Research Article

A Non Randomized, Open-Label, Non Comparative, Prospective Study to Investigate the Efficacy of Herbsulin In The Treatment of Diabetes As Adjuvent Therapy

Tapobrata Basu

SMO, Microdose Lifescience, 6D Krishnaram Bose Street, Kolkata-700 004, West Bengal, India.

1 Study Synopsis

<table>
<tr><td>Introduction</td><td colspan="2">HERBSULIN is the result of many years' research and experiment of Dr. Tapobrata Basu, MD. Dr. Basu is an eminent physician of Eastern India visiting hundreds of patients of different diseases since 2004. He is a faculty member of the 'CLINICAL RESEARCH CENTRE' under the department of Pharmaceutical Technology of Jadavpur University of Kolkata, West Bengal. HERBSULIN was initially formulated in the year 2007 for treating the own patients of Dr. Basu. Gradually after many experiments and clinical practice, and after obtaining adequate confidence the formulation of HERBSULIN was finalized. In the year 2015. The formulation was shared with Deekay Pharma as the authorized manufacture of HERBSULIN and after getting the manufacturing license, commercial production was started. Through an legal agreement, Ms Deekay Pharma is engaged as the sole manufacturer for HERBSULIN in INDIA. For better understanding and acceptability, the collection of research data and statistical analysis of the data is planned. The target patient is who has high blood glucose (blood sugar), either because insulin production is inadequate, or because the body's cells do not respond properly to insulin, or both. HERBSULIN works in both conditions well.</td></tr>
<tr><td rowspan="2">Name of Sponsor/Company:
Dr. Tapobrata Basu

119 Ramsita Ghat Street,
Po- Bhadrakali
Hooghly
PIN- 712232</td><td>Name of Investigational Product:</td><td><u>Name of Active Ingredients</u></td></tr>
<tr><td>HERBSULIN</td><td>Kerela: Momordica charantia,
Amla: Officinalis emblica,
Haridre: Curcuma longa,
Baheda: Belerica terntinalia,
Jamun: Syzygium cumini,
Neem: Azadirachta indica,
Gurmar: Gymnema sylvestre,
Methi: Trigonella foenum-graecum.</td></tr>
<tr><td colspan="3">Title of Study: A non randomized, open-label, non comparative, prospective clinical study to investigate the efficacy of HERBSULIN in the treatment of diabetes as adjuvant therapy.</td></tr>
<tr><td colspan="3">Principal Investigator: Dr. Asis Chakraborty</td></tr>
<tr><td colspan="3">SMO: MICRODOSE LIFESCIENCE, KOLKATA.</td></tr>
<tr><td colspan="3">Study Site: Namita Medical Hall, Amarapuri, Sodepur
Kolkata- 700 111, West Bengal.</td></tr>
<tr><td colspan="3">Studied Period: From 3rd October 2015 to 15th December 2015</td></tr>
<tr><td colspan="3">Objectives:
To evaluate safety and efficacy of HERBSULIN in patients with Diabetes.</td></tr>
<tr><td colspan="3">Methodology:
This is a non randomized, open-label, non comparative, prospective study to investigate the efficacy of HERBSULIN in the treatment of diabetes as adjuvant therapy.
Subjects were evaluated at screening/enrolment, and at the end of treatment. Patients were treated with 15 ml of HERBSULIN with a small amount of water 2 times per day for a period of 60 days.</td></tr>
<tr><td colspan="3">Number of Patients: 20</td></tr>
<tr><td colspan="3">Diagnosis and Main Criteria for Inclusion
1. Male or female outpatients aged 10 to 80 years
2. Patients with Diabetes.
3. The patient will take his regular medicines along with this adjuvant therapy.
4. Patients ready to give written informed consent and willing to comply the study protocol.</td></tr>
<tr><td colspan="3">Test Product: HERBSULIN
Dose & Mode of Administration: 15 ml of HERBSULIN taken with a small amount of water 2 times per day for a period of 60 days.</td></tr>
</table>

Duration of Treatment: 60 days
Criteria for Evaluation:
Efficacy: **Primary Efficacy End Point.** To evaluate reduction in fasting blood glucose level in patients with Diabetes. Secondary **Efficacy End Point.** To Determine the development in quality of life through General Health & debility assessment by subjective scoring (VAS) and clinical assessment.
Safety: 1. Adverse Events 2. Overall safety will be assessed by local symptoms of itching, rash or any other allergic reactions.
Statistical Methods Data of efficacy and safety were presented descriptively. Descriptive statistics was used for efficacy end points. Blood Sugar data (Fasting) was examined using baseline demographics and at the end of study. General Health & debility was assessed by subjective scoring (VAS) and clinical assessment.
CONCLUSION **HERBSULIN** has been found to be a safe and effective herbal product as the adjuvant therapy of Diabetes.
Date of Report: 20th December 2015

Ethics

1.1 Independent Ethics Committee

The study was carried out according to the protocol approved by the Sponsor. The study would be conducted in accordance with the "Good Clinical Practices for Clinical Research in India" guidelines and pertinent regulatory requirement.

The investigators would report promptly to the Sponsor any new information that may adversely affect the safety of the patients or the conduct of the trial. The investigator would submit written summaries of the trial status to the Sponsor if requested. Upon completion of the trial, the investigator would provide the Sponsor with a brief report of its outcome, if required. The original documents would be sent to the sponsor and the investigator would keep a copy.

1.2 Ethical Conduct of the Study

The study was performed in accordance with the requirements of the International Conference on Harmonisation (ICH) guidelines for current Good Clinical Practice (GCP)as well as the demands of national drug and data protection laws and other applicable regulatory requirements.

