Research Paper

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The comparative effect of an antidiabetic supplement-Diabetall™ and an antidiabetic drug on the BS level of STZ induced diabetic rats

SCIENCE

KEYWORDS : Diabetall™, Blood sugar level (BS), Nutraceuticals, Anti-diabetic supplement, Reversal of Type 2 Diabetes

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ABSTRACT

Ageing population, changing consumer lifestyles, unhealthy & poor dietary habits and a focus on preventive medicine is driving the growth of the nutraceutical market globally due to its lower or no risk of side effects. Major part of the population at a global level is suffering from lifestyle disorder i.e. Type 2 Diabetes & Pre-Diabetes. Due to risk of toxicity or adverse side effects of drugs, consumers are massively turning to have nutraceutical product in order to improve their health. Looking over to such scenario, a unique formulation has been formulated which helps to maintain the healthy blood sugar level and has a potential to reverse the type 2 diabetic and pre-diabetic condition. The aim of the study is to study the comparative effect of an antidiabetic supplement-Diabetall™ and an antidiabetic drug on the BS level of STZ induced diabetic rats. In this study, it was found that Diabetall™ has a significant antidiabetic effect. The study results clearly demonstrated that the solution form of Diabetall™ had promising results in controlling the blood sugar levels along with the maintenance of the normal level of glycosylated haemoglobin, total protein, total cholesterol, HDL and creatinine in the blood stream. The results of Diabetall™ were very near to the results of antidiabetic drug which was taken as a standard control. The biopsy report of the tested animal with Diabetall™ has shown the regeneration of Islet cells of pancreas of STZ induced diabetic rat. Thus, this study concludes that, the Diabetall™ can be considered as a safe and effective supplement for the long term & for the effective management of Type 2 diabetic and Pre-diabetic conditions.

INTRODUCTION

Nutraceuticals are products that provide health and medicinal benefits, including the prevention and treatment of diseases in addition to the basic nutritional value found in foodstuff. Nutraceuticals are particularly of interest to the present generation as they have the potential to substantially reduce the expensive, high-tech, disease treatment approaches that are presently being employed in western healthcare. Primarily used in functional foods and dietary supplements, nutraceutical ingredients are natural, bioactive, chemical compounds that have health promoting, disease preventing or medicinal properties[1].

Nutraceutical health supplements provide an opportunity to improve the human health, reduce health care costs and support economic development in rural communities. The global nutraceutical product market is primarily categorized on the basis of functional foods, functional beverages and dietary supplements[1]. Nutritional food supplements can be defined as a "a food (or part of a food) that provides medical or health benefits, including the prevention and/or treatment of a disease"[1].

The nutraceutical ingredients market is emerging with an increased awareness among people and growing health concerns. People are inclined to buy healthy foods that fulfill the need of essential nutrients in the body. With the rise in educational level, people are gaining awareness regarding the types of nutraceutical dietary supplements, functional foods & beverages that help in maintaining balanced diet and proper health[2].

In the western countries, people began to eat more meat, dairy products, vegetable oils, sugary foods, and alcoholic beverages during the latter half of the 20th century. People also developed sedentary lifestyles which resulted in greater rates of obesity. Rates of colorectal cancer, breast cancer, prostate cancer, endometrial cancer and lung cancer started increasing after this dietary change. Today, a poor dietary habit combined with an unhealthy lifestyle among the growing population of a world, has weakened the immune system which has made us prone to various lifestyle disorders. Drug abuse, tobacco smoking, and alcohol drinking, as well as a lack of exercise may also increase the risk of developing certain diseases, especially later in life[3].

Lifestyle disorders (also sometimes called diseases of longevity or diseases of civilization interchangeably) have appeared to increase in frequency as countries become more industrialized and people live longer. Lifestyle disorders include Arthritis, Type 2 diabetes, Obesity, Atherosclerosis, Asthma, certain kinds of Cancer, Chronic liver disease or Cirrhosis, Chronic obstructive pulmonary disease, heart disease, metabolic syndrome, chronic renal failure, osteoporosis, stroke and depression[4]. Due to risk of toxicity or adverse side effect of drugs, consumers are turning massively to food supplements to improve their health where pharmaceuticals have failed[5].

