CLINICAL STUDY REPORT

MEHYOG POWDER

5/4/2012

A pilot open-label clinical study to assess the efficacy of MEHYOG Powder in gaining glycemic control and reducing symptoms of patients with Type II Diabetes Melitus over 12 weeks

Francis Ayurveda

A Division of Francis Vaidyans Ayurveda Vaidyasala Pvt Ltd)

CLINICAL STUDY REPORT

1. TITLE PAGE

Study title:	A pilot open-label clinical study to assess the efficacy of MEHYOG Powder in gaining glycemic control and reducing symptoms of patients with Type II Diabetes Melitus over 12 weeks
Test drug / investigational product:	MEHYOG Powder
Indication:	Type II Diabetes Melitus
Study No:	FA/DM/DL 01/2011
Phase of development:	Pilot
Study start date:	02 Dec 2011
Study end date:	04 April 2012
Principal / Coordinating investigator:	1. Dr. Sreejith Sreekumar Chief Physician Kumaramangalam Ayurvedic Clinic & Research Center
Report date:	04 May 2012

2. SYNOPSIS

Name of the sponsor: Francis Ayurveda,Kerala,India
Name of the finished product: MEHYOG Powder
Name of Active Ingredient(s): Polyherbal compound
Title of Study: A pilot open label clinical study to assess the efficacy of MEHYOG Powder in gaining glycemic control and reducing symptoms of patients with Type II Diabetes Melitus for 12 weeks.
Publications: None
Study Period: 12 weeks
Phase of Development: Pilot
Methodology: Patients diagnosed with Type II DM were introduced to the study by the principal investigator. After explaining the study, they were invited to join the study. The study participants were interviewed to evaluate their medical history, social habits and health status. Screening examinations included General and Clinical examination, Evaluation of disease, recording of vital signs and baseline Symptomatic Questionnaires. Lab Examinations and questionnaires were repeated at the end of each 4 weeks till End of Study Visit (week 12).
Number of Subjects (Planned and Analyzed): Planned: 100 Analyzed: 100
Diagnosis and Main Criteria for Inclusion: Subjects meeting all of the following criteria were eligible to participate in the study: **Inclusion Criteria:** 1. 30-65 years of age of both sexes 2. Confirmed diagnosis of Type II DM **Exclusion Criteria** 1. IDDM&NIDDM patients with acute complications of diabetes 2. Pregnant and lactating women 3. Patients with concomitant severe illness necessitating other medications 4. Patients with severe hypertension 5. History of severe unstable angina, myocardial infarction, CVAs, renal failure

Criteria for Evaluation:

Primary efficacy variable:

1. Mean Fasting Blood Glucose
2. Mean Post Parandial Blood Glucose
3. Symptomatic changes from Baseline to End-of-Treatment visit

Statistical Methods:

Paired t-test was used to assess the percentage change from baseline to endpoint in all parameters. All statistical tests were two-sided with a significance level of α=0.05, unless otherwise specified. Data were summarized using descriptive statistics (number of subjects [n], mean, standard deviation [SD] and median) for continuous variables, and using frequency and percentage (i.e., number and proportion of subjects – n, %) for discrete/categorical variables, unless otherwise specified. Efficacy analyses were performed only for subjects who had completed all visits. All the safety analyses were performed using the ITT population.

SUMMARY – CONCLUSION:

MEHYOG powder twice daily dose were found to have significant effect in reducing mean blood glucose levels in patients with Type II Diabetes melitus.There was significant reduction in the subject symptoms as well.

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ETHICS

Independent Ethics Committee (IEC) or Institutional Review Board (IRB)

The protocol, informed consent form (ICF) and information for the subject were approved by the IEC/IRB prior to enrolment of subjects. Any amendments to the protocol or the ICF were approved by the IEC/IRB prior to recruiting patients under amended protocol / ICF.

Ethical conduct of the study

The Sponsor and investigator conducted the study in accordance with the protocol, EU Directive 2001/20/EC, all applicable local regulations, GCP regulations, and the Declaration of Helsinki. In addition, the investigator followed local and institutional requirements pertaining but not limited, to investigational product, clinical research, informed consent (including the use and disclosure of protected health information) and IEC/IRB regulations.