1.3 Patient Information and Consent

The investigator was responsible for ensuring that no patient enters in the trial before obtaining his written informed consent. Informed Consent means that the person involved is capable to give consent and he is able to exercise free power of choice. It is the explicit acceptance that the individual's data would be known to the investigator(s), sponsor and possibly the regulatory authorities. The consent shall be given in writing after detailed information about the trial and trial medication is provided. Informed written consent will be obtained from each patient in the form provided by the investigator. The patient who refuses to give written informed consent shall not be included in the trial. The investigators will give the patient complete information about the nature, meaning and importance of the study and description of the procedures to be followed by the investigator. They were further given a description of any foreseeable risks and discomforts. Patient will also be told that they have the right to opt out of the trial at any time without having to give reasons if they so wish and without prejudice to further treatment. The patient/guardian will be given sufficient time to consider the implications of the study before deciding whether or not to participate in the trial. The patient and the principal investigator must sign the informed consent form. A copy of the ICF signed by the investigator and subject and/ or LAR and/ or independent witness will be given to the subject. The patient should have legal capacity and be able to comprehend the nature, meaning, importance and risks of the study and to make up his mind accordingly. If the patient is unable to comprehend and understand the necessary information pertaining to his participation in the study, then, an impartial witness (a person, who is independent of the trial and who cannot be influenced by people involved in the trial) would attend the informed consent process and would explain the contents of the informed consent form, in a language understood by the patient.

1.4 Investigators and Study Administrative Structure
1.5 Study Centres
1.6 Administrative Structure
This was a non randomized, Prospective, Open Label, Non-Comparative study in subjects having Diabetes.
Each patient received treatment for the duration of 60 days. Outpatients (male or female aged between 10-80 years) who had Diabetes were enrolled.
A total of 20 patients were enrolled and analysed in order to receive the proper data.

2 INTRODUCTION

Use of Herbal preparations are widely used for prevention and treatment of Diabetes.. There are several preparations available for Diabetes. The selection of any herbal preparation depends on its antimicrobial spectrum, minimal risk of irritation and allergenicity.

Kerela (*Momordica charantia)*
A lot has been written lately about the very beneficial aspects of bitter melon in the treatment of diabetes. Bitter melon has a host of bitter chemicals, which are hypoglycemic in action. It also has at least one substance that is like the insulin secreted by the human pancreatic glands. Hence, bitter melon is extremely effective in the treatment of diabetes mellitus. Doctors all over the world prescribe having either bitter melon juice early in the morning or to include it in some other fashion in the daily diet. Regular use of bitter melon over a period of time helps to bring the blood sugar level down.

Amla (*Emblica officinalis)*
emblica juice contains high levels of ascorbic acid (vitamin C). Ayurvedic preparations that contain Phyllanthus emblica may increase the concentration of ascorbic acid by up to three times. Various parts of this plant show antidiabetic, hypolipidemic, antibacterial, antioxidant, antiulcerogenic, hepatoprotective, gastroprotective, and chemopreventive properties.

Haridra (*Curcuma Longa)*
Curcumin is the principal curcuminoid found in turmeric (*Curcuma longa* Linn.), a popular spice in Asian cuisine. Curcumin extract from rhizomes of turmeric has been shown to contain anti-inflammation and antidiabetic properties. In addition, it could delay development of T2DM, improve β-cell functions, prevent β-cell death, and reduce insulin resistance in animals. We found that curcumin extract effectively reduced the number of prediabetic individuals who progressed toward T2DM as well as improved functions of β-cells
The turmeric (Curcuma longa L. rhizomes) extract significantly suppressed an increase in blood glucose level in type 2 diabetis.

Baheda *(Beleirica Terntinalia)*
Beleirica fruit is powdered and used to dress wounds to arrest the bleeding. Beleric fruits and kernels are used in making medicated hair oil, used to alleviate pain and burning sensation, boost hair growth and impart black color to the hair. The paste of the fruit is applied on eyelids, in case of conjunctivitis. The herb is used in various eye ailments, such as myopia, corneal opacity, pterigium, immature cataract, chronic and acute infective conditions. Beleric helps in loss of appetite, flatulence, thirst, piles and worms. The ripened fruit acts as an astringent and anti-diarrheal. The decoction of the kernels is used in case of excessive thirst and vomiting. Beleric plant alleviates cough, relieves blocked phlegm, controls bleeding in the sputum and eases bronchospasms. It prevents ageing, imparts longevity, boosts immunity, improves mental faculties and enhances the body resistance against diseases. It helps in lowering cholesterol and blood pressure.

Jamun (*Syzygium cumini)*
This plant is acrid, sweet, digestive, astringent to the bowels, anthelmintic and used for the treatment of sore throat, bronchitis, asthma, thirst, biliousness, dysentery and ulcers. It is also a good blood purifier. The fruit is acrid, sweet, cooling and astringent to the bowels and removes bad smell form mouth, biliousness, stomachic, astringent, diuretic and antidiabetic. The fruit has a very long history of use for various medicinal purposes and currently has a large market for the treatment of chronic diarrhea and other enteric disorders. The seed is sweet, astringent to the bowels and good for diabetes.

Neem (*Azadirachta indica)*
Anti-inflammatory, Antidiabetic , Anti-thelmintic, Antiarthritic , Antipyretic , Hypoglycaemic , Antigastric ulcer, Spermicidal ,Antifungal, Antibacterial, Anti-inflammatory, Antibacterial, Antiviral, Antiulcer effect, Antimalerial, Antifungal Anticancer, Antioxident, Anti-inflammatory ,Immunmodulatory. Effect on central nervous system, pathogenic fungi, bacteria, viral, protozoan and Helminthes are sensitive to neem preparations, with antiseptic properties. NSO and leaves extract significantly inhibited fertility in males, but not anti-ovulatory, hence “sensal” a contraceptive.

