Clinical Protocol Title

MULTICENTRIC OPEN LABELED CLINICAL TRIAL ON NEERIZHIVU (DIABETES MELLITUS)

Phase of investigations

PHASE 3

Investigational Drug

Sponsor

CCRS

CENTRAL COUNCIL FOR RESEARCH IN SIDDHA

MULTICENTRIC OPEN LABELED CLINICAL TRIAL ON NEERIZHIVU (DIABETES MELLITUS)

I. BACKGROUND

Diabetes and its significance:

Diabetes is a chronic disorder especially of carbohydrate, fat and protein metabolism characterized by increased fasting and post prandial blood sugar levels. The global prevalence of diabetes is estimated to increase, from 4% in 1995 to 5.4% by the year 2025. WHO has predicted that the major burden will occur in developing countries. Studies conducted in India in the last decade have highlighted that not only is the prevalence of diabetes high but also that it is increasing rapidly in the urban population [4]. It is estimated that there are approximately 33 million adults with diabetes in India. This number is likely to increase to 57.2 million by the year 2025.

Diabetes mellitus is a complex metabolic disorder resulting from either insulin insufficiency or insulin dysfunction. Type I diabetes (insulin dependent) is caused due to insulin insufficiency because of lack of functional beta cells. Patients suffering from this are therefore totally dependent on exogenous source of insulin while patients suffering from Type II diabetes (insulin independent) are unable to respond to insulin and can be treated with dietary changes, exercise and medication. Type II diabetes is the more common form of diabetes constituting 90% of the diabetic population.

Symptoms of both diabetic conditions may include: (i) high levels of sugar in the blood; (ii) unusual thirst; (iii) frequent urination; (iv) extreme hunger and loss of weight;

(v) blurred vision; (vi) nausea and vomiting; (vii) extreme weakness and tiredness; (viii) irritability, mood changes etc.

Though pathophysiology of diabetes remains to be fully understood, experimental evidences suggest the involvement of free radicals in the pathogenesis of diabetes [5] and more importantly in the development of diabetic complications [6–8]. Free radicals are capable of damaging cellular molecules, DNA, proteins and lipids leading to altered cellular functions. Many recent studies reveal that antioxidants capable of neutralizing free radicals are effective in preventing experimentally induced diabetes in animal models [9, 10] as well as reducing the severity of diabetic complications [8]. For the development of diabetic complications, the abnormalities produced in lipids and proteins are the major etiologic factors. In diabetic patients, extra-cellular and long lived proteins, such as elastin, laminin and collagen are the major targets of free radicals. These proteins are modified to form glycoproteins due to hyperglycemia. The modification of these proteins present in tissues such as lens, vascular wall and basement membranes are associated with the development of complications of diabetes such as cataracts, microangiopathy, atherosclerosis and nephropathy [11].

During diabetes, lipoproteins are oxidized by free radicals. There are also multiple abnormalities of lipoprotein metabolism in very low density lipoprotein (VLDL), low density lipoprotein (LDL), and high density lipoprotein (HDL) in diabetes. Lipid peroxidation is enhanced due to increased oxidative stress in diabetic condition. Apart from this, advanced glycation end products (AGEs) are formed by non-enzymatic glycosylation of proteins. AGEs tend to accumulate on long-lived molecules in tissues and generate abnormalities in cell and tissue functions [12, 13]. In addition, AGEs also contribute to increased vascular permeability in both micro and macrovascular structures by binding to specific macrophage receptors. This results in formation of free radicals and endothelial dysfunction. AGEs are also formed on nucleic acids and histones and may cause mutations and altered gene expression. As diabetes is a multifactorial disease leading to several complications, it needs a multiple therapeutic approach. Patients of diabetes either do not make enough insulin or their cells do not respond to insulin. In case of total lack of insulin, patients are given insulin injections. Whereas in case of those where cells do not respond to

insulin many different drugs are developed taking into consideration possible disturbances in carbohydrate-metabolism. For example, to manage post-prandial hyper-glycaemia at digestive level, glucosidase inhibitors such as acarbose, miglitol and voglibose are used. These inhibit degradation of carbohydrates thereby reducing the glucose absorption by the cells. To enhance glucose uptake by peripheral cells biguanide such as metphormine is used. Sulphonylureas like glibenclamide is insulinotropic and works as secretogogue for pancreatic cells.

Although several therapies are in use for treatment, there are certain limitations due to high cost and side effects such as development of hypoglycemia, weight gain, gastrointestinal disturbances, liver toxicity etc [14]. Based on recent advances and involvement of oxidative stress in complicating diabetes mellitus, efforts are on to find suitable antidiabetic and antioxidant therapy. Medicinal plants are being looked up once again for the treatment of diabetes. Many conventional drugs have been derived from prototypic molecules in medicinal plants. Metformin exemplifies an efficacious oral glucose-lowering agent. Its development was based on the use of *Galega officinalis* to treat diabetes. *Galega officinalis* is rich in guanidine, the hypoglycemic component. Because guanidine is too toxic for clinical use, the alkyl biguanides synthalin A and synthalin B were introduced as oral anti-diabetic agents in Europe in the 1920s but were discontinued after insulin became more widely available. However, experience with guanidine and biguanides prompted the development of metformin. To date, over 400 traditional plant treatments for diabetes have been reported, although only a small number of these have received scientific and medical evaluation to assess their efficacy. The hypoglycemic effect of some herbal extracts has been confirmed in human and animal models of type 2 diabetes.