Patient information and consent

Prior to entering the study, all subjects or their legally acceptable representative were fully informed of the nature and the aim of the study. A study-specific subject information sheet was prepared to clearly explain the nature of the study and study drug, including the study objectives, the potential risks and benefits and the procedures involved for the subject. Subjects were reminded that participation in the study was voluntary and that they could withdraw at any time without affecting their relationship with the investigator, without justification, and without penalties or loss of benefits.All subjects freely gave their written informed consent before their enrolment in the study.

INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE.

Key Study Administrative Information

Principal Investigators	1. Dr.Sreejith Sreekumar
Study Sites	1. Kumaramangalam Ayurvedic Clinic &Research Centre, Thodupuzha

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder in which blood glucose levels become too high, as the body produces little or no insulin (a hormone produced by the pancreas that aids in the utilization of glucose for energy), or cannot use insulin properly. The disorder has been growing at an alarming pace not only in the developed countries but also in the developing countries where noncommunicable diseases are rapidly surpassing communicable diseases as the commonest cause of death.

The World Health Organization (WHO) has suggested that over the next two decades, DM in the developing countries will be seen more in the lesser age group ranging from 20 to 45 years. India, with a population over 1 billion has the largest number of diabetic patients in the world, (estimated over 32 million in the year 2000) and this figure is predicted to increase to nearly 80 million by the year 2030.

Characterized by chronic hyperglycemia (high blood glucose), long-term DM is associated with damage to various organs such as the nerves (neuropathy), eyes (retinopathy), kidneys (nephropathy) and the heart (cardiovascular diseases). The cornerstone of therapy revolves around disease prevention, motivation toward healthy lifestyle choices and complication surveillance. Education of partner or caretakers is important in maintaining positive lifestyle changes in diabetic patients. Oral hypoglycemic agents (OHAs) are the primary treatment of type 2 DM. Intensive treatment with insulin has been shown to have significant benefits in both type 1 and type 2 diabetic patients.

Type 2 diabetes mellitus comprises an array of dysfunctions resulting from the combination of resistance to insulin action and inadequate insulin secretion. It is disorders are characterized by hyperglycemia and associated with microvascular , macrovascular , and neuropathic complications.

Unlike patients with type 1 diabetes mellitus, patients with type 2 are not absolutely dependent upon insulin for life. This distinction was the basis for the older terms for types 1 and 2, insulin dependent and non–insulin dependent diabetes. However, many patients with type 2 diabetes are ultimately treated with insulin. Because they retain the ability to secrete some endogenous insulin, they are considered to require insulin but not to depend on insulin. Nevertheless, given the potential for confusion due to classification based on treatment rather than etiology, these terms have been abandoned.

Another older term for type 2 diabetes mellitus was adult-onset diabetes. Currently, because of the epidemic of obesity and inactivity in children, type 2 diabetes mellitus is occurring at younger and younger ages. Although type 2 diabetes mellitus typically affects individuals older than 40 years, it has been diagnosed in children as young as 2 years of age who have a family history of diabetes.

STUDY OBJECTIVES

A pilot open label clinical study to assess the efficacy of MEHYOG Powder in gaining glycemic control and reducing symptoms of patients with Type II Diabetes Melitus for 12 weeks.

INVESTIGATIONAL PLAN

This is a single center, open label, pilot study to evaluate the effectiveness of MEHYOG capsule with Type II Diabetes Melitus.

Subjects were screened from outpatient clinic. After obtaining the written informed consent, subjects willing to take part in the study were screened for eligibility. The study participants were interviewed to evaluate their medical history, social habits and health status. Screening examinations included General and Clinical examination, Evaluation of disease, recording of vital signs and baseline Symptomatic Questionnaires. Lab Examinations and questionnaires were repeated at the end of each 4 weeks till End of Study Visit (week 12).