Gurmar (*Gymnema sylvestre)*
The active ingredients are thought to be the family of compounds related to gymnemic acid: purified gymnemic acids are widely used as experimental reagents in taste physiology and have also an anti-diabetic effect in animal models, reduce intestinal transport of maltose in rats when combined with acarbose, and reduce absorption of free oleic acid in rats.
This *in vitro* data suggests that extracts derived from Gymnema sylvestre may be useful as therapeutic agents for the stimulation of insulin secretion in individuals with diabetes. The rise in insulin levels may be due to regeneration of the cells in the pancreas. G. sylvestre can also help prevent adrenal hormones from stimulating the liver to produce glucose in mice, thereby reducing blood sugar levels. Clinical studys with type 2 diabetics in India have used 400 mg per day of water-soluble acidic fraction of the Gymnema leaves administered for 18–20 months as a supplement to the conventional oral drugs.

Methi (*Trigonella foenum-graecum)*
Fenugreek seed powder in the diet reduces blood sugar and urine sugar with concomitant improvement in glucose tolerance and diabetic symptoms in type 2 diabetic patients. The hypoglycemic effects of fenugreek have been attributed to several mechanisms. In vitro the amino acid 4-hydroxyisolcucine in fenugreek seeds increased glucose-induced insulin release in human and rat pancreatic islet cells; it was observed that 4- hydroxyisoleucine extracted from fenugreek seeds has insulin tropic activity. This amino acid appeared to act only on pancreatic beta cells, since the levels of somatostatin and glucagon were not altered. In human studies, fenugreek reduced the area under the plasma glucose curve and increased the number of insulin receptors, although the mechanism for this effect is unclear. In humans, fenugreek seeds exert hypoglycaemic effects by stimulating glucose dependent insulin secretion from pancreatic beta cells, as well as by inhibiting the activities of alpha-amylase and two intestinal enzymes involved in carbohydrate metabolism.

3 Study Objectives

3.1 Primary Objective

To evaluate reduction of blood glucose level in patients with Diabetes.

Selection of Study Population

3.1.1 Inclusion Criteria

To be eligible for study entry patients had to satisfy all of the following criteria:

1. Male or female outpatients aged 10 to 80 years
2. Patients with Diabetes.
3. The patient will take his regular medicines along with this adjuvant therapy.
4. Patients ready to give written informed consent and willing to comply the study protocol.

3.1.2 Exclusion Criteria

Patients were excluded from the study if one or more of the following criteria were applicable:

1. Patients with deep cuts and wounds, raw wound and weeping wounds.
2. Patient with known allergy to any ingredients used in 8 in 1 Juice.
3. Patients with signs of cellulitis, osteomyelitis, necrotic or avascular bed.
4. Patients with documented peripheral arterial disease
5. Patients with Cancer.
6. Patient receiving corticosteroids or any other immunosuppressive treatment
7. Patient with clinical evidence of anemia or malnutrition
8. Pregnant and lactating females.
9. Patients who have received any investigational drug within 1 month prior to study entry or such treatment is planned for during the study period.

3.1.3 Removal of Patients from Therapy or Assessments

Patients would be free to withdraw from the study anytime without stating the reason, however, every attempt would be made by the investigator to find out and record the reason for the same. Conversely, if the principal investigator feels appropriate he/she may withdraw the patient from the study. A record of reasons for the same would be made in the patient CRF. In the event of a patient requiring any other medication/intervention during the course of the trial, which can interfere with the study, that patient will be withdrawn from the trial. The withdrawn patients would be subjected to physical and systemic examination and efficacy endpoint assessment.

It would be documented whether or not each patient completed the study phase. If for any patient either study treatment or observations were discontinued, the reason for the same would be recorded. Reasons that a patient may discontinue study treatment may be one of the following:

- ✓ Adverse event(s)
- ✓ Abnormal laboratory value(s)
- ✓ Unsatisfactory therapeutic effect
- ✓ Patients conditions no longer requires study treatment
- ✓ Protocol violation
- ✓ Patient withdrew consent
- ✓ Administrative problems
- ✓ Lost to Follow up

3.2 Investigational Products

3.2.1 Investigational Products Administered

The investigational product is **HERBSULIN**. 15 ml. was taken two times daily with little amount of water for a period of 60 days.

3.2.2 Identity of Investigational Products

The details of the investigational products are described below.

Drug name / product	Test
Product	**HERBSULIN**
Dosage form	Liquid
Formulation	Dr. Tapobrata Basu
Route of administration	Oral
Frequency	Two times daily
Manufacturer Batch number(s) License no	Deekay Pharma Batch No: HS-01 AL698M

The investigational products should be stored at a temperature from 15 ^{o}C to 30^{o}C.

3.2.3 Method of Assigning Patients to Treatment Groups
As it is a single arm study, all the patients were assigned the same treatment without any randomization.

3.2.4 Selection of Doses in the Study
Dose selection was not the case in this study.

3.2.5 Selection and Timing of Dose for Each Patient
15 ml. **HERBSULIN** to be taken two times daily with little amount of water for a period of 60 days.. No specific timings were followed and required.

3.2.6 Blinding
The treatment was administered without any randomization. So, blinding was not performed and maintaining was not required.