The World Health Organization Expert Committee on diabetes has recommended that traditional medicinal herbs be further investigated. (Indian Herbal Drugs for Diabetes Vol. 40, No. 3, 2007 , 165) Major hindrance in amalgamation of herbal medicine in modern medical practices is lack of scientific and clinical data proving their efficacy and safety. There is a need for conducting clinical research in herbal drugs, developing simple bioassays for biological standardization, pharmacological and toxicological evaluation,

and developing various animal models for toxicity and safety evaluation. It is also important to establish the active component/s in these plant extracts. (Indian Medicinal Plants with antidiabetic and related beneficial effects). There are many herbal remedies suggested for diabetes and diabetic complications. Medicinal plants form the main ingredients of these formulations. A list of medicinal plants with antidiabetic and related beneficial effects is given. Conventional modern medicine provides a number of drugs of choice for controlling the blood sugar level in the patients of diabetes mellitus type-2. However, with the prolonged treatment doses of the drugs often needs to be increased to control the blood sugar level and a time comes when the patient has to switch over to insulin. Such patients become cases of insulin dependent diabetes mellitus. With a view to help the suffering community there is a need to find a safer drug, which can be used to control the blood sugar level and such drug can be used safety for longer periods.

Diabetes in Siddha:

Diabetes Mellitus which is called as Neerizhivu in Siddha is caused by inherent / acquired defect in udal thee where biocombustion is challenged. Dominated Iyam slowly wipe out Azhal kutram which leads to further deterioration. Vali kutram is involved leading to complications. Seven thathus slowly degenerate. When all the thathus are deranged dyspnoea, coma, delirium occurs leading to death. This is called Sanni in Siddha.

ETIOLOGY IN SIDDHA

Kodhaiyar kalavi bodhai
Kolutha meen iraichi padhai
Paadhuvai neiyum palum
Parivudan unbeeragil—
sodha pandu uruvamikka
Sukkila prameham than
Odhu neerizhivum sera
undana arinthu kollen

The above version explains that Diabetes Mellitus is caused due to excessive sex indulgence and diet rich in fatty foods. Iyakuttram increases which in turn reduces Anila pitham of the body which is the base of udal thee and due to which proper digestion and Metabolic functions take

place. When Vali kutram is involved slowly the complications set off {Vathamalathu meni kedathu}. This is reflected in the following symptoms :

- ✓ Neer miguntu irangal (Excessive urination)
- ✓ Udal melivu (Emaciation)
- ✓ Varatchi (Dryness)
- ✓ Athi thagam (Excessive thirst)
- ✓ Mayakkam (Syncope)
- ✓ Kan padalam (Pterygium)
- ✓ Thamaraga vayu (Heart disease)
- ✓ Narambu thalarchi (Nervous weakness)
- ✓ Kara patha soolai (Peripheral neuritis)

II. AIM

To study the clinical efficacy of Siddha formulation in controlling blood sugar level of the patients suffering from Type-2 Diabetes mellitus.

OBJECTIVES:

A. **Primary: To study the clinical efficacy of investigational drug in Diabetes Mellitus**

B. Secondary: To study the effect of investigational drug in lipid metabolism

III. CENTRE

Centers of CCRS

IV. SAMPLE SIZE AND METHODS

Sample size-30 in each center

Level of study- Open labeled trail, Multicentric OPD level.

V. SOURCE OF PROCUREMENT OF DRUG

Siddha Central Research Institute, Chennai

VI. TREATMENT

A. Dietary regimen: Annexure I

B. Trial drug:

Tab. D5 chooranam 500mg, 4 b.i.d, half an hour before meals for ninety days.

Diet: - Patients will be advised to take their diet as described in Patient information sheet and do brisk walking / jogging or light exercise for half hour daily.

VII. CRITERIA FOR INCLUSION

1. Age between 30 years to 60 years
2. If yes in any of the three

   Blood sugar – Fasting > 110 and =< 200 mg/dl or

   PP > 160 mg/dl and<= 350 mg/dl or

   Glycated hemoglobin> 6.5% and <10%
3. Recently diagnosed (< 1 year) cases of Type-2 Diabetes mellitus.
4. Patients who are in mono therapy alone.

VIII. CRITERIA FOR EXCLUSION

1. Age below 30 and above 60 years.
2. If yes, in any one of the three

   Blood sugar – Fasting =< 109 and > than 201 mg/dl or

   PP=< 159 mg/dl>351 mg/dl or

   Glycated hemoglobin<=6.4% and =>10.1%
3. Malignant and accelerated hypertensive
4. CVS disorder (CAD)
5. Pregnant woman and planning to be pregnant within six months
6. Lactating mother
7. Secondary Diabetes mellitus
8. Patient undergoing regular treatment for Diabetes or any other severe illness
9. CNS disorder e.g. encephalopathy

IX.CRITERIA FOR WITHDRAWAL: - **The investigator shall withdraw the patients from the study if**

1. fasting blood sugar rises to >200 mg. /dl. Or post- prandial blood sugar level increases to>350 mg/dl and are not controllable within fifteen days.
2. any serious complication develops which requires urgent treatment with any other Drug / Therapy

The investigator will mention the probable cause of withdrawal and provide possible medical treatment to manage the illness.

