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STEVIA REBAUDAINA – A MIRACLE HERB FOR PATIENTS WITH NON-INSULIN DEPENDENT DIABETES MELLITUS AND IMPAIRED GLUCOSE TOLERANCE

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Diabetes Mellitus is a disorder of carbohydrate metabolism which is characterized by a defect in insulin production, liberation and action. Diabetes is a major public health problem all over the world. It is estimated that by 2030 the number of people with diabetes will rise to 438 million. India shelters the most number of people with Diabetes and is termed as the Diabetic Capital of the World. *Stevia rebaudiana*is one such miracle herb which helps in the management of diabetes and can be used by diabetics to satisfy their urge for sweet consumption. The present study was conducted to assess the nutritional composition of Stevia leaves and to assess its hypoglycaemic and hypolipidaemic effect in diabetic patients and in patients suffering from Impaired Glucose Tolerance (IGT). Chemical analysis revealed Stevia to be a nutritious herb with 7% moisture, 9.8% protein, 4% fat, 12% fibre, 62.5% Carbohydrate, 9.2% ash, 0.18% iron and 0.16% Calcium. Dietary intake of fat by the subjects was found to be higher than the Recommended Dietary Allowance whereas the fibre intake was found to be low. Intervention with Stevia leaf powder reduced the fasting and PP Glucose levels in diabetics and in IGT patients. The serum Triglyceride levels were reduced from 103.64±36.3 mg/dl to 70.07+44.2 mg/dl in diabetics and from 137.5 ± 70.2 mg/dl to 120.5 ± 66.3 mg/dl in IGT patients. Hence it can be used as an anti-diabetic herb with a great deal of safety.

Keywords: Diabetes, Hypoglycaemia, Hypolipidaemia, IGT, Stevia

Introduction

The World Health Organisation has defined Diabetes Mellitus as a heterogeneous group of disorders, characterized by a state of chronic hyperglycaemia resulting from a diversity of aetiologies. The underlying cause of diabetes is the defective production or action of insulin, a hormone that controls glucose, fat and amino acid metabolism. In diabetes, the body either fails to properly respond to its own insulin, does not make enough insulin, or both. These cause glucose to accumulate in the blood, often leading to various complications[1,2]

The pancreas plays a primary role in the metabolism of glucose by secreting the hormones insulin and glucagon. The Islets of Langerhans secrete insulin and glucagon

directly into the blood. Insulin is a protein that is essential for proper regulation of glucose and for maintenance of proper blood levels[3].Glucagon is a hormone that opposes the action of insulin. It is secreted when blood glucose level falls. It increases blood glucose concentration partly by breaking down stored glycogen in the liver.

Types of Diabetes: The two most common types of diabetes are Insulin-Dependent Diabetes Mellitus (IDDM) or Type-1 and Non- Insulin Dependent Diabetes Mellitus (NIDDM) or Type-2. WHO classification has also recognized malnutrition related diabetes mellitus and gestational diabetes. Malnutrition related diabetes was omitted from the new classification because its etiology is uncertain, and it is unclear whether it is a separate type of diabetes or not [4-5]

Type-1 Diabetes Mellitus: It is a result cellular mediated autoimmune destruction of the insulin secreting Beta –cells of the pancreas, which results in an absolute deficiency of insulin for the body. Patients are more prone to ketoacidosis. It occurs in children and in young persons, usually before 40 years of age, although the onset of the disease can occur at any age. The patients with Type-1 diabetes must rely on insulin medication for survival. It may account for 5-10 per cent of all diagnosed cases of diabetes. Autoimmune, genetic and environmental factors are the major risk factors for Type – 1 diabetes[6]

Type -2 Diabetes Mellitus: Two key features in the pathogenesis of Type-2 diabetes mellitus are a decreased ability of insulin to stimulate glucose uptake in peripheral tissues, insulin resistance, and the inability of the pancreatic Beta cells to secrete insulin adequately, Beta cell failure. The major sites of insulin resistance in Type-2 diabetes are the liver, skeletal muscle and adipose tissue [7-8]. Both defects, insulin resistance and Beta cell failure, are caused by a combination of genetic and environmental factors. Environmental factors such as lifestyle habits (i.e. physical inactivity and poor dietary intake), obesity and toxins may act as initiating factors or progression factors for Type-2 diabetes. The genetic factors are still poorly understood[9-10].