3.2.7 Prior and Concomitant Therapy
Medications other than the study drugs which would be considered necessary for the patient' welfare and which would not interfere with the study medication or efficacy evaluation may be allowed at the discretion of the investigator, and an appropriate record would be maintained in the CRF.

3.3 Efficacy, and Safety Variables
3.3.1 Efficacy, and Safety Measurements Assessed
3.3.1.1 Efficacy Assessments
Parameters
Blood Sugar Level (Fasting) was evaluated at the beginning and at the end of therapy. Also the signs and symptoms of General Health and Debility was assessed before and after of treatment by VAS score.

Primary Efficacy End Points
Proportion of patients achieving reduction in blood sugar level and developing general welling being.

Secondary Efficacy End Point
To Determine the development in quality of life through General Health & debility assessment by subjective scoring (VAS) and clinical assessment.

3.3.1.2 Safety Assessments
Assessments of safety were based on the following:
- ✓ Adverse Events
- ✓ Overall safety was assessed by local symptoms of itching, rash or any other allergic reactions.

3.3.1.2.1 Adverse Events
Expected Adverse Events
There is no significant adverse event expected with **HERBSULIN**. However, few patients may develop constipation, irritation or local reaction at the site of application.

Serious Adverse Event
Any "serious adverse effects" resulting in withdrawal from the study must be notified by the Investigator within 24 hours to the study sponsor. In case of "Death", it should be reported to Sponsor within one working day. Any unexpected serious adverse event (SAE) occurring during a clinical trial should be communicated promptly (within 14 calendar days) by the Sponsor to the Licensing Authority and to the other Investigator(s) participating in the study.
All the serious adverse effects (SAE) occurring during study at each centre will be recorded into SAE reporting form.

A serious adverse event or reaction is any untoward medical occurrence that at any dose
1. Is life threatening [Note: The term "life threatening" in the definition of "serious" refers to an event in which the patient was at risk of death at the time of the event; if appropriate help was not available (it does not refer to an event, which hypothetically might have caused death, if it were more severe)].
2. Results in death.

3. Requires in patient hospitalization or prolongation of existing hospitalization.
4. Results in persistent or significant disability / incapacity.
5. Results in congenital anomaly.

Causality Assessment

Causality of adverse Event were based on investigator's assessment of the event as certain, probable, possible, unlikely, unclassified and un-assessable as per WHO scale (as given in the table below).

Relationship	Description
CERTAIN	A clinical event, including laboratory test abnormality, occurring in a plausible time relationship to drug administration, and which cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the drug (dechallenge) should be clinically plausible. The event must be definitive pharmacologically or phenomenologically, using a satisfactory rechallenge procedure if necessary.
PROBABLE	A clinical event, including laboratory test abnormality, with a reasonable time sequence to administration of the drug, unlikely to be attributed to concurrent disease or other drugs or chemicals, and which follows a clinically reasonable response on withdrawal (dechallenge). Rechallenge information is not required to fulfil this definition.
POSSIBLE	A clinical event, including laboratory test abnormality, with a reasonable time sequence to administration of the drug, but which could also be explained by concurrent disease or other drugs or chemicals. Information on drug withdrawal may be lacking or unclear
UNLIKELY	A clinical event, including laboratory test abnormality, with a temporal relationship to drug administration which makes a causal relationship improbable, and in which other drugs, chemicals or underlying disease provide plausible explanations.
UNCLASSIFIED	A clinical event, including laboratory test abnormality, reported as an adverse reaction, about which more data is essential for a proper assessment or the additional data are under examination
UNASSESSIBLE	A report suggesting an adverse reaction which cannot be judged because information is insufficient or contradictory, and which cannot be supplemented or verified

Intensity of adverse events

Intensity of adverse events was assessed as per the following classification:

Mild

An event that is usually transient, and requires no special treatment or intervention. The event does not generally interfere with usual daily activities. Includes transient laboratory test alteration.

Moderate

An event that is alleviated with simple therapeutic treatments. The event impacts usual daily activities, which includes alteration in the laboratory tests indicating injury, but without long-term risk