X. ROUTINE EXAMINATION AND ASSESSMENT

The full details of history and physical examination of the patients will be recorded as per the proforma (Forms I & IA). Clinical and physiological assessment will be done before drug administration and after every two weeks. The laboratory investigations will be recorded before drug administration (Form-III), after every 4 weeks (FBS & PPBS only) and at the end of treatment (Form-III)

XI. PERIOD OF STUDY

Duration of the study: Six months

Duration of medication – 90 days

XII. CRITERIA FOR SUCCESS OF TREATMENT

If during treatment or after treatment fasting Blood sugar become<110 mg/dl. & post prandial Blood sugar < 160 mg/dl and HbA1c < 6.5 % it will be considered as successful outcome of the treatment.

XIII. STATISTICAL ANALYSIS

Data on Fasting /Post prandial blood sugar and HbA1c will be analyzed by using appropriate statistical methods.

XIV. TRIAL MONITORING AND DATA ANALYSES

The progress of the trial will be monitored by CCRS Head Quarters, Chennai consisting of one expert each of Allopathy and Siddha besides one outside expert. Data analysis will be undertaken at Central Council for Research in Siddha.

XV. ETHICAL REVIEW

Institutional Ethical Committee (IEC) of the participating center should give clearance certificate before the project is initiated. Patient's information sheet and informed consent form should be submitted along with project proposal for approval by IEC. Both should be maintained in duplicate with one copy given to the patient at the time of entry to the trial.

REFERENCE

1. Harrison's Principle of Internal Medicine 15th Edition Page 2109-2135.
2.
3. The Expert Committee on Diagnosis and classification of Diabetes Mellitus : Report of the Expert Committee on Diagnosis and Classification of Diabetes Mellitus, Diabetic care 1997; 207:1183-97.
4. Siddharth N Shah, Asshit Shah, API Text Book of Medicine 5th Edition Page-1460.
5. Vaisajya Ratnawali, Saptam Sanskaran 2040 Page 812.
6. P.V. Sharma, Dravya Guna Vigyan Vol-II, Dasham Sanskaran Page 103-105, 661-63, 684-685.
7. P.V. Sharma, Dravya Guna Vigyan Vol-III, Tritiya Sanskaran 2041 Page 99-100.
8. B.G. Vaidya Nighantu Adarsh, Pratham Sanskaran 2025, Vol-I, Page 581-585.

CENTRAL COUNCIL FOR RESEARCH IN SIDDHA

MULTICENTRIC OPEN LABELED CLINICAL TRIAL ON NEERIZHIVU (DIABETES MELLITUS)

CONSENT FORM

CERTIFICATE BY INVESTIGATOR

I certify that I have disclosed all the details about the study in the terms easily understood by the patient.

Date: _____ Signature_____

Name_____

CONSENT BY SUBJECT

I have been informed to my satisfaction, by the attending physician, the purpose of the clinical trial and the nature of drug treatment and follow-up, including the laboratory investigations to be performed to monitor and safeguard my body functions.

I have been informed about the possible side effects and procedures to report when encountered. I am also aware of my right to opt out of the trial at any time during the course of the trial without having to give the reasons for doing so.

I, exercising my free power of choice, hereby give my consent to be included as a subject in the clinical trial on "Multicentric open labeled clinical trial on Neerizhivu (diabetes mellitus)" Clinical Trial of a investigational drug in Controlling Blood Sugar Level in Type 2 Diabetes mellitus.

Date: _____ Name of the Subject: _____

Signature or Thumb impression_____

Date: _____ Name of witness: _____

Signature or Thumb impression: _____

Relationship _____

Translate into regional Language

CENTRAL COUNCIL FOR RESEARCH IN SIDDHA

MULTICENTRIC OPEN LABELED CLINICAL TRIAL ON
NEERIZHIVU (DIABETES MELLITUS)

PATIENT INFORMATION SHEET

STUDY DOCTOR:

SITE OF INVESTIGATION:
CONTACT No:

You are being asked to participate in a clinical research study. However, before you decide to be a part in this study, you need to understand the risks and benefits as well as what is expected of you as a study participant. Please read the following information carefully. This consent form may contain word (s) that you do not understand. Do not hesitate to ask the doctor and/or doctor's staff any questions you may have. You should not sign this form until you understand all of the information presented in the following pages and until all of your questions about the research have been answered to your satisfaction.

What is the study about?

Research is going on to find a suitable natural product for the treatment of Type-2 Diabetes mellitus. You are invited to participate in such a study in which you will receive Siddha trial drug.

The aim of the present study is to clinically evaluate the anti-diabetic effect of a investigational drug in the management of Type 2 Diabetes mellitus.

Totally 30 patients from this hospital will be taking part in this study.

What will you have to do?

Your doctor will explain clearly what you have to do. It is important that you follow the instructions scrupulously. The study will take approximately three months to complete. After this period, you are expected to visit the hospital every fortnight. The interval between the first and second visit will be around 14 days.

Before you start treatment, during the first visit to the clinic, you will undergo a complete physical examination. Blood and urine samples will also be taken. This is to make sure that you are eligible for the study.

One week later, at your second visit, if you are eligible, you would be put on trial treatment for 90 days. You may receive trial drug for 90 days. You should follow life style modifications (Diet Advice, Exercise) as given along with information Sheet.

From the first visit onwards, you will be required to fast overnight before attending each visit. Blood and urine samples will be taken at every visit. At each visit, you will be supplied with sufficient quantity of drug to last until your next visit.

What happens at the end of the study?