Inclusion criteria

1. 30-65 years of age of both sexes
2. Confirmed diagnosis of Type II DM

Exclusion criteria

1. Both IDDM &NIDDM patients with acute complications of diabetes
2. Pregnant and lactating women
3. Patients with concomitant severe illness necessitating other medications
4. Patients with severe hypertension
5. History of severe unstable angina, myocardial infarction, CVAs, renal failure

Removal of patients from therapy or assessment

Subjects were withdrawn from the trial in case of the following conditions:

1. Subject did not take 3 doses of medicine continuously.
2. Adverse events, in investigator's discretion did not allow the subject to continue.
3. Subject wanted to discontinue and withdrew the consent.
4. Progression of disease requiring withdrawal of patient.

TREATMENTS

Treatments administered

All subjects were given oral powder of the study product in a thrice daily dose.

Identity of investigational product(s)

The study drug label included following information:

1. Common name : MEHYOG
2. Name to be used in report : MEHYOG
3. Test Item code : DL/01
4. Physical appearance : powder
5. Storage conditions : ambient (+18 to +36^{o}C)

Indication.

MEHYOG Powder is indicated for both insulin dependent and non insulin dependent Diabetes Mellitus. When used as an adjuvant to existing therapy, the product exhibits anti diabetic properties. MEHYOG is expected to enhance cardio and hepato protective activities.

Dosage and Administration.

MEHYOG capsule is administered orally on thrice daily basis until the targeted sugar level is achieved. It is advised to continue the medication to prevent the risk of micro and macro vascular complications of diabetes.

Contra Indications and Interactions.

MEHYOG is a poly herbal medication containing herbs that has been in use widely in traditional ayurvedic treatments. Animal studies on individual herbs have shown these drugs to be safe and thus the product does not produce any anaphylactic or untoward reactions even after prolonged use. MEHYOG does not produce any Drug to Drug or Drug to Food interactions.

Pharmacokinetics.

MEHYOG is well absorbed from the gastro intestinal tract. Any diseases related to the GUT may affect the normal absorption pattern of the drug.

Blinding

This is an open-label study.

Prior and concomitant therapy

Subjects who were required to take medicines for any other complaints were to do so only in consultation with the Investigator. Use of any concomitant medication was to be recorded in the case report form (CRF). Subjects were not advised any specific lifestyle & dietary changes upon enrolment in the study & throughout the duration of the study.

Treatment compliance

In order to ensure treatment compliance, adequate instructions were to be given to subjects regarding trial procedures during the informed consent process. At each visit, a record of dispensed and returned medication was to be maintained to determine subject's compliance to treatment

EFFICACY VARIABLES

Primary efficacy variable:

1. Mean Fasting Blood Glucose
2. Mean Post Parandial Blood Glucose

Secondary Outcome measures

1. Symptomatic changes from Baseline to End-of-Treatment visit

The schedule of the assessments conducted during the study is presented in Table 1

Table 1: Schedule of study procedure

Assesment ParameteR	**Baseline**	**VI**	**V-II**	**EOT**
Informed consent	X			
Medical history	X			
Treatment history for current disease	X			
Demographics	X			
Physical examination (general/systemic)	X	X	X	X
Vital signs	X	X	X	X
Blood Sugar	X	X	X	X
Quality of life questionaire	X	X	X	X
Assessment of treatment compliance		X	X	X
Adverse events		X	X	X
Concomitant medication		X	X	X
Study drug dispensing	X	X	X	X

Screening Examinations (Base line)

After obtaining informed consent and before starting therapy, the following assessments/procedures were done.

General and Clinical examination, Evaluation of disease, recording of vital signs, Quality of life questionnaire were done. Study drug was distributed.Blood sugar was checked

Visit 2 AND Visit 3

General and Clinical examination, Evaluation of disease, recording of vital signs,blood investigations and questionnaires were repeated.

Visit 4 End of study:

General and Clinical examination, Evaluation of disease, recording of vital signs,blood examinations and questionnaires were repeated. All samples were taken back and looked for compliance.