Table 1. WHO Diagnostic Criteria for Diabetes (2006)

Condition	Parameter	Diagnostic level
Diabetes	a. Fasting plasma glucose	$\geq$ 7.0 mmol L^{-1} (126mg dL^{-1})
	b. 2 h Plasma glucose	$\geq$ 11.1 mmol L^{-1} (200 mg dL^{-1})
Impaired glucose tolerance (IGT)	a. Fasting plasma glucose	$\geq$ 7.0 mmol L^{-1} (126mg dL^{-1})
	b. 2 h Plasma glucose	$\geq$ 7.8 and <11.1 mmol L^{-1} (140mg dL^{-1} and 200 mg dL^{-1})
Impaired fasting glucose	a. Fasting plasma glucose	1- 6.9 mmol L^{-1} (125mg dL^{-1})
	b. 2 h Plasma glucose	and (if measured) < 7.8 mmol L^{-1} (140mg dL^{-1})

Source : WHO Technical Report & Recommendation 2006[11]

Artificial Sweeteners: There are five dangerous sugar substitutes that are approved for consumer use – (i) saccharin, (ii) neotame, (iii) accesulfame – potassium,

(iv) aspartame and (v) sucralose. Of the five, sucralose and aspartame are the most pervasive and dangerous substitutes available. These sweeteners qualify as calorie-free but come with significant limitations and health risks.

Herbalism is a traditional medicinal or folk medicine practice based on the use of plants and plant extracts. Herbalism is also known as botanical medicine, medical herbalism, herbology and phytotherapy[12].The species ***Stevia rebaudiana***, commonly known as sweet leaf, sugar leaf or simply Stevia, is widely grown for its sweet leaves. As a sugar substitute, Stevia's taste has a slower onset and longer duration than that of sugar. With its extract having up to 300 times the sweetness of sugar, Stevia has garnered attention with the rise in demand for low carbohydrate, low sugar food alternatives.

Two French chemists isolated the glycosides that give Stevia its sweet taste [13]. These compounds were named stevioside and rebaudioside A, B, C, D and E; dulcoside A, and are 250-300 times sweeter than sucrose, heat stable, pH stable and non-fermentable [14]

Medicinal Properties of Stevia : Stevia is a completely safe specific herb for diabetes and hypoglycaemia, a flavour enhancer, contains a variety of constituents, besides steviosides and rebaudiosides, the nutrients and good deal of sterols, triterpenes, flavonoid, tannins. Stevia also contains an extremely rich volatile oil comprising rich preparations of aromatic aldehyde, monterpens and sesquiterpens. So far these constituents probably have some impact on human physiology and may help explain some of the reported beneficial therapeutic uses of Stevia [14]

Safety in the use of Stevia: In 2006, the World Health Organisation (WHO) performed a thorough evaluation of recent experimental studies of stevioside and steviols conducted on animals and humans, and concluded that "stevioside and rebaudioside A are not genotoxic in vitro or in vivo.

Major objectives of the Research Study

1. To estimate the nutrient composition of Stevia leaves (carbohydrate protein, fat, fibre, moisture, ash, iron and calcium).
2. To assess the nutritional status of Type -2 Diabetes Mellitus (DM) and Impaired Glucose Tolerance (IGT) subjects by anthropometry, biochemical and dietary methods.
3. To assess the hypoglycemic and hypolipidaemic effect of Stevia leaves after intervention trials of 60 days on Type -2 Diabetics and IGT subjects.

Methodolgy

PHASE – I

Chemical Analysis of Nutrient Composition of Stevia leaf powder :

PHASE – II

- Initial Screening and Assessment of Nutritional Status of Type-2 Diabetes Mellitus (DM) and Impaired Glucose Tolerance (IGT) Subjects.
- Intervention with Stevia Leaf Powder on Type-2 DM and IGT Subjects Followed by Biochemical Testing after 30 and 60 days.

Selection of Subjects- For the present piece of experimental study, patients suffering from Type-2 Diabetes Mellitus (DM) and Impaired Glucose Tolerance (IGT) of Ajmer city (Rajasthan) were selected by convenience sampling method.

The criteria kept for selection was - Patients (males and females) suffering from Type – 2 DM and IGT aged between 40-60

years were chosen to be the subjects for the research.