The trial treatment will be stopped at the end of 90 days. You will be referred to the General OPD of SCRI.

Are there any risks?

The trial drug may cause hypoglycemia (very low blood sugar) in some cases. The symptoms of hypoglycemia are sweating, drowsiness, nausea, confusion and in-coordination. In case of such symptoms, you should immediately take sugar, glucose/biscuits and milk/fresh lime juice/orange juice with sugar and report to the doctor.

What are the alternatives?

Your doctor will be pleased to explain to you the available alternative treatment to control your blood sugar?

When can you leave the study?

Your participation in the study is entirely voluntary. You can choose to leave the study at any time. Your decision to leave the study will not affect your medical care or relationship with your doctor.

Your doctor may decide that you should not continue in the study if, a) your blood sugar becomes very high or very low, b) you start on insulin or other medication that affect blood sugar, c) you take part in any other trial.

What is the cost of the study?

All medication and tests to be done during the study will be free of charge.

If you do not want to participate, you are free to do so. It will not affect your medical care or relationship with your doctor in any way.

What happens now if you decided to take part?

You will be asked to sign a consent form saying that you have been given information about the study and you voluntarily agree to take part.

It is important to follow all instructions given by your doctor or doctor's assistant carefully.

What about the confidentiality?

The study data in your name or address will be coded with initials and number in your records. The confidentiality will be maintained. Unless required by law, only the Study Doctor, the Study Team and its authorized agents and the Institutional Ethics Committee will have access to confidential data which identifies you by name.

Any other additional information regarding this trial?

If you have any questions regarding the research study or if you need emergency medical treatment while you are participating in this study, or have questions or additional concerns about the study, you should contact the study doctor

Do not sign this form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions

Translate into regional Language

மண:	நாள 1	நாள 2	நாள 3	நாள 4	நாள 5	நாள 6	நாள 7
8-9 மண	பால மிலி 100 இட்லி 2 சாம்பா ½ கப	பால மிலி 100 தோசை 2 சடன	பால மிலி 100 இட்லி 2 சாம்பா ½ கப	பால மிலி 100 உப்புமா சட்ன	பால மிலி 100 கேழ்வரகு கள கொ துவையல்	பால மிலி 100 தோசை 2 சடன	பால மிலி 100 உப்புமா சட்ன
11 மண	கறிவேபபல பொடி கலந்த மோ மிலி 150	கறிவேபபல பொடி கலந்த மோ மிலி 150	கறிவேபபல பொடி கலந்த மோ மிலி 150	கறிவேபபல பொடி கலந்த மோ மிலி 150	கறிவேபபல பொடி கலந்த மோ மிலி 150	கறிவேபபல பொடி கலந்த மோ மிலி 150	கறிவேபபல பொடி கலந்த மோ மிலி 150
1 மண	சாதய 1½கப கததிர், சாம்பா கறிவேபல துவையல சரைகாய் கூடு	சாதய 1½கப முளங்கி சாம்பர் அவரை பொரியல கீரை கூட்டு	எலுமிசசை/ தக்காளி/ புள சாதய எ துவையல வாழைதண்டு பொரியல் தய் 1½ கப	சாதய கப 1 ம or அவயல சண்டைகாய சாம்பா	சாதய 1½கப வெண்டைகாய சாம்பா அவரை பொரியல கீரை கூட்டு தய 1½ கப்	சாதய 1½கப முருங்கைகாய சாம்பா வாழைப்பூ பொரியல் தய் 1½ கப	சாதய கப 1 கறி குழப்பு or கோவைகாய பொரியல வெங்காய சாபா
4-5 மண	பால/ பழய	பால/ பழய	பால/ பழய	பால/ பழய	பால/ பழய	பால/ பழய	பால/ பழய
8-9 மண	2 சபாதி 70 கிரா கறிவேபலை/ கொதுமல்லி/ புதினா/ வெங்காயய/ தக்காள சட்ன	கேழ்வரகு தோசை 2 கறிவேபலை/ கொதுமல்லி/ புதினா/ வெங்காயய/ தக்காள சட்ன	தோசை 2 கறிவேபலை/ கொதுமல்லி/ புதினா/ வெங்காயய/ தக்காள சட்ன	சபாதி 70 கிராகறிவேபல லை/ கொதுமல்லி/ புதினா/ வெங்காயய/ தக்காள சட்ன	இடலி 2 கறிவேபலை/ கொதுமல்லி/ புதினா/ வெங்காயய/ தக்காள சட்ன	கேழ்வரகு தோசை 2 கறிவேபலை/ கொதுமல்லி/ புதினா/ வெங்காயய/ தக்காள சட்ன	70 சபாதி 2 கிரா கறிவேபலை/ கொதுமல்லி/ புதினா/ வெங்காயய/ தக்காள சட்ன

CENTRAL COUNCIL FOR RESEARCH IN SIDDHA

MULTICENTRIC OPEN LABELED CLINICAL TRIAL ON NEERIZHIVU (DIABETES MELLITUS)

FORM I - SCREENING PROFORMA

1. Code No (of clinical trial) ☐
2. Centre:
3. Name of the Patient _____
4. S.No. of Patients _____
5. Gender Male ☐ (1) Female ☐ (2)
6. Date of Birth ☐☐ ☐☐ ☐☐ Age (Yrs) ☐☐
7. Address _____