One of the major Lifestyle disorders which is a serious matter of health concern at a global level i.e. Diabetes. Diabetes is described as a group of metabolic diseases in which the person has high blood sugar levels, either because insulin production is inadequate, or because the body's cells do not respond properly to insulin, or both[6]. Patients with high blood sugar typically experience polyuria (frequent urination), become increasingly thirsty (polydipsia) and hungry (polyphagia). Diabetes, earlier considered as a genetic disorder, has now inclined itself and has become more of a lifestyle related disorder[5].

WHO projects that diabetes will be the 7th leading cause of death in 2030[7]. Today, there are around 382 million people living with diabetes at a global level. Another 316 million with impaired glucose tolerance are at high risk from the disease, an alarming number that is set to reach 471 million by 2035. Type 2 diabetes accounts for 85% to 95% of all diabetes in high-income countries and may account for an even higher percentage in low- and middle income countries[8].

In India around 67 million DIABETIC and 30 million PRE-DIABETIC patients (Nov., 2013) are there. By 2030, India will have the largest number of patients in the world[7]. Type 2 diabetes is currently incurable and a common treatment approach is used to control the disease with lifelong use of anti-diabetic drugs causing various other side effects[8].

Looking at the demand for an alternative treatments for diabetes, Diabetall™ was introduced which has the potential in reversing the of Type 2 diabetic & prediabetic conditions. Diabetall™, a nutritional food supplement, which is a blend of unparalleled combination of the following botanicals - Gymnema sylvestre, Momordica charantia, Pterocarpus marsupium, Cinnamomum cassia, Syzgium cumini, Salacia reticulata, Curcuma longa, Cassia fistula, Lawsonia inermis, Berberis aristata, Phylanthus emblica, Zingiber officinalae, Piper nigrum, Piper longum, which in combination, provide not only an immediate reduction in BS (Blood Sugar) levels, but also reduces the inflammation in the body, sensitizes the insulin, thereby reducing the quantity and improving the quality of insulin released. Diabetall™ heals the beta cells of the pancreas, exerts an anti-alpha glucosidase effect, increases the glycogen storage in the liver, lessens the conversion into triglycerides and reduces the total oxidative stress on the body. As a complimentary effect, it also, Normalizes the levels of total cholesterol , Increases HDL, Reduces LDL, Increases insulin sensitivity when taken over a period, Reduces the amount of endogenous insulin released, Brings down the Inflammation, Reduces the Oxidative stress , Promotes healing and recuperation of the Pancreas and Creates a sense of well being

If the Diabetall™ is taken with the right amount of dosage within a particular time period, we can expect a reduction in a blood sugar level by 20-30mg/dl within a week and a reduction of 50-70mg/dl within a month. This supplement can be taken along with the oral hypoglycemic. People who are borderline diabetics can choose this as a first line management with lifestyle changes like right eating and exercising.

The product complies with the most stringent parameters for the presence of pesticides, herbicides, heavy metals and is free of infestation. There are absolutely no side effects of this product and it can be taken with any Oral Hypoglycemic (diabetic Medication) drug and insulin. It does not interfere with any medication.

This supplement works primarily through the following mechanisms:

1. Sensitizing insulin (the person's own)
2. Reducing the quantity of insulin produced and increasing the quality of insulin produced
3. Reduces the absorption of glucose in the intestines (alpha-glycosidase inhibition)
4. Anti-inflammatory effect on the pancreas and the body on the whole, allowing it to recover and heal.

This supplement supports healthy blood sugar level and glucose metabolism by mediation of insulin release and activity and augmentation of healthy pancreatic function along with the beta cells regeneration/repairing in type 2 diabetic patients.