Severe

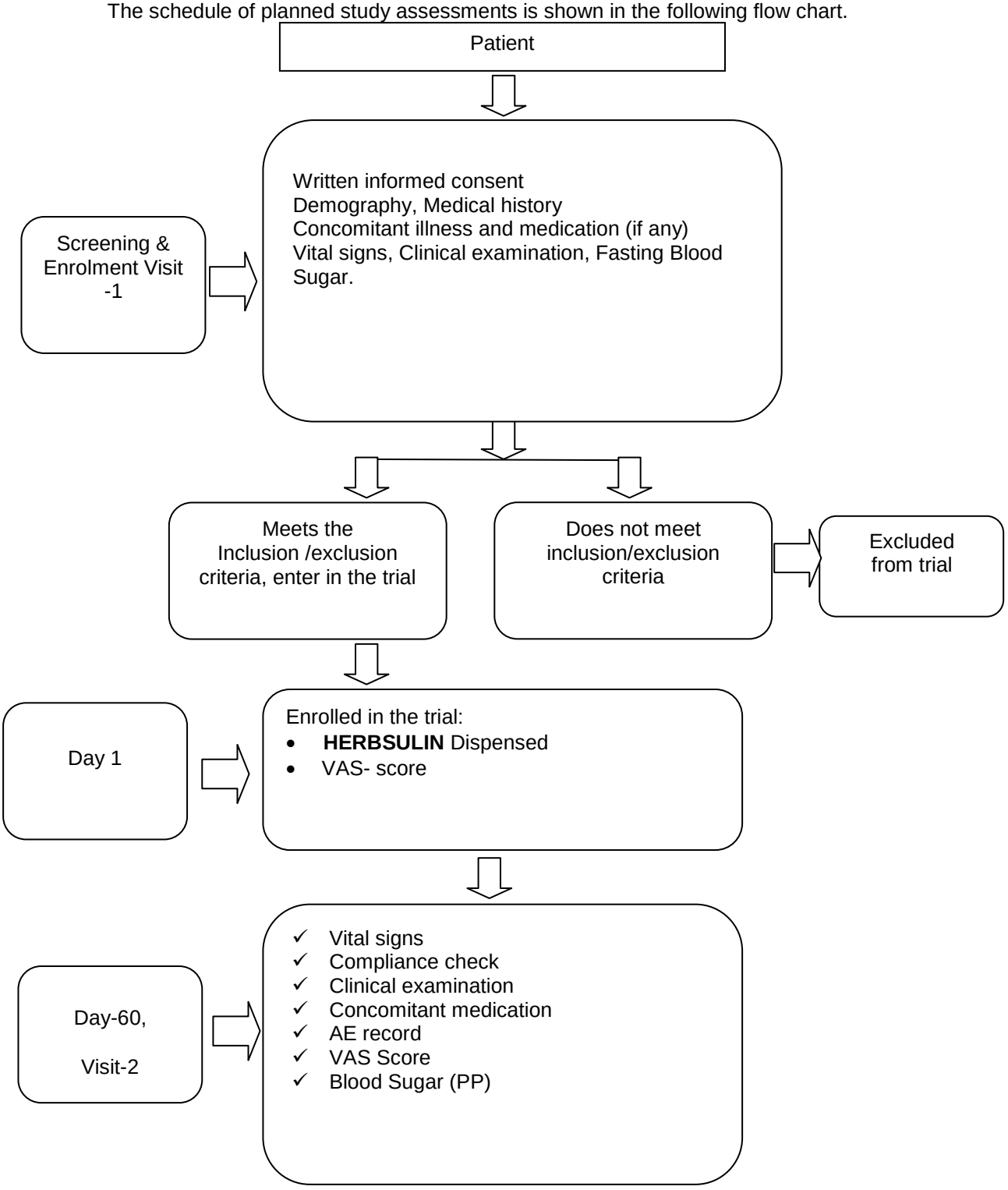
An event that requires therapeutic intervention. The event interrupts usual daily activities, which also include laboratory test indicating a serious health threat or permanent injury. If hospitalization is required for treatment it becomes a serious adverse event.

Abnormal laboratory values will be reported as adverse events under the following circumstances:

- ✓ When the abnormal lab report is accompanied with associated symptoms.
- ✓ When medical/surgical intervention is required.
- ✓ When an additional diagnostic test is required.
- ✓ Leads to a serious adverse event.
- ✓ When it is considered by clinical investigator as an adverse event.

Flow Chart

The schedule of planned study assessments is shown in the following flow chart.



3.3.2 Drug Concentration Measurements

Not applicable.

3.4 Data Quality Assurance

The Sponsor implemented and maintained quality assurance and quality control systems with written Standard Operating Procedures (SOPs) in accordance with the Guidelines of Good Clinical Practice of CDSCO.

The study was monitored as per the requirement of CDSCO GCP guidelines. A monitor or auditor appointed by the sponsor could meet the investigator and visit the study facilities at any time in order to maintain current knowledge of the study through review of the records, comparison with source documents, observation and discussion of the conduct and the progress of the study. Prior to the start of the study, the principal investigator will be contacted and informed of any impending visits and the frequency of such visits. The investigator will allow and assist the Sponsor's study monitor to review study progress, allow source data verification (checking of CRFs against original source documents) for accuracy of data recording, review of study drug logs and facilities, collect completed documents. Any deficiency found will be reported, and signed by the principal investigator and Sponsor Monitor. Also action taken for the last visits decision will be signed. Site monitoring visit log will be updated after every monitoring visit.

In addition, a study site might be audited by the Sponsor's Quality Assurance unit (QA) or by an external Auditor on behalf of Sponsor and/or inspected by the representative of Regulatory Authority. This audit might include review of all source documents, drug records, original clinical case notes, facilities used in the trial.

3.5 Changes in the Conduct of the Study or Planned Analyses

3.5.1 Changes in the Conduct of the Study

No amendments were generated for the study.

3.5.2 Changes in the Planned Analyses

No changes in the conduct of the study or planned analyses were instituted after the start of the study.

4 Study Patients and Results

4.1 Disposition of Patients

A total of 30 patients were screened at 1 centre in Kolkata, India. A total of 30 patients were assigned and all of them received study medication and completed the study. The patients were recruited from Namita Medical Hall, Amarapuri, Sodepur, Kolkata - 700 111, West Bengal, India for this study.

4.2 Demographic and Other Baseline Characteristics

Demographic data are summarised for all the patients in Table 1 Demographic Characteristics.

