

Hyperglycemia and hyperlipidemia mitigating impact of *Catharanthus roseus* (Sadabahar) leaves aqueous extract on type2 diabetes mellitus subjects

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ABSTRACT

Type 2 diabetes is increasing at a very high rate especially in developing countries. This disease is co associated with several complications, CVD is one of them. With the disturbing rise in the prevalence of this metabolic disease and associated healthcare cost, interest in alternative or complementary therapies has been grown. *Catharanthus roseus* has been used for centuries to treat a variety of ailments and was a favorite ingredient of magical charms in the middle ages. To assess the efficacy of *Catharanthus roseus* leaves aqueous extracts (75 mg/day) on diabetes and lipid profile and to observe whether the sustained use of *Catharanthus roseus* aqueous leaves extract produces any side effects. 60 diabetic subjects were divided into two groups (In Group A and B, n= 30 per group) and supplemented with *Catharanthus roseus* water extract for 30 days .The results were compared with control group by measuring blood glucose levels and lipid profile. On analyzing the fasting blood glucose level, post prandial blood glucose level, glycated Hb and total cholesterol, total triglyceride, Low density lipoprotein-Cholesterol (LDL-C), High density lipoprotein-Cholesterol (HDL-C), Very low density lipoprotein-Cholesterol (VLDL-C), a significant reduction was observed except High density lipoprotein-Cholesterol was found to be non significant in this study. No side effects of the sustained use of *Catharanthus roseus* aqueous leaves extract were seen. Result suggest that *Catharanthus roseus* can be used as prophylactic agent in the progressively abnormalities related to the diabetes.

Keywords: Diabetes Mellitus, *Catharanthus roseus*, lipid profile, blood glucose level, glycosylated Hb.

INTRODUCTION

Diabetes mellitus also known as “Madhumeha” is a degenerative disease. The word ‘Diabetes’ meaning “siphon” was first given by the Greek physician “Arateus” in the 2nd century which describe patients with excessive thirst and urination. In the 17th century, Willis observed that urine of diabetic patients was sweet, as if imbued with honey or sugar so the word “Mellitus” meaning “honey- honey” was added to it. The presence of sugar in the urine of diabetics was demonstrated by Dobson in 1755 ¹Type 2 diabetes accounts for about 95% of diagnosed diabetes in adults. Several studies have shown that healthy eating and regular physical activity, used with medication if prescribed, can help to control health complications from type 2 diabetes or can prevent or delay the onset of type 2 diabetes ².

While tendency to develop diabetes mellitus is strongly hereditary, yet environmental factors also play no less role in NIDDM occurrence. Lack of exercise and obesity are the major contributors to NIDDM. Roughly, 90% of the individuals with NIDDM are obese. This condition can predispose one to the condition of insulin resistance, which is characterized by hypersecretion of insulin (hyperinsulinemia). Insulin resistance results in increased fasting and

postprandial blood glucose levels which lead to beta cell burn out and eventually occurrence of diabetes. The condition of Insulin resistance may exist for many years before pancreatic beta cell function actually becomes impaired³. Long term complications include cardiovascular diseases, hypertension, chronic renal failure, retinal damage, nerve damage, erectile dysfunction and macro vascular damage which may cause poor healing of wounds particularly of the feet and can lead to gangrene which may require amputation⁴. Hypercholesterolemia is an important factor contributing to the high prevalence of accelerated atherosclerosis and coronary heart diseases⁵. The World Health Organization has predicted a global increase in diabetes prevalence of 39% between the years 2000 and 2030 which will increase the absolute number to 366 million people⁶. Diabetes mellitus can be found in almost every population in the world but this disease becomes a real problem of public health in developing countries, where its prevalence is increasing steadily⁷.

The World Health Organization⁸ has also realized that an effective health agenda for developing countries can never be achieved by western medicine alone, unless it is complemented by alternative medicines including traditional herbal medicine and has accordingly advised and urged developing countries of the world to utilize their medicinal plant resources and other traditional medicine systems in order to achieve the goal of primary health care. Estimates of the current and future economic burden on the health care system can assist decision-makers understand the magnitude of the problem, prioritize research efforts, and plan resource allocation to properly manage the condition. Disease cost estimates also help prioritize interventions, which must be done in the face of limited health care resources. Since the Ayurvedic practice started in India, plant extracts are being used in the cure of diseases. The exact mechanism of these plant-derived preparations is not well understood which requires being scientifically investigated. Although the *Catharanthus roseus* have been used for their alleged health benefits, there is no scientific investigation in this regard. To fill these scientific lacunae, the present work was undertaken.