The solution form of Diabetall shows a promising result in controlling blood sugar levels, since nano sized molecules have and increased cell permeability and surface area for binding with the targeted molecules. They also have an advantage of enhanced uptake and bioavailability of nutrients into the body.

MATERIALS AND METHODS

Experimental Animals:

For toxicity studies:

Wister albino mice were chosen having an average weight of 20-25g of either sex. Animals were housed under standard environment having controlled temperature of 25 ± 2°C with a 12 hours light-dark cycle and humidity 50-60% of the lab has been maintained.

For anti-diabetic studies:

Wister albino rat having weighing about 180-200g of either sex were chosen. Animals were housed under standard environment having controlled temperature 22 ± 1°C with a 12 hours light-dark cycle and humidity 60-70% of the lab was maintained. The animals were acclimatized to laboratory condition for seven days before the commencement of the experiment. The animals were fed with commercially available rat pelleted diet and drinking water.

Nutritional Anti-Diabetic Food Supplement:

Diabetall™, a nutritional food supplement, which is a blend of unparalleled combination of herbs (Gymnema sylvestre, Momordica charantia, Pterocarpus marsupium, Cinnamomum cassia, Syzgium cumini, Salacia reticulata, Curcuma longa, Cassia fistula, Lawsonia inermis, Berberis aristata, Phylanthus emblica, Zingiber officinalae, Piper nigrum and Piper longum) was provided to the experimental animals in three different forms i.e. crude, granules & solution forms.

Drugs & Chemicals:

Streptozotocin (STZ) was obtained from Sigma Chemical Co, St Louis, MO, USA. Biochemical kit for biochemical studies were obtained from Autospan, Span Diagnostic Ltd., Surat, Gujarat. Metaformin was purchased from Sigma-aldrich. All chemicals used are of analytical grade.

Acute Toxicity study:

The acute toxicity for crude, granules & solution forms of Diabetall™, were determined in mice, maintained under standard conditions. The animals were fasted overnight prior to the experiment. Fixed dose (OCED Guideline no. 423, Annexure 2d) method of CPCSEA was adopted for toxicity studies. The tested extracts were administrated orally. The mortality was not observed at (2000 mg/kg for sample I & II, 6ml/kg for sample III) in the all cases (OECD, 1997). Common side effects such as, mild diarrhoea, loss of weight and depression of treated groups of animals were not recorded within the 14 days of observation.

Selection of dose of extracts:

LD50 was done as per OECD guidelines for fixing the dose for biological evaluation and the samples dose, not showed mortality at the dose of 2000 mg/kg & 6ml/kg respectively.

Therefore, 2000 mg/kg (Sample I & II) & 6ml/kg (Sample III) dose was considered as LD50 cut off the dose under Globally Harmonized Classification System (GHS) category 5 (safe dose) and OECD guideline 423, Annexure 2d. Common side effects such as, mild diarrhea, lose of weight and depression in treated group of animals were not recorded within the 14 days of observation.

The biological evaluation of the extracts was carried out at doses of 100mg/kg (crude & granules) & 6 ml/kg (solution) respectively.

Anti-Diabetic Activity:

Effect of a given sample on normoglycemic and glucose fed-hyperglycemic rats:

A combined methodology was preferred for the activity assessment of Diabetall™. In order to rationalize the use of animals, there were some modifications which were incorporated in the time pattern for blood glucose level determination. After over-

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night fasting (16 h) the blood glucose level of rats were determined and treated with test samples and standard.

Test samples and standard were given immediately after the collection of initial blood samples. The blood glucose levels were determined in the following pattern of 30 and 60 min to access the effect of test samples on normoglycaemic animals. The rats were then loaded orally with 2g/kg glucose and the glucose concentrations were determined at 60, 90 and 210 min after glucose load.

The animals were divided into five groups of 6 rats in each.
Group I - Animals to be received normal saline 5ml/kg b.w/p.o.

Group II - Animals to be received metformin 650mg/kg.

Group III - Animals to be received crude sample of Diabetall™ 100mg/kg.