Subject Identification Number	Subject Initials	ICF Signed by subject	Gender	Age years	Weight Kg	Height cm
1	P-K-C	03-OCT-2015	Male	61	55.00	160
2	J-S	03-OCT-2015	Male	65	60.00	164
3	A-J	03-OCT-2015	Male	49	72.00	170
4	B-T	03-OCT-2015	Male	64	74.00	172
5	B-C	03-OCT-2015	Male	75	70.00	168
6	H-B	04-OCT-2015	Male	31	64.00	170
7	P-S	04-OCT-2015	Male	68	75.00	174
8	D-S	04-OCT-2015	Male	19	40.00	150
9	M-M-B	05-OCT-2015	Male	13	35.00	138
10	D-P	05-OCT-2015	Male	35	50.00	160
11	R-B	05-OCT-2015	Male	14	15.00	75
12	J-B	05-OCT-2015	Female	24	45.00	150
13	L-B	07-OCT-2015	Male	51	70.00	172
14	N-B	07-OCT-2015	Male	58	65.00	165
15	T-M	07-OCT-2015	Female	63	55.00	156
16	G-P	07-OCT-2015	Male	46	78.00	180
17	H-S	08-OCT-2015	Male	72	81.00	172
18	R-K-M	09-OCT-2015	Male	34	41.00	161
19	C-C	09-OCT-2015	Male	18	32.00	159
20	R-B	10-OCT-2015	Male	39	70.00	170
Mean				**44.95**	**57.35**	**159.3**

4.3 Vital Signs

	1st Visit Date	1st Visit Vital Signs				2nd Visit Date	2nd Visit Vital Signs			
		PR	BP	RR	Temp		PR	BP	RR	Temp
1	03-OCT-2015	80	124/80	14	98	04- DEC -2015	80	120/84	16	98
2	03-OCT-2015	76	122/82	14	99	05- DEC -2015	74	124/80	14	98
3	03-OCT-2015	76	130/86	14	99	04- DEC -2015	72	130/84	14	99
4	03-OCT-2015	84	150/100	16	99	04- DEC -2015	76	146/100	14	98
5	03-OCT-2015	80	154/100	14	99	06- DEC -2015	78	154/100	16	98
6	04-OCT-2015	74	120/80	16	99	07- DEC -2015	74	120/80	14	99
7	04-OCT-2015	80	140/90	16	99	06- DEC -2015	80	140/90	16	99
8	04-OCT-2015	74	120/80	14	99	04- DEC -2015	79	120/80	14	98
9	05-OCT-2015	74	120/80	14	99	08- DEC -2015	80	120/80	16	99
10	05-OCT-2015	74	120/80	14	99	05- DEC -2015	80	120/80	14	99
11	05-OCT-2015	90	124/80	18	99	07- DEC -2015	90	120/80	20	99
12	05-OCT-2015	74	120/80	14	99	08- DEC -2015	80	120/80	14	98
13	07-OCT-2015	76	120/80	16	99	11- DEC -2015	82	120/80	16	99
14	07-OCT-2015	74	120/80	14	99	10- DEC -2015	80	120/80	14	98
15	07-OCT-2015	76	120/80	14	98	09- DEC -2015	84	120/80	14	99
16	07-OCT-2015	74	120/80	14	99	09- DEC -2015	80	120/80	14	99
17	08-OCT-2015	80	120/90	14	99	12- DEC -2015	78	120/90	14	98
18	09-OCT-2015	81	110/85	15	98.6	15- DEC -2015	78	110/80	14	98.6
19	09-OCT-2015	79	100/80	17	98.3	09- DEC -2015	72	100/80	17	98.7
20	10-OCT-2015	76	120/80	15	98.9	14- DEC -2015	78	120/80	17	98.1
	Mean	**77.6**		**14.85**	**98.84**		**78.75**		**15.1**	**98.52**

No significant change in vital signs of medically important has been observed compared to baseline after treatment with HERBSULIN for 60 days.