The study was conducted in two phases. In phase I, chemical analysis of the nutrient composition of stevia leaf powder was carried out. This included estimation of moisture content[15], protein[15] (microkjeldhal method), fat[16] (solvent extraction method), crude fibre[16] (weende's dry ashing method), ash content[15], carbohydrate[15], calcium content[17] (volumetric titration method) and iron[17] (spectrophometric technique) .

The phase II included the initial screening and assessment of 30 subjects, 20 suffering from Type II diabetes mellitus and 10 suffering from impaired glucose tolerance. The subjects were intensively studied for complete psychosocial and socioeconomic information, medical history, anthropometric parameters[18] which included height and weight body mass index, waist/hip ratio, mid upper arm circumference and biochemical estimations which included fasting and post prandial blood glucose levels (GOD method)[19], triglycerides (enzymatic method)[20], total cholesterol[21], LDL[22] and VLDL cholesterol, HDL cholesterol, LDL/HDL ratio and atherogenic index. In addition a detailed dietary study was done by 24 hrs dietary recall method for 3 consecutive days plus and oral questionnaire was used to collect information. The nutrients analysed[23] were energy, carbohydrate, protein, fat and fibre. The diabetic subjects were further divided into two groups of 10 subjects each. Group I served as control group and group II served as experimental group I and IGT subjects (Group III, experimental group II) were given intervention with 1 gm stevia leaf powder which was procured from Jeevan Herbs and agro farms, Anand (M.P.) India. The biochemical parameters of the control group as well as both the experimental groups were studied initially and then after a period of 30 and 60 days.

Statistical Analysis: The data collected during the study was tabulated and was statistically analysed.[24] All the data was expressed as Mean±SD. Statistical significance was calculated using 2-tailed t-test. Significance was calculated at $p<0.01$ and also at $p<0.05$.

Results

Nutrient composition of Stevia leaf powder (per100gm) which was analysed on dry weight basis indicated that it contains 9.87 gm percent protein, 4 gm percent fat, total carbohydrate 62.5 gm percent, crude fibre 12 gm percent, moisture 7.05 gm percent, total ash 9.2 gm percent, iron 0.18 gm percent and calcium 0.16 gm percent.

Table 2. Nutrient Composition of Stevia leaf powder

Nutrients	Per 100 gm
Moisture (gm)	7.05
Protein (gm)	9.87
Fat (gm)	4
Crude Fibre (gm)|	12
Total Carbohydrate (gm)	62.58
Ash (gm)	9.2
Iron (gm)	0.18
Calcium (gm)	0.16

All values are per 100 gm (dry weight basis)

It was found to be a nutritious and very low calorie sweetener which could be of immense help in restricting the calorie intake in the diet of affluent diabetic patients and also prove to be beneficial where calorie restricted diets are prescribed.

Table 3. Intake of Nutrients by Control Group (CG), Type-2 Diabetics (Experimental Group1 EG -1) and Patients with Impaired Glucose Tolerance (Experimental Group2 EG -2)

	CG (n=10)		**EG - 1 (n=10)**		**EG - 2 (n=10)**	
	Males n=4	**Females n=6**	**Males n=4**	**Females n=6**	**Males n=4**	**Females n=6**
Energy (Kcal)	2357 ± 417.5	1799.5 ± 138.88	2227.75 ± 370.66	1533± 262.24	2585.75 ± 407.99	1664.16 ± 170.03
Carbohydrate (gm)	381.5 ± 79.5	256.33 ± 37.03	311.25 ± 29.7	215.16 ± 58.7	395.75 ±68.54	219.0 ± 21.3
Protein (gm)	50.5 ± 6.02	39.16 ± 7.8	75.25 ± 4.49	47.65± 12.45	78.0 ±8.04	52.83 ± 9.62
Fat (gm)	61.25 ± 10.30	38.83 ± 7.75	72.0 ± 3.55	34.16 ± 9.10	68.25 ±19.46	42.0 ± 4.8
Fiber (gm)	10.0 ± 2.16	10.16 ± 3.06	11.0 ± 0.81	7.55 ± 2.5	15.25± 2.5	11.0 ± 0.89

All values are Mean ± SD

Results of dietary assessment of diabetic subjects revealed that the mean daily intake of energy by male subjects was 2357±417.5 kcal by the diabetics of the control group and 2227.7±370.6 and 2585.75± 407.99by diabetics of the Experimental group and by the IGT subjects respectively. This intake was lower in the case of female subjects. The fat intake was higher than the Recommended Dietary Allowance in all the groups and the intake of fiber was also found to below.

