Multicentric Open Clinical Study on

Azhal Keel Vayu

[Osteo arthritis- Knee Joint]

CENTRAL COUNCIL FOR RESEARCH IN SIDDHA
Chennai

CLINICAL PROTOCOL: Summary Information

Study title:

Clinical evaluation of coded drug *OA- 1 Churnam* and *xxx in* the management of *Azhal Keel Vayu* - Osteo arthritis (Knee joints).

Phase of clinical investigation: Phase – 2

Investigational drug(s):

1. OA-1 Churnam – Oral administration

2. xxx - External application

Sponsor:

CCRS, Chennai

Study Monitor:
CCRS, Chennai

Study Centers:
Peripheral Institutes of CCRS

Team Leader:

Study Investigator(s):

Clinical Laboratory (ies), Technical Department(s), and Institution(s) Providing Clinical &

other Study Services:

Clinical Protocol

1. Introduction:

1.1 Background:

Siddha System of medicine has broadly classified the joint diseases. *Azhal Keel Vayu* is one among them. *Azhal Keel Vayu* or *Pitha Keel Vayu* is often referred and correlated to Osteo arthritis by its symptomatic relevance. An old poem insists this disease pattern as follows,

அழல் கீல்வாயு

"பித்தக்கீல் வாய்வு தள்ளாற்
பிறங்குகீள் மூட்டு வீங்கிச்
சித்தஞ்செய் மருத்து வத்துஞ்
சீபடாத் தள்ளைத் தாகித்
தத்தறு காய்ச்சல் கண்டு
சாலவே தளைதாள் தந்தே
மெத்தறு சிகிச்சை தள்ளால்
மெள்ளமல் நீங்கு மப்பா."

- சபாபதி கைவியடு

Sabapathi Kaiyedu, a Traditional text, states that *Pitha Keel Vayu*[15] is a condition in which the articular joints swell and later become very difficult to treat which is accompanied with fever and pain. And moreover this condition may be resolved with a kind

of good treatment. This clinical condition can be well correlated with Osteo arthritis of Knee joints.

Osteo arthritis is one of the most prevalent articular disorders affecting human kind and a major cause of disability and socio economic burden, [2]. Osteo arthritis is a chronic degenerative disorder of multifactorial aetiology, including acute and / or chronic insults from normal wear and tear, age, obesity and joint injury[3, 4]. Osteo arthritis is characterised by the degradation of the articulate cartilage resulting in an alteration of its biochemical properties[5].

There is higher prevalence of Osteo arthritis with advanced age and in females[6, 7].Regarding prevalence of Osteo arthritis with estimates of 7.2% in those of age 40 or older[8], 12.5% in those aged over 45[9] and 14.8% in those aged 50 or older[10]. Drug therapy includes non-opioid analgesics such as paracetamol non-steroidal anti-inflammatory drugs (NSAIDS). Topical analgesics, opioid analgesics and intra-articular steroid injections. Such treatment may prove ineffective in some patients and NSAIDS often have serious adverse effects.[11, 12] Gastro intestinal complications are frequently reported with NSAIDS. Hence, there appears to be a need for drugs with good efficiency and toxic free in the treatment of OA. Specifically there is a need for safe and effective medicine for patients with OA.

1.2

Rationale:

The existing current drug therapy includes non - opioid analgesics such as paracetamol non- steroidal anti-inflammatory drugs (NSAIDS).Topical analgesics, Opioid analgesics and intra- articular steroid injections. Such treatment may prove ineffective in some patients and NSAIDS often have serious adverse effects.[2, 3] Gastro intestinal complications are frequently reported with NSAIDS.

Hence, there appears to be a need for drugs with good efficacy and toxic free in the treatment of OA. Specifically there is a need for safe and effective medicine for patients with OA. Many Siddha medicines are indicated for *Azhal Keel Vayu*. The New drug application, Coded Siddha drug *OA-1 Churnam* and *xxx* are selected for this