_____

Mobile: ☐☐☐☐☐☐☐☐☐☐ Phone no: ☐☐☐☐☐☐☐☐

CRITERIA FOR INCLUSION	**Yes(1)**	**No(0)**
8. Age between 30 years to 60 years	☐	☐
9. If yes in any one of the three in GTT	☐	☐
Fasting >110 mg/dl	☐	☐
1/2 hr >160mg/dl	☐	☐
1 hr >170mg/dl	☐	☐
1 ½ hr >140mg/dl	☐	☐
2 hr >125mg/dl	☐	☐
Post prandial >140mg/dl	☐	☐

10. Recently diagnosed (<1 year) cases of Type-2 Diabetes mellitus

Blood sugar – Fasting > 110 and =< 200 mg/dl ☐ ☐

PP > 160 mg/dl and<= 350 mg/dl or ☐ ☐

Glycated hemoglobin>6.5% and <10% ☐ ☐

11. Patients who are in Mono therapy alone. ☐ ☐

VII. CRITERIA FOR EXCLUSION

12Glycated hemoglobin<=7% and =>10% ☐ ☐

13. Malignant and accelerated hypertensive ☐ ☐

14. CVS disorder (CAD) ☐ ☐

15. Pregnant woman or the women planning to be pregnant in next six months ☐ ☐

16. Lactating mothers ☐ ☐

17. Secondary Diabetes mellitus ☐ ☐

18. Patient undergoing regular treatment for Diabetes or for any other severe illness ☐ ☐

19. CNS disorder e.g. encephalopathy ☐ ☐

If yes to S.No.8-11 admit the patient into the study.

If admitted subjects _____ No. _____

Date: _____ Signature of the Doctor _____

CENTRAL COUNCIL FOR RESEARCH IN SIDDHA

MULTICENTRIC OPEN LABELED CLINICAL TRIAL ON NEERIZHIVU (DIABETES MELLITUS)

FORM I A – SELECTION PROFORMA

1. Code No. (Clinical trial) ☐

2. Centre :

3. Name of the Patient _____

4. S.No. of Patients _____

5. Gender Male ☐ (1) Female ☐ (2)

6. Date of Birth ☐☐ ☐☐ ☐☐ Age (Yrs) ☐☐

7. Address _____
   _____
   _____

8. Educational status
   Illiterate ☐ (1) Read & Write ☐ (2)
   Educational qualifications_____ (3)

9. Occupation
   Desk Work ☐ (1) Field Work ☐ (2) Other Specify_____(3)

10. Income per capita per month in Rs _____

Chief complaint with duration (if any) in days

	Absent(0)	**Present(1)**
11. Polyuria (Excessive urination)	☐	☐
12. If present, duration in Days_____		
13. Polyphagia (excessive hunger)	☐	☐
14. If present, duration in Days_____		
15. Polydipsia (excessive thirst)	☐	☐
16. If present, duration in Days_____		

	Absent (0)	**Present (1)**
17. Exhaustion / Tiredness	☐	☐
18. If present, duration in Days_____		
19. Loss of body weight	☐	☐
20. If present, duration in Days_____		
21. Body ache	☐	☐
22. If present, duration in Days_____		
23. Giddiness	☐	☐
24. If present, duration in Days_____		
25. Polyneuritis (Numbness / Tingling)	☐	☐
26. If present, duration in Days_____		
27. Visual disturbance	☐	☐
28. If present, duration in Days_____		

29. Other (specify), if any_____

Personal History:

30. Diet Veg ☐ (1) Non-veg ☐ (2) Lacto-veg ☐ (3)

31. Presence of anxiety No ☐ (0) Yes ☐ (1)

32. Constipation No ☐ (0) Yes ☐ (1)

Addiction

33. Smoking No ☐ (0) Yes ☐ (1)

If yes specify:
(a) Quantity [packs] _____ (b) Total duration in years _____

34. Tobacco No ☐ (0) Yes ☐ (1)

if yes, specify: (a) quantity_____ b) Total duration in years_____

☐ ☐

35. Alcohol No (0) Yes (1)

36. If yes specify: quantity(ml)_____

37. Total duration in years_____

38. Any other(specify)_____

39. Yakkaiyin Ilakkanam ☐

VITAL SIGNS

12.Pulse rate/min ☐☐

13.Heart rate/min ☐☐

14.BP(mmHg) ☐☐☐ / ☐☐☐

15.Temperature ºF ☐☐☐.☐

	PRESENT(1)	ABSENT (2)
16.Cyanosis	☐	☐
17.Anaemia	☐	☐
18.Jaundice	☐	☐
19.Clubbing	☐	☐
20.Lymphadenopathy	☐	☐
21.Oedema	☐	☐

22.Height/cm ☐☐☐.☐

23.Weight/Kg ☐☐☐.☐

24.BMI ☐☐

SIDDHA ASPECTS

25.KAALA NILAI					
1. Kaarkaalam	☐	2.Koothirkaalam	☐	3. Munpanikaalam	☐
4.Pinpanikaalam	☐	5.Ilavenirkaalam	☐	6.Muduvenirkaalam	☐

AYMPORIGAL	**NORMAL(1)**	**AFFECTED(2)**	
26.Mei	☐	☐	_____
27.Vaai	☐	☐	_____
28.Kan	☐	☐	_____
29.Mookku	☐	☐	_____
30.Sevi	☐	☐	_____