Group IV - Animals to be received Granular sample of Diabetall™ 100mg/kg.

Group V - Animals to be received solution form of Diabetall™ 6ml/kg.

Effect of a given sample on blood glucose level in STZ induced diabetic rats:
The animals were divided into six groups. Group I consists of normoglycaemic rats. The remaining groups consisted of 5 STZ induced diabetic rats.

Group I - Normal control animals received normal saline 5ml/kg b.w/p.o. for 21 days.

Group II - Streptozotocin (45mg/kg b.w) induced animals received normal saline 5ml/kg b.w/p.o. for 21 days. (Control)

Group III - Streptozotocin (45mg/kg b.w) induced animals received metformin / p.o for 21 days.(Standard Control)

Group IV - Streptozotocin (45mg/kg b.w) induced animals received crude form of Diabetall™ sample for 21 days.

Group V - Streptozotocin (45mg/kg b.w) induced animals received granules form of Diabetall™ sample for 21 days.

Group VI - Streptozotocin (45mg/kg b.w) induced animals received solution form of Diabetall™ sample for 21 days.

The above mentioned treatment schedules are followed for the respective group of animals for 21 days. Changes in the blood glucose level were observed on 0th, 7th, 14th and 21st day of treatment.

Biochemical Studies:
Biochemical studies done to measure the levels of Glycosylated Haemoglobin, Total Cholesterol, Total Protein, HDL level and Creatinine level, which were determined by using ERBA Semi Autoanalyser (chem. 7) and the procedure of analysis was followed as mentioned on kit.

Histopathology:
At the end of the study, all the animals were sacrificed under light ether anesthesia. The rats were sacrificed by decapitation and blood was collected by bleeding of carotid artery. Serum was separated to study the biochemical parameters. Pancreas of one animal from each group was removed, dissected out and washed with ice-cold saline. All tissues were preserved in 10% (v/v) formalin fluid for histopathological studies. Histopathological studies were carried out by Vijaya Diagnostic center at Hyderabad.

Statistical analysis:
Statistical analysis of the result was carried out by one way ANOVA method followed by Dunnett's test by using Graph Pad Instant Version 3.0, USA. Results are expressed as mean ±SEM from six rats in each group.

TABLE – 1

Group	Day 1	Day 7	Day 14	Day 21
Control (Normal Rat)	99.97 ± 4.64	101.73 ± 4.89	105.3 ± 4.15	107.85 ± 4.52
Control (Diabetic Rat)	233.78 ± 19.48***	249.01 ± 17.54	248.47 ± 17.20***	246.88 ± 19.22***
Standard (Drug)	271.60 ± 6.95***	238.88 ± 5.30***	198.23 ± 5.54**	165.6 ± 3.80***
Crude (Diabetall)	270.75 ± 10.98***	249.45 ± 9.72***	235.08 ± 10.96***	222.32 ± 10
Granules (Diabetall)	266.13 ± 19.17***	262.67 ± 18.23**	250.35 ± 17.33***	235.8 ± 17.75***
Solution (Diabetall)	278.92 ± 24.21***	244.17 ± 22.98	222.98 ± 22.26***	201.52 ± 20.91***
Values are the mean ± S.E.M., n=6. ***p<0.001, **P<0.01, *P<0.005 (vs. control)				

EFFECT OF THE GIVEN SAMPLE ON A BLOOD SUGAR LEVEL OF A STZ INDUCED DIABETIC RATS

TABLE – 2
ESTIMATION OF GLYCOSYLATED HAEMOGLOBIN (%), TOTAL PROTEIN(G/DL), TOTAL CHOLESTEROL (MG/DL), HDL CHOLESTEROL (MG/DL) & CREATININE (MG/DL) LEVEL IN THE BLOOD STREAM OF A DIABETIC RATS ADMINISTERED WITH THE GIVEN DIFFERENT SAMPLES