DATA QUALITY ASSURANCE

Source data were original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Original documents and data records included, but were not limited to, hospital records, clinic and office charts, laboratory notes, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, X-rays, and subject files and records kept at the pharmacy, at the laboratories, and medico-technical departments involved in the clinical trial.

The sites maintained appropriate medical and research records for this trial, in compliance with ICH and regulatory and institutional requirements for the protection of confidentiality of subjects. Sites permitted authorized representatives of Mayden Vedic Pharmaceuticals to examine (and when required by applicable law, to copy) clinical records for the purposes of quality assurance reviews, audits, and evaluation of the study safety and progress.

STATISTICAL METHODS PLANNED IN THE PROTOCOL AND DETERMINATION OF SAMPLE SIZE

8.7.1 *Statistical and analytical plans*

All statistical tests were two-sided with a significance level of α=0.05. Data were summarized using descriptive statistics (number of subjects [n], mean, standard

deviation [SD], median, minimum, and maximum) for continuous variables, and using frequency and percentage (i.e., number and proportion of subjects – n, %) for discrete/categorical variables, unless specified otherwise. Students T-test was used to assess primary outcome of the trial.

STUDY SUBJECTS

Disposition of subjects

A summary of subject disposition is provided in Table 2. Two sites were selected and initiated on this protocol. The recruitment was competitive. A total of 50 subjects were screened to enroll 40 subjects into the study. All subjects completed all visits in accordance with protocol and were selected for both safety and efficacy analysis.

EFFICACY EVALUTION

Data sets analysed

Table 2 Populations for Analysis

Number Of Subjects	Number
Screened	120
Randomized	100
Evaluable Population	100

Evaluable Population: These are subjects in each group who had completed end of study visit.

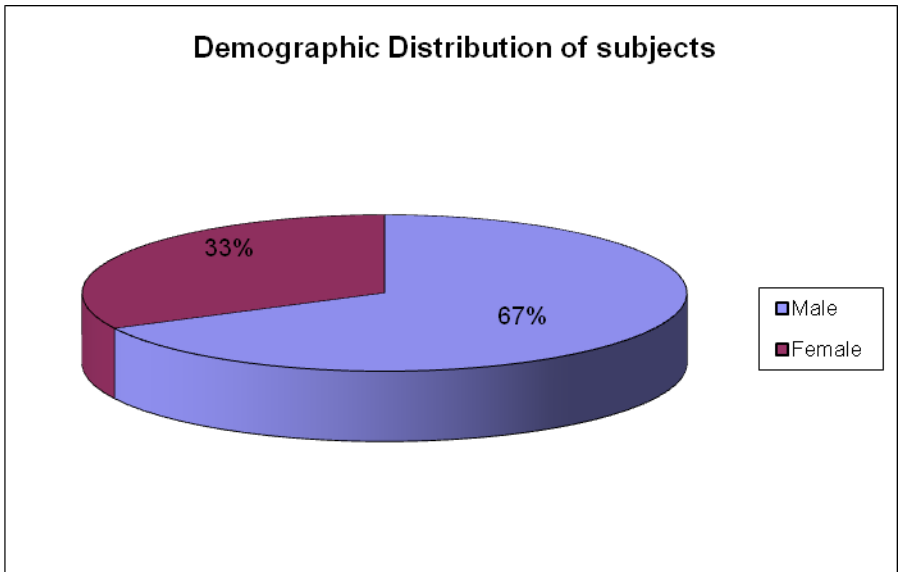
Demographic and other baseline characteristics