AYMPULANGAL	**NORMAL(1)**	**AFFECTED(2)**	
31.Ooru	☐	☐	_____
32.Suvai	☐	☐	_____
33.Oli	☐	☐	_____
34.Oosai	☐	☐	_____
35.Naatram	☐	☐	_____

KANMENDRIYUM	**NORMAL(1)**	**AFFECTED(2)**	
36.Kai	☐	☐	_____
37.Kaal	☐	☐	_____
38.Vaai	☐	☐	_____
39.Eruvaai	☐	☐	_____
40.Karuvaai	☐	☐	_____

UYIR THATHUKKAL

VALI - ABSENT (0) NORMAL (1)DECREASED(2)INCREASED(3)

41. Uyirkkal (Pranan)

42. Digestion ☐ _____

43. Kizhnokkukkal(Abanan)

Excretion of Urine ☐ _____

Excretion of Faeces ☐ _____

44 .Paravukal(Viyanan)

Blinking ☐ _____

Movement of limbs ☐ _____

45.Melnokkunkal(Uthanan)

Speech ☐ _____

Complexion ☐ _____

Hiccup ☐ _____

46. Nadukkal (Samanan)

Digestion ☐ _____

47. Nagan

Hearing ☐ _____

Intelligence ☐ _____

Closing & opening of eyelids ☐ _____

48. Koorman

Winking (of eyelids) ☐ _____

Yawning ☐ _____

Closing of mouth ☐ _____

49.Kirukaran

Salivary Secretions ☐ _____

Hunger ☐ _____

50. Devathathan

Occular Movements ☐ _____

Laziness ☐ _____

51. Thananjeyan

Abnormal noise (Tinnitus) ☐

in the ears ----------

Condition of Sinuses ☐

AZHAL - ABSENT (0) NORMAL (1) DECREASED (2) INCREASED (3)

52. Aakkanal(Anar pitham)

Digestion ☐ _____

53.Vannayeri(Ranjagam)

Pallor ☐ _____

54. Aattralangi(Sathagam)

Movements ☐ _____

55. Olloli Thee (Alosagam)

Complexion ☐ _____

Lustre of Skin ☐ _____

Vision ☐ _____

56. Nokkazhal (Prasagam)

Brightness of Skin ☐ _____

IYAM - ABSENT (0) NORMAL (1) DECREASED (2) INCREASED (3)

57. Aliiyam (Avalambagam)

Respiration ☐ _____

58. Neerppiyam (Kilethagam)

Digestion ☐ _____

59. Suvaikanaiyam (Pothagam)

Taste ☐ _____

60. Niraivaiyam (Tharpagam)

Cooling of eyes ☐ _____

61. Ondriyaiyam (Santhigam)

Movements of joints ☐ _____

VATHAM ☐ PITHAM ☐ KABAM ☐ _____

UDAL THATHUKKAL	INCREASED(1)	DECREASED(2)
62. **SAARAM**	◯	
Indigestion	☐	
Loss of weight		☐
Tiredness		☐
Lassitude		☐
Dryness of the skin		☐
Diminished activity of sense organs		☐
63. **SENNEER**	◯	
Boils	☐	
Throbbing pain	☐	
Anorexia	☐	
Mental disturbance	☐	
Splenomegaly	☐	
Colic pain	☐	
Increased BP	☐	
Reddish eye & skin	☐	
Jaundice	☐	
Haematuria	☐	

Anaemia

Tiredness

Lassitude

Neuritis

Pallor of body

64**. OON**

Cervical lymph adenitis

Ulcers & Tumor

Muscularity in cervical region

Impairment of sense organs

65. **KOZHUPPU**

Dyspnoea

Loss of activity

Pain in hip

66. **ENBU**

Splitting & Falling of Hair

Loosening of Teeth & Nail

67. **MOOLAI**

Non healing ulcer

Swollen phalanges

Swollen eyes

Oliguria

Heaviness of body

Weakness of bone

Sunken eyes

68.**SUKILAM/SURONITHAM**

Love & Lust towards women/men

Urinary calculi

Failure in reproduction ☐

Pain in genitalia ☐

ENVAGAI THERVUGAL

NAA

69.Maa padithal Present ☐ Absent ☐

70.Niram Black ☐ Red ☐ Pale ☐ Others ☐

71. Suvai Inippu ☐ Pulippu ☐ Kaippu ☐ Thuvarppu ☐ Uvarppu ☐ Karppu ☐

72.Vedippu Present ☐ Absent ☐

73.Vai neerural Normal ☐ Excess ☐ Scanty ☐ Absent ☐

74. NIRAM (SKIN)

Karuppu ☐ Manjal ☐ Veluppu ☐ Maa niram ☐

75.MOZHI

Sama oli ☐ Uratha oli ☐ Thazhntha oli ☐

76. VIZHI

.Niram Black ☐ Red ☐ Yellow ☐ Pale ☐

77.Kanneer Normal ☐ Abnormal ☐ _____

78.Yeritchal Present ☐ Absent ☐ _____

79.Peelai Present ☐ Absent ☐ _____

MEI

80. Veppam Mitha Veppam ☐ Miku Veppam ☐ Thatpam ☐ _____

81. Viyarvai Normal ☐ Increased ☐ Reduced ☐ _____

82. Thoduvali Present ☐ Absent ☐ _____

83. Vali Present ☐ Absent ☐ _____

84. NAADI

Vali ☐ Azhal ☐ Iyam ☐ Valiazhal ☐ Valiiyam ☐

Azhaliyam ☐ Azhalvali ☐ Iyavali ☐ Iyaazhal ☐

MALAM	**NORMAL (1)**	**AFFECTED (2)**		
85. Niram	Black ☐	Red ☐	Yellow ☐	Pale ☐
86. Thanmai (Consistency)	Irukal ☐	Ilakal ☐	Thin ☐	Bulky ☐
87.Alavu	Normal ☐	Increased ☐	Reduced ☐	