Subjects of the control group did not receive Stevia intervention while those in the experimental groups received intervention. Fasting and PP blood Glucose levels were measured prior to and post intervention. On completion of 60 days the difference between the Fasting and PP blood glucose levels of diabetic and IGT subjects was found to be statistically significant $p \leq 0.05$ whereas no significant reduction in glucose levels was seen in subjects of the control group who did not receive

Table 4. Impact of Intervention with Stevia Leaf Powder on the Fasting and PP blood Glucose Levels of Diabetic Subjects and in Patients suffering from IGT

Blood Glucose	Prior to Intervention Control	Prior to Intervention EG 1	Prior to Intervention EG 2	Post Intervention Control	Post Intervention EG 1	Post Intervention EG 2
Fasting mg/dl	155.62±36.83	156.61±31.32	117.24±9.3	155.29±36.54	123.55±22.94	104.51±23.52**
PP mg/dl	232.79±29.10	225.17±43.86	185.38±11.07	228.35±9.52	200.60±43.80**	168.27±13.22**

** p≤0.05

Table 5. Impact of Intervention with stevia leaves for 60 days on the lipid profile of diabetic subjects (EG1)

Lipid	**Prior to intervention**		**Post- intervention, 60 days**	
	Control	**Experimental**	**Control**	**Experimental**
Total cholesterol	175.18 ± 38.45	179.78 ±31.58	172.80 ± 0.67	172.05 ± 26.20
Tryglyceride	87.36 ± 8.66	103.64 ± 36.33	79.03 ± 12.7	70.07 ± 44.29**
HDL-C	51.26 ± 6.46	43.05± 7.07	52.35 ± 4.92	42.97 ± 7.39
LDL-C	107.79 ± 33.76	118.22 ± 27.90	105.02 ± 36.90	111.63 ± 30.06
VLDL-C	17.44 ± 1.73	20.68 ± 7.27	15.78 ± 2.55	17.96 ± 8.82**
LDL/HDL ratio	2.10 ± 00.12	2.75 ±0.09	2.0 ± 0.20	2.60 ± 0.10
Atherogenic index	2.44 ± 0.52	3.22 ± 0.89	2.30 ± 0.63	3.01 ± 0.91

Results are given as mg dL-1

** p≤ 0.05

Table 6. Impact of Intervention with stevia leaves for 60 days on the lipid profile of IGT subjects (EG2)

Lipid Profile (mg/dl)	**Pre - intervention level (n=10)**		**Post - intervention level (n=10)**		**t* value**
	Mean	**SD**	**Mean**	**SD**	
Total cholesterol	159.95	14.48	155.34	20	1.26
TG	137.54	70.23	120.53**	71.91	1.01
HDL – C	46.38	6.65	42.9	4.92	2.05
LDL – C	87.1	9.91	96.07	14.69	2.22
VLDL - C	27.47	14.05	24.58	14.97	1.48
LDL/HDL Ratio	0.37	0.92	0.39	0.09	0.82
Atherogenic Index	3.29	0.89	3.06	0.94	1.72

All vaules are Mean ± SD

** - Significant at p <0.05

t value : Two –tailed test for difference between the mean of samples prior to and post intervention

intervention with Stevia. The results are similar to other research findings which have reported a significant reduction in blood glucose levels of rats fed with Stevioside, a glycoside found in Stevia [25]Scientists have reported that the glycosides in Stevia have insulinotropic effects and may serve a potential role in the treatment of Type 2 Diabetes.

Stevia leaf powder had a beneficial role in reducing in serum cholesterol, triglycerides, VLDL-C levels significantly both in the diabetic subjects and in patients suffering from IGT.Similar results were obtained in earlier studies on the lipid profile of hypertensive patients.[26]

Conclusion

In conclusion it can be said that Stevia which is a sweet herb is an extremely safe plant, totally non toxic with multiple health benefits. It can thus be used for the management of Diabetes and Hyperlipidemia and as a sweetenersubstitute by patients with longstanding Diabetes.

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