study:

(1) Current use of other blood glucose-regulating agents;
(2) Daily intake of alcoholic beverages;
(3) Smokers consuming >1 pack/day;
(4) Diagnosis of type I and insulin-dependent type II diabetes; and
(5) Patients with hepatic or renal disease, pancreatitis, cardiac problems, uncontrolled hypertension, malnutrition, and severe immune deficiency.

Before commencement of the study, the objectives, the nature of drugs to be taken ("GSPF *kwath*"), the rationale, and the duration of therapy were conveyed to all participating subjects in the local language. They were asked to avoid a carbohydrate-rich diet and advised to walk regularly for about 4–5 km during the course of the study. The patients who consented to participate in the study were registered; anthropometric measurements such