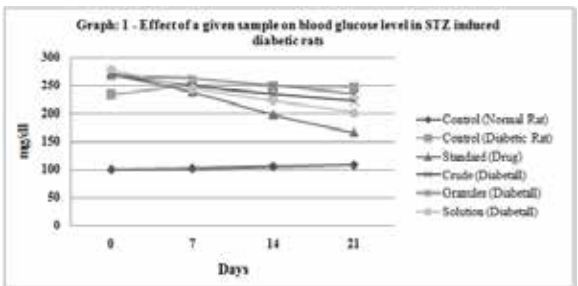
Group	Glycosylated Haemoglobin (%)	Total Protein (g/dl)	Total Cholesterol (mg/dl)	HDL Cholesterol (mg/dl)	Creatinine (mg/dl)
Control (Normal Rat)	7.64 ± 0.80	5.88 ± 0.39	134.41 ± 5.70	30.01 ± 2.17	1.54 ± 0.31
Control (Diabetic Rat)	16.17 ±0.55***	2.35 ± 0.65**	171.93 ± 4.99**	12.07 ± 1.61***	3.25 ± 0.4
Standard (Drug)	8.18 ± 0.72	5.62 ± 0.55	140.08 ± 4.94	30.40 ± 2.17	1.48 ± 0.32
Crude (Diabetall)	14.01 ± 0.76***	3.21 ± 0.53*	145.92 ± 8.16	22.06 ± 2.48	2.25 ± 0.35
Granules (Diabetall)	14.75 ± 1.11***	2.83 ± 0.36**	163.45 ± 7.72*	19.80 ± 2.40*	2.53 ± 0.59
Solution (Diabetall)	11.75 ± 1.18*	5.16 ± 0.76	148.36 ± 6.50	27.08 ± 2.86	1.79 ± 0.51
Values are the mean ± S.E.M., n=6. ***p<0.001, **P<0.01, *P<0.005 (vs. control)					

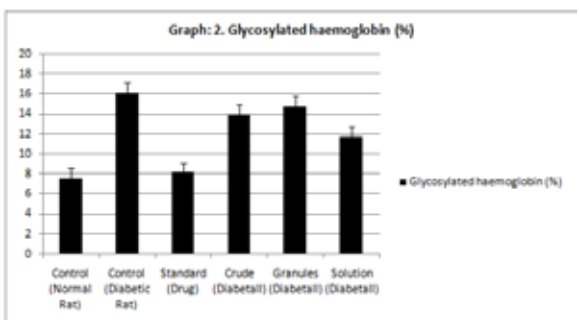
Results & Discussions:
In this study, it was found that the animals were safe up to a maximum dose level of 2000mg/kg bodyweight. There were no changes in normal behavioral pattern and no signs and symptoms of toxicity and mortality were observed.

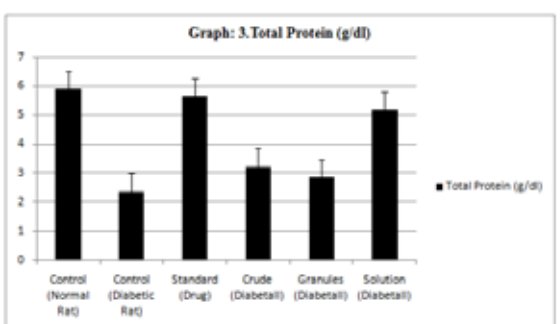
Animal treated with three different forms of Diabetall™ showed a remarkable decrease in their blood sugar level. After 21 days of study on a STZ induced diabetic rat, crude form of Diabetall™ reduced blood sugar levels from 270.75±10.98 to 222.32±10 mg/dl, granule form of Diabetall™ reduced blood sugar levels from 266.13±19.17 to 235.8±17.75 mg/dl and solution form of Diabetall™ reduced blood sugar levels from 278.92±24.21 to 201.52±20.91 mg/dl respectively. These results show that the solution form of Diabetall™ shows better results when compared to its other forms. During the 21 days treatment with the solution form of Diabetall™, there was a decrease in the blood sugar level around 77.4 ± 3.3 mg/dl, while crude form has 48.43 ± 0.98 mg/dl and granules form has 30.33 ± 1.42 mg/dl. While the drug i.e. Metformin reduces blood sugar level from 271.60 ± 6.95 to