4.4 *Medical History and Examinations*

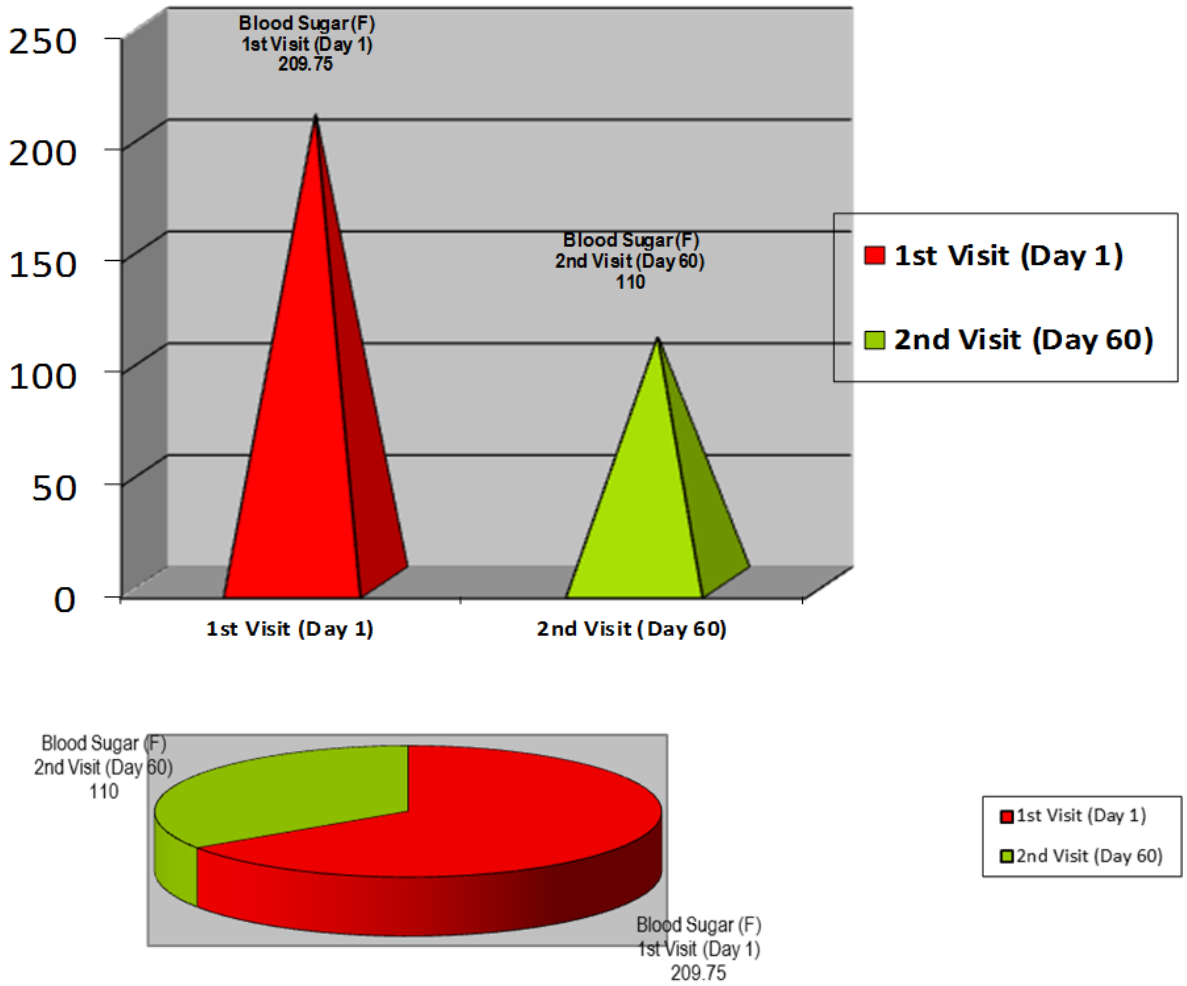
Subject No	Subject Initial	Physical Examination	Medical History	Allergies	Recent Hospitalization	Medical History	Surgical History
1	P-K-C	None	None	None	None	None	None
2	J-S	None	None	None	None	None	None
3	A-J	None	None	None	None	None	None
4	B-T	None	None	None	None	None	None
5	B-C	None	None	None	None	None	None
6	H-B	None	None	None	None	None	None
7	P-S	None	None	None	None	None	None
8	D-S	None	None	None	None	None	None
9	M-M-B	None	None	None	None	None	None
10	D-P	None	UTI	None	5 Months ago	None	Renal Stone
11	R-B	None	None	None	None	None	None
12	J-B	None	PCO	None	4 Months ago	None	Hysterectomy
13	L-B	None	None	None	None	None	None
14	N-B	None	None	None	None	None	None
15	T-M	None	None	None	None	None	None
16	G-P	None	None	None	None	None	None
17	H-S	None	None	None	None	None	None
18	R-K-M	None	None	None	None	None	None
19	C-C	None	None	None	None	None	None
20	R-B	None	None	None	None	None	None

8.5 Baseline Characteristics (Visit 1)

Sl. No.	Subject Initial	Fasting Blood Glucose
1	P-K-C	220
2	J-S	208
3	A-J	190
4	B-T	260
5	B-C	169
6	H-B	185
7	P-S	278
8	D-S	190
9	M-M-B	240
10	D-P	210
11	R-B	230
12	J-B	205
13	L-B	170
14	N-B	168
15	T-M	277
16	G-P	240
17	H-S	186
18	R-K-M	149
19	C-C	173
20	R-B	247
Fasting Blood Glucose Mean = 4195/20= 209.75		

8.5 Study End Characteristics (Visit 2)

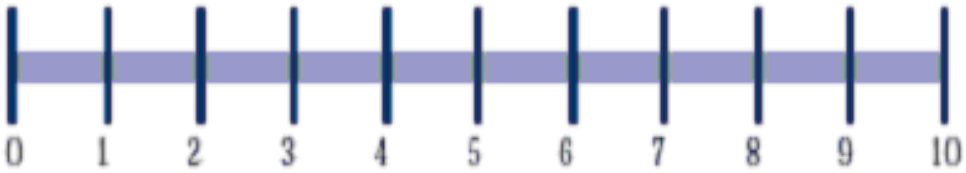
Sl. No.	Subject Initial	Fasting Blood Glucose
1	P-K-C	120
2	J-S	98
3	A-J	100
4	B-T	116
5	B-C	109
6	H-B	95
7	P-S	110
8	D-S	130
9	M-M-B	140
10	D-P	110
11	R-B	130
12	J-B	105
13	L-B	115
14	N-B	108
15	T-M	95
16	G-P	114
17	H-S	96
18	RKM	99
19	C-C	103
20	R-B	107
Fasting Blood Glucose Mean = 2200/20= 110		



Graphical Representation of study start and close mean data of Fasting Blood Glucose

4.5 Quality of life Analysis by Visual assessment & voluntary subjective declaration. Patients were asked about the difficulties they are facing in everyday life due to urinary incontinence, urge of urination and overactive bladder at the beginning and end of treatment.