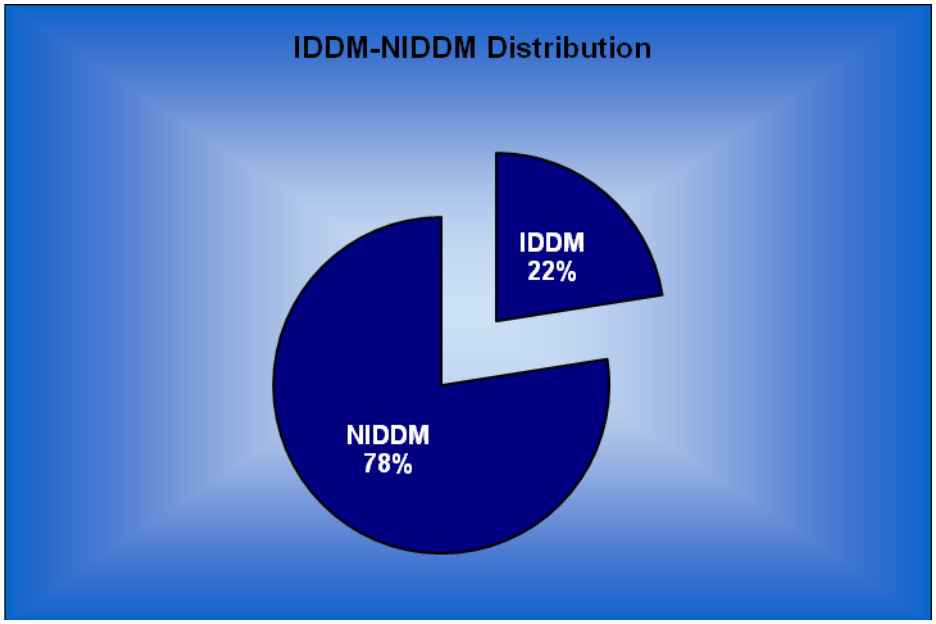
The study recruited 40 patients of both sexes. Baseline characteristics are listed in the table below.

Table 10-2 Demographics and baseline characteristics (Safety set)

Parameters	**Values**
Age(years)	
N	100
Mean	57.85
S.D	8.06

Parameters	**Values**
Weight(Kgs)	
N	100
Mean	76.60
S.D	11.40
Height(cms)	
N	100
Mean	161.00
S.D	8.92
BMI(Kg/m^2)	
N	100
Mean	29.55
S.D	3.61
Gender	
Male	67
Female	33
Type of Diabetes Melitus	
Insulin Dependent	22
Non Insulin Dependet	78





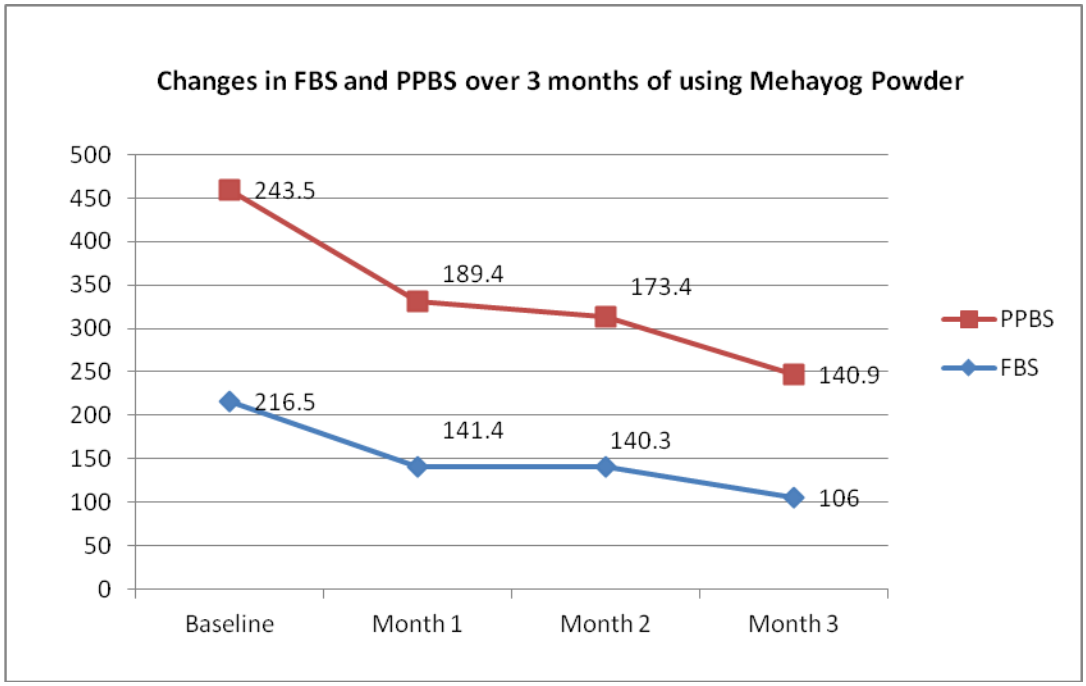
9.1 Efficacy results and tabulations of patient data