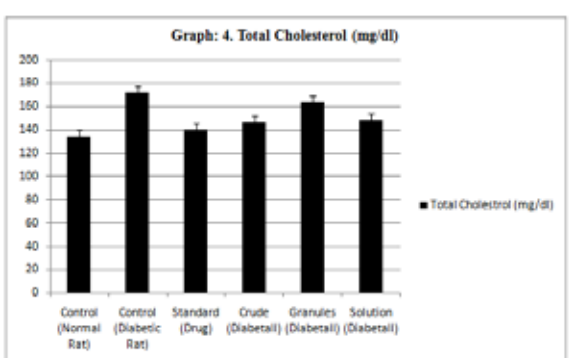
165.6 ± 3.80 mg/dl i.e. a total decrease in the blood sugar level was around 106 ± 3.15 mg/dl (as shown in Graph 1).

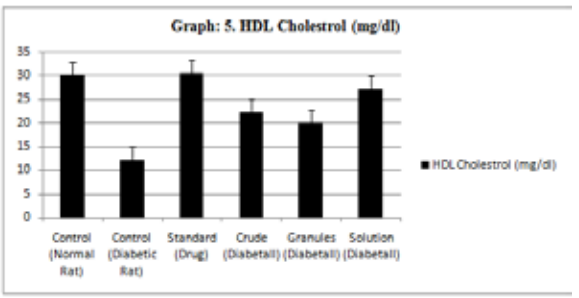
The solution form of Diabetall™ shows positive results which are close to the results obtained with Metformin drug. Diabetall™ does not have shown any kind of side effects as it is a pure blend of botanicals.

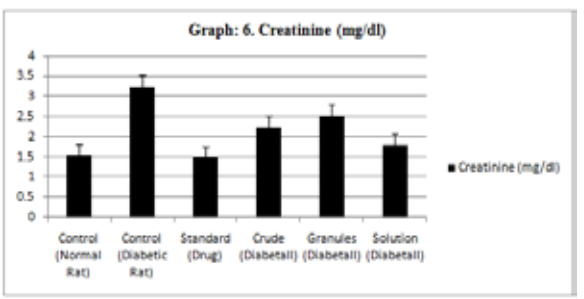












The glycosylated haemoglobin level was normal in diabetic rats administered with Diabetall™ in solution form when compared to its other forms after the 21 days study (as shown in Graph 2). Similarly, the results of the total protein level & total cholesterol level were also normal in rat having administered with the solution form of Diabetall™ as compared to other forms (as shown in Graph 3 & 4). The total HDL cholesterol level increased and creatinine level reduced in diabetic rat having administered with Diabetall™ solution form (as shown in Graph 5 & 6).

The histopathological reports also show that diabetic rats have shown only fibro fatty tissue and no islets, while diabetic rats treated with different forms of Diabetall™ have shown pancreas with small islets.

CONCLUSION

The study shows that Diabetall™ has a significant antidiabetic effect. The results of the present study clearly demonstrated that the solution form of Diabetall™ had promising results in controlling the blood sugar levels and was better as compared to other forms of Diabetall™ along with the maintenance of the normal level of glycosylated haemoglobin, total protein, total cholesterol, HDL and creatinine. The biopsy report of the tested animal with the Diabetall™ shows the regeneration of Islet cells of pancreas. Thus, Diabetall™ can be considered as a safe and effective supplement for the long term & for the effective management of Type 2 diabetic and Pre-diabetic condition.

Further studies can be done by increasing the Diabetall™ dosage levels which might give better results. Also, with the use of nanotechnology along with biopolymers as nanocarriers, an increase in the bio-accessibility and bio-availability of the supplement can be obtained.

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