Catharanthus roseus belong to the family apocynaceae⁹ *Catharanthus roseus* is commonly called as *Periwinkle*, *Madagascar periwinkle* and *Sadabahar*. It grows throughout India and found as an escape in waste places and sandy tracts¹⁰. In the wild, it is an endangered plant; the main cause of decline is habitat destruction by slash and burn agriculture. It is also however widely cultivated and is naturalised in subtropical and tropical areas of the world. It is an evergreen subshrub or herbaceous plant growing to 1 m tall. The leaves are oval to oblong, 2.5–9 cm long and 1–3.5 cm broad, glossy green, hairless, with a pale midrib and a short petiole 1–1.8 cm long. *Catharanthus roseus* leaves extract made significant changes in each cardiovascular parameter after investigation with hypotensive and hypolipidemic effects in animals¹¹. Hot water extract of dried leaves were taken orally to rabbits was active¹². More than 130 different compounds have been reported including about 100 monoterpenoid indole alkaloids¹³. As an important medical plant, it has a good antioxidant potential throughout its parts under drought stress¹⁴. As many others herbal plants established in the indigenous system of medicine for their antidiabetic potentials and this plant has to be established in this indigenous system of medicines. There is a scanty research available on *Catharanthus roseus* leaves. So with this background in mind, this study was embarked on, to study the hypoglycemic, hypolipidemia effect of *Catharanthus roseus* leaves extract in type 2 Diabetes Mellitus.

MATERIALS AND METHODS

Locale

The study was conducted on Type 2 Diabetes Mellitus Subjects of middle age group (40-60 years). Subjects were sought from the main campus of Banasthali University, Tonk in eastern Rajasthan, India.

Plant Material

Catharanthus roseus leaves were collected from the Botanical garden of Banasthali University, campus. The leaves were washed thoroughly with tap water followed with sterilized distilled water for the removal of dust and sand particles.

Preparation of Aqueous Extract from the Fresh *Catharanthus roseus* Leaves

To prepare the extract, 50 g of *Catharanthus roseus* leaves were soaked in 400 ml of distilled water for 12 hours in a beaker and then it was put on water bath. When the volume comes one fourth, then filtered through muslin cloth. Take filtrate in another beaker and heated on water bath till it gets concentrated. Then put into the oven at 40°C till it gets into crystallized form, grounded into the fine powder with an auto-mix blender and stored in air tight container at 4-7 °C until the time of use. Powder of *Catharanthus roseus* leaves extract then manually filled in the capsules.

Experimental Design

Type 2 Diabetes Mellitus Subjects aged between 40-60 years, who were volunteer to be the part selected for the study. The following criterion was used for the selection of type 2 diabetic individuals:-Patients of type II diabetic both sexes with well diagnosed diabetes. Fasting blood glucose in a range of 126-400 mg/dl, in spite taking their usual antidiabetic medicines. Patients not on insulin therapy. Patients taking any medication, other than that of diabetes. Patients not taking *Catharanthus roseus* in any form or any other herbal treatment to control diabetes. Pregnant women could not be the part of study. Selected subjects (n=60) were randomly divided into two groups (In Group A and B, n= 30 per group). Baseline information regarding their dietary practices and disease was collected from the selected samples. Group A was Experimental and was supplemented with *Catharanthus roseus* leaves aqueous extract in the form of powder and Group B served as control group. 75 mg of *Catharanthus roseus* (*Sadabahar*) Leaves aqueous extract equivalent to the 3.2g of *Catharanthus roseus* (*Sadabahar*) Leaves was supplemented to the experimental group for 30 days. Control group was given placebo in capsules

Biochemical Assay

Approximately 5 ml fasting blood samples were taken from each individual on day 0 and day 30. Blood (1ml approximately) samples were transferred to sterilized vial adding 0.5 gm of EDTA (for glycosylated Hb). Rest blood sample (4 ml approximately) were centrifuged for 10 minutes at 4000 rpm for serum separation (blood glucose level and lipid profile). All samples were coded prior to the analysis. Biochemical analysis involved evaluation of blood glucose level (Fasting and post prandial blood glucose level), Glycated Hb and Lipid profile. The levels of glycosylated haemoglobin were estimated by the method Ion Exchange Resin Method¹⁵. Serum was separated and analyzed for fasting blood glucose and post blood glucose level by using the methods of GOD/POD enzymatic method based on end point colorimetric^{16,17} and total cholesterol¹⁸, total triglycerides¹⁹, HDL-C¹⁸ using span diagnostic kit.

LDL-C and VLDL-C were calculated by Friedewald's equation²¹.

$$\text{VLDL-C} = \text{TG}/5 \quad \text{LDL-C} = \text{TC} - (\text{HDL-C} + \text{VLDL-C})$$

Statistical Analysis

Analysis of data was performed using the Statistical Package for the Social version 16.0 (SPSS) computer software. Descriptive statistics were adapted to display data in means \pm SD. The statistical method paired t-test was used to compare the mean values obtained between pre intervention and post intervention on samples. Differences were considered significant whenever the p-value was ($P < 0.01$) and ($P < 0.05$).