	Present	Absent	
88. Kazhichal	☐	☐	
89. Seetham	☐	☐	
90. Vemmai	☐	☐	

MOOTHIRAM

NEERKURI	NORMAL (1)	AFFECTED (2)		
91. Niram	Venmai ☐	Manjal ☐	Sivappu ☐	Others ☐
92. Nurai	Normal ☐	Increased ☐	Reduced ☐	
93. Edai	Normal ☐	Increased ☐	Reduced ☐	
94. Enjal	Normal ☐	Increased ☐	Reduced ☐	

(Alavu) Normal ☐ Increased ☐ Reduced ☐

---

95. Manam Present ☐ Absent ☐ _____

96. Thadavai (Frequency) Day ☐ Night ☐ _____

NEIKKURI

97. Aravam ☐ 93.Mothiram ☐ 94.Muthu ☐

Date: Signature of Investigator/ Medical Officer

CENTRAL COUNCIL FOR RESEARCH IN SIDDHA

MULTICENTRIC OPEN LABELED CLINICAL TRIAL ON NEERIZHIVU (DIABETES MELLITUS)

FORM II - CLINICAL & PHYSIOLOGICAL ASSESSMENT

[Before Treatment & Fortnightly during Treatment]

1. Code No.(of clinical trial) ☐
2. Centre :
3. Name of the Patient _____
4. S. No. of the Patient _____
5. Gender Male ☐ (1) Female ☐ (2)
6. Date of Birth ☐☐ ☐☐ ☐☐ Age (Years) ☐☐
7. Address _____

_____

Chief complaint with duration (if any) in days

	Absent(0)	**Present(1)**
8. Polyuria (excessive urination)	☐	☐
9. Polyphagia (excessive hunger)	☐	☐
10. Polydipsia (excessive thirst)	☐	☐
11. Exhaustion/Tiredness	☐	☐

	Absent(0)	Present(1)
12. Bodyache	☐	☐
13. Giddiness	☐	☐
14. Polyneuritis(Numbness / Tingling)	☐	☐
15. Visual disturbance	☐	☐

16. Others (specify),if any_____

VITAL SIGNS

12.Pulse rate/min ☐☐

13.Heart rate/min ☐☐

14.BP(mmof Hg) ☐☐☐ / ☐☐☐

15.Temperature ºF ☐☐☐ . ☐

	PRESENT(1)	ABSENT (2)
16.Cyanosis	☐	☐
17.Anaemia	☐	☐
18.Jaundice	☐	☐
19.Clubbing	☐	☐
20.Lymphadenopathy	☐	☐
21.Oedema	☐	☐

22. Height/cm ☐☐☐ . ☐

23. Weight/Kgs ☐☐☐ . ☐

24.BMI ☐☐

UYIR THATHUKKAL

VALI - ABSENT (0) NORMAL (1) DECREASED(2) INCREASED(3)

37.Uyirkkal (Pranan)

Digestion ☐ _____

38.Kizhnokkunkkal (Abanan)

Excretion of Urine ☐ _____

Excretion of Faeces ☐ _____

39.Paruvukal (Viyanan)

Blinking ☐ _____

Movement of limbs ☐ _____

40.Melnokkunkal (Uthanan)

Speech ☐ _____

Complexion ☐ _____

Hiccup ☐ _____

41.Nadukkal (Samanan)

Digestion ☐ _____

42.Nagan

Hearing ☐ _____

Intelligence ☐ _____

Closing&opening of eyelids ☐ _____

43.Koorman

Winking of eyelids ☐ _____

Yawning ☐ _____

Closing of mouth ☐ _____

44.Kirukaran

Salivary Secretions ☐ _____

Hunger ☐ _____

45.Devathathan

Occular Movements ☐ _____

Laziness ☐ _____

46. Thananjeyan

Abnormal noise (Tinnitus) ☐

in the ears ----------

Condition of Sinuses ☐

AZHAL - ABSENT(0) NORMAL (1) DECREASED(2) INCREASED(3)

47.Aakkanal (Anar pitham)

Digestion ☐ _____

48.Vannayeri (Ranjagam)

Pallor ☐ _____

49.Aattralangi (Sathagam)

Movements ☐ _____

50. Olloli Thee (Alosagam)

Complexion ☐ _____

Lustre of Skin ☐ _____

Vision ☐ _____

51.Nokkazhal (Prasagam)

Brightness of Skin ☐ _____

IYAM - ABSENT (0) NORMAL (1) DECREASED (2) INCREASED (3)

52.Aliiyam (Avalambagam)

Respiration ☐ _____

53.Neerppiyam (Kilethagam)

☐

Digestion _____

54.Suvaikanaiyam (Pothagam)

Taste ☐ _____

55.Niraivaiyam (Tharpagam)

Cooling of eyes ☐ _____

56.Ondriyaiyam (Santhigam)