Efficacy was analyzed using percent change from baseline in the following variables:
Mean Blood Glucose levels [Table 10-3.1]
Symptom Questionnaire[Table 10-3.2]

Table 10-3.1 Efficacy Results –Mean Blood Glucose

	Baseline	**V1**	**V2**	**End of Treatment**	**% Change**	***p****
FBS	216.5 ±95.9	141.4 ±48.4	140.3 ±37.8	106 ± 6.3	51	<0.05
PPBS	243.5 ±64.3	189.4 ±64.7	173.4±56.4	140.9±44	**42**	<0.05

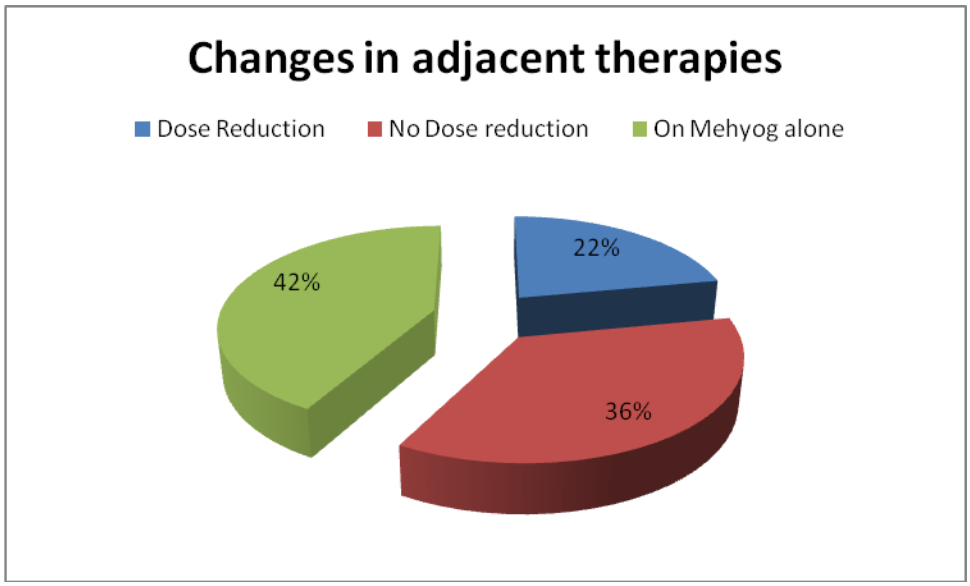
**Paired t-test was used*.



9.1.1 *Changes in Dosage*

Of the 58 subjects who were on allopathic medication 22(38%) had a dosage reduction towards end of treatment. 42 subjects who were not on allopathic medication, completed the study with Mehyog powder alone .

Adjuan Therapies	Number of Subjects
Dose Reduced	22
No Dose Reduction	36
Mehyog alone	42