RESULTS AND DISCUSSION

The present findings and drawn the inferences, with respect to the specific objectives of the study on the basis of analysis by using relevant statistical methods. The results showed a significant decrease at both level ($p \leq 0.01$) and ($p \leq 0.05$) in the mean fasting blood glucose level, post prandial blood glucose level, glycosylated Hb, total cholesterol, total triglyceride, LDL-C, VLDL-C in experimental group A. whereas group B has no significant decrease ($p \geq 0.05$) in pre and post intervention stages. The calculated value of t is greater than tabulated value, hypothesis is accepted. Hence the supplementation is useful for the diabetic patients at ($p \leq 0.01$). The hypoglycemic activity of *Catharanthus roseus* leaves may be due to the presence of alkaloids like vincristine and vinblastine through stimulation of β cell activity leading to increased insulin production and release⁷. Hence the HDL-C results showed in experimental group A and control group B has no significant decrease ($p \geq 0.05$) in pre and post intervention stages. The calculated value of t is less than tabulated value, hypothesis is rejected. Consequently we can also say that *Catharanthus roseus* leaves stabilized the HDL-C in diabetes subjects.

TABLE 1:- Effect of Aqueous Extract *Catharanthus roseus* leaves on Experimental group

Biochemical Tests	Pre intervention (0 day) (Mean±SD) (mg/dl)	Post intervention (30 days) (Mean±SD) (mg/dl)	Difference between pre and post	Paired t test
Fasting Blood Glucose Level	149.45± 37.90	147.44± 21.00	2.01	5.55**
Post Prandial Blood Glucose Level	240.67± 62.87	228.32± 68.35	12.35	3.60**
Glycosylated Haemoglobin Level	7.15±4.08	7.22±3.51	0.86	3.37**
Total Cholesterol Level	170.40±41.48	165.15±44.27	5.25	2.60*
Total Triglyceride Level	204.96±82.42	198.19±78.2	6.77	2.57*
HDL- Cholesterol Level	28.32 ±16.80	27.88±16.36	0.52	0.15NS
LDL- Cholesterol Level	105.04± 42.28	102.42± 43.92	2.36	2.57*
VLDL- Cholesterol Level	41.0 ± 16.48	39.63 ± 15.64	1.36	2.60*

** Significant at both level ($p \leq 0.01$) and ($p \leq 0.05$)* Significant at ($p \leq 0.01$) level

NS= non significant

TABLE 2:- Biochemical results of control group

Biochemical Tests	Pre intervention (0 day) (Mean±SD) (mg/dl)	Post intervention (30 days) (Mean±SD) (mg/dl)	Difference between pre and post	Paired t test
Fasting Blood Glucose Level	179.06± 0.92	182.23± 32.61	1.88	0.83
Post Prandial Blood Glucose Level	252.89± 0.76	253.65± 0.45	1.33	0.1
Glycosylated Haemoglobin Level	6.93±1.07	6.99±0.98	0.23	0.94
Total Cholesterol Level	269.91±79.71	270.00±46.32	1.23	0.1
Total Triglyceride Level	210.00±70.42	211.34±65.2	0.94	0.1
HDL- Cholesterol Level	37.50±2.46	40.90±2.01	0.21	0.11
LDL- Cholesterol Level	190.40± 34.06	188.90± 23.80	1.03	0.09
VLDL- Cholesterol Level	90.34± 18.23	96.90± 13.78	4.65	0.09

All found to be non significant

However, it can be concluded that *Catharanthus roseus* leaves showed a positive impact on blood glucose and lipid profile of type-2 diabetics. The significant reduction of serum lipid level in the diabetic rats after *Catharanthus roseus* treatment may be directly attributed to the improvement in insulin level²¹. Feeding of *Catharanthus roseus* leaves enriched powder led to marked improvement in antidiabetic activity and their complications. No side effects of *Catharanthus roseus* (*Sadabahar*) Leaves extract were seen.

CONCLUSION

Globally, the prevalence of chronic, non-communicable disease is increasing at an alarming rate and Diabetes is one of them²². If diabetes is not controlled then a lot of complication like coronary artery disease, cerebrovascular disease, peripheral vascular disease, retinopathy, nephropathy and neuropathy arise in diabetic patients and causes morbidity or mortality³. The direct and indirect social or economic cost of treating diabetes and its complication have the potential to cripple the countries health care budgets. *Catharanthus roseus* (*Sadabahar*) is easily available and very cheap. Therefore, it may be concluded from the above results, that the aqueous extracts obtained from the leaves of *Catharanthus roseus* may be used enough as drug to treat diabetes and its complications. These also lead to the conception of this project and the objectives designed under the study were successfully attained. With the disturbing rise in the prevalence of this metabolic disease and associated healthcare cost, interest in alternative or complementary therapies has been grown.

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