Movements of joints ☐ _____

VATHAM ☐ PITHAM ☐ KABAM ☐ _____

UDAL THATHUKKAL	INCREASED(1)	DECREASED(2)
57. **SAARAM**	◯	
Indigestion	☐	
Loss of weight		☐
Tiredness		☐
Lassitude		☐
Dryness of the skin		☐
Diminished activity of sense organs		☐
58. **SENNEER**	◯	
Boils	☐	
Throbbing pain	☐	
Anoerxia	☐	
Mental disturbance	☐	
Splenomegaly	☐	
Colic pain	☐	
Increased BP	☐	
Reddish eye & skin	☐	
	☐	

Jaundice

Haematuria ☐

Anaemia ☐

Tiredness ☐

Lassitude ☐

Neuritis ☐

Pallor of body ☐

59. **OON** ◯

Cervical lymph adenitis ☐

Ulcers & Tumor ☐

Muscularity in cervical region ☐

Impairment of sense organs ☐

60. **KOZHUPPU** ◯

Dyspnoea ☐

Loss of activity ☐

Pain in hip ☐

61**. ENBU** ◯

Splitting & Falling of Hair ☐

Loosening of Teeth & Nail ☐

62. **MOOLAI** ◯

Non –healing ulcer ☐

Swollen phalanges ☐

Swollen eyes ☐

Oliguria ☐

Heaviness of body ☐

Weakness of bone

Sunken eyes

63.**SUKILAM / SURONITHAM**

Love & lust towards women/men

Urinary calculi

Failure in reproduction

Pain in genitalia

Date: _____

Signature of Doctor _____

CENTRAL COUNCIL FOR RESEARCH IN SIDDHA

MULTICENTRIC OPEN LABELED CLINICAL TRIAL ON NEERIZHIVU (DIABETES MELLITUS)

FORM III - LABORATORY INVESTIGATIONS

1. Code No.(of clinical trial) ☐

3. Centre:

3. S.No. of Patient _____

4. Name of the Patient _____

5. Address _____

_____

6. Gender Male ☐ (1) Female ☐ (2)

7. Date of Birth ☐☐ ☐☐ ☐☐ 8. Age(Yrs) ☐☐

9. Date of Assessment _____

Urine Examination
Routine

10. Sugar_____ 11.a) Albumin_____ b) Microalbumin_____

12. Deposits_____

Microscopic

13. Pus cell _____ (HPF)

14. RBC_____ (HPF)

15. Cast_____ (HPF)

Stool examination
16. Routine _____

Microscopic
17. Ova_____ 18. Cyst_____19. Occult Blood_____

Blood

20. TC(Cells/Cumm)_____

Differential Count

21. P (%) _____ 22. L(%) _____ 23. E(%) _____ 24. M(%) ____ 25.B (%) ___

26. Hb (g/dl) _____.

27. ESR (1/2 hour.) _____ ESR (1 hour.) _____

28. Blood Sugar- Fasting(mg/dl) _____

29. Blood Sugar – PP (mg/dl) _____

30. Glycated Hemoglobin (HbA1c)_____ (to be done before treatment after three months and end of treatment)

31. Blood Urea (mg/dl) _____

32. S.Creatinine (mg/dl) _____

33. Uric acid (mg/dl) _____

LIPID PROFILE

34. Serum total Cholesterol (mg/dl) _____

35. S. Triglycerides (mg/dl) _____

36. HDL(mg/dl) _____

37. LDL (mg/dl) _____

38. VLDL(mg/dl) _____

LIVER FUNCTION TESTS
Serum Bilirubin

39. Total(mg/dl) _____

40. Direct(mg/dl) _____

41. SGOT(IU/L) _____

42. SGPT (IU/L) _____

43. Alk.Phosphatase(KA units) _____

44. Total proteins (gm/dl) _____

45. Albumin (gm/dl) _____

46. Globulin (gm/dl) _____

47. A/G Ratio _____

Serum Electrolytes

48. Sodium(mEq/L) _____

49. Potassium (mEq/L) _____

Sl.No.10-49 will be done before and after treatment except Sl.No.28& 29 (Blood Sugar) which will be done before treatment and fortnightly during treatment period. HbA1c will be repeated after three months also.

Date: _____ Signature of Doctor _____

CENTRAL COUNCIL FOR RESEARCH IN SIDDHA

MULTICENTRIC OPEN LABELED CLINICAL TRIAL ON NEERIZHIVU (DIABETES MELLITUS)

FORM IV
DRUG COMPLIANCE REPORT FORM – I

(To be filled by the trial participant)

(To be issued on 1st visit – 0th day and taken back on 2nd visit – 15th day)

Registration No. of the participant _____

Name of the participant _____

Please come for next visit on..... (Date and time is to be filled by the Investigator)

Instructions to trial participant

- Please take single Capsule twice a day before food
- Please return the unused capsules along with the drug compliance report duly filled.
- Please be prepared for the blood investigations during next visit.

S.no	Date	Morning dose (around 9 AM)		Evening dose (around 8PM)	
		Please put mark after taking the Medicine	Please enter the time	Please put mark after taking the Medicine	Please enter the time
1.					
2.					
3.					
4.					
5.					
6.					

S.no	Date	Morning Dose (around 9 AM)		Evening dose (around 8PM)	
		Please put mark after taking the Medicine	Please enter the time	Please put mark after taking the Medicine	Please enter the time
7.					
8.					
9.					
10.					
11.					
12.					
13.					
14.					

Name of the Participant: _____

Date: _____

Signature or Thumb impression of the participant

Signature of the Investigator with date