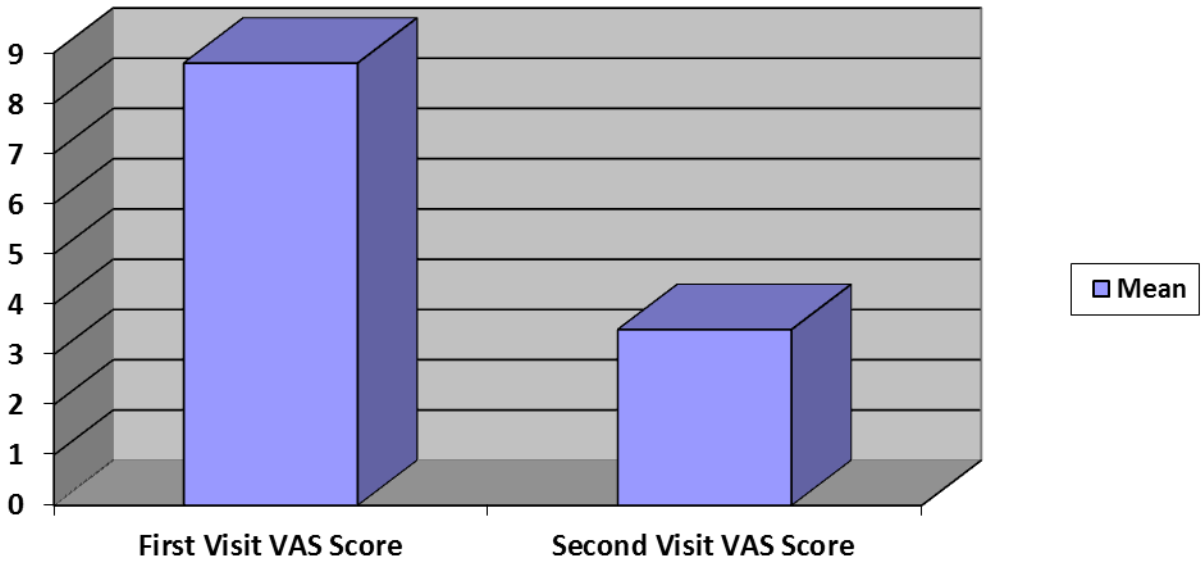
The Visual Analog Scale (VAS) is a psychometric response scale which can be used in questionnaires. It is a measurement instrument for subjective characteristics or attitudes that cannot be directly measured. When responding to a VAS item, respondents specify their level of agreement to a statement by indicating a position along a continuous line between two end-points. This continuous (or "analogue") aspect of the scale differentiates it from discrete scales such as the Likert scale. There is evidence showing that visual analogue scales have superior metrical characteristics than discrete scales, thus a wider range of statistical methods can be applied to the measurements.

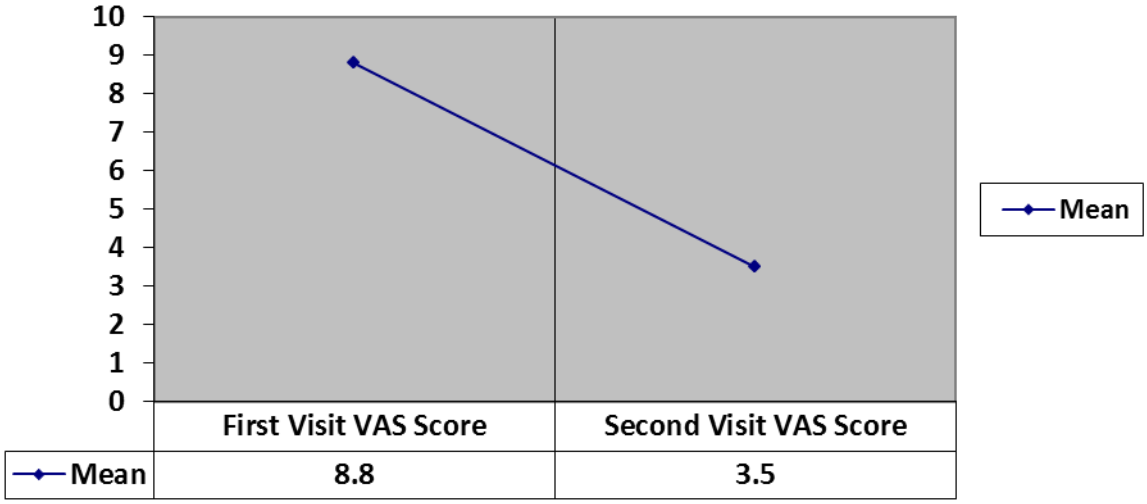


Enjoying Normal Life (No UI) **Worst Possible (Severe UI)**

Subject No	Quality of Life (Visit 1)	Quality of life (Visit 2)
1	10	3
2	10	4
3	08	3
4	10	4
5	09	4
6	10	3
7	08	3
8	08	2
9	08	4
10	09	5
11	08	4
12	10	4
13	08	2
14	07	3
15	08	2
16	10	5
17	07	3
18	08	3
19	10	5
20	10	4
Mean	**8.8**	**3.5**

The mean VAS score has been decreased from 8.8 (Visit 1) to 3.5 (Visit 2). This decrement in VAS score is statistically significant for reduction of Fasting Blood Glucose Mean from Visit 1 to Visit 2 The analysed data is graphically presented below.





Summary

VAS score	Visit 1	Visit 3
Score	8.8	3.5
Inference		**Highly significant development**

4.5.1 Efficacy Conclusions

After application of **HERBSULIN** for 60 days on 20 patients.

- ✓ This reduction in number of Fasting Blood Glucose mean at the end of treatment is statistically significant in support of efficacy of **HERBSULIN** in treatment of Diabetes.
- ✓ The decrement of VAS score from Visit 1 to Visit 2 is statistically significant in support of development of QUALITY OF LIFE of the patients suffering from diabetes.

4.5.2 Safety Conclusions

After application of **HERBSULIN** for 30 days on 20 patients.

- ✓ No medically important adverse change in vital signs has been observed
- ✓ No adverse event either treatment related or unrelated has been reported during the course of the study.

5 CONCLUSION

HERBSULIN has been found to be a safe and effective herbal product and excellent for the treatment of Diabetes as adjuvant therapy.