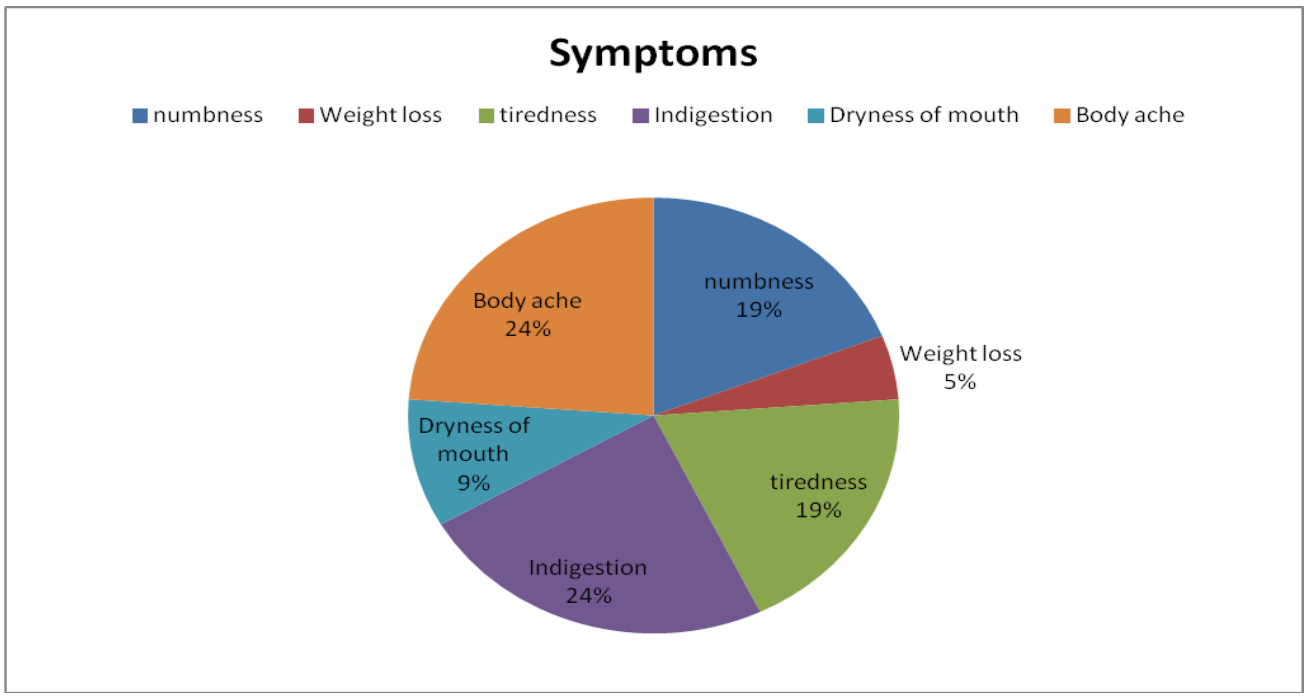


9.1.2 *Symptomatic Changes*

The symptoms that were generally present were

1. Numbness in extremities
2. Weight loss
3. Tiredness
4. Indigestion
5. Dryness of Mouth

The symptoms were present in the following percentages. After 2 months of treatment Numbness, indigestion and tiredness were completely relieved. Dryness of mouth was contained to a large extent and further weight loss was arrested.



9.1.3 *Efficacy conclusions*

The study showed conclusive evidence that MEHYOG reduced both FBS and PPBS in a systematic mode over the visits. There was a palpable improvement symptoms and subjects were well tolerated towards a reduction of dose in 22 cases.

10 SAFETY EVALUATION

Safety was evaluated as extent of exposure, AEs, including serious and other significant adverse events, physical examinations and vital signs measurements,. There e no serious adverse events reported that were related to the study drug.

10.1 *Withdrawals and Dropouts*

There were no withdrawals or dropouts during the study.All 30 patients completed the study and a compliance rate of 99% was maintained.

10.2 *Adverse Events*

10.2.1 *Brief summary of adverse events*

There were no treatment emergent adverse events reported during the study.

10.3 *Vital Signs, and Other Observations Related to Safety*

No significant changes were observed in any of the vital signs.

11. Overall Conclusion

Diabetes has already become a threat to the nation and the individual due to its high prevalence rates and high medical expenses. Therefore, preventing diabetes at an earlier stage is very important. Despite advances in antidiabetic agents, we have not yet achieved any satisfying results in treating diabetes. Among various treatments, medicinal herbs and supplements for diabetes are reported to show generally good efficacy and safety data.MEHYOG powder once daily dose was found to have significant effect in reducing mean blood glucose levels in patients with Type II Diabetes melitus.There was significant reduction in the subject symptom score as well.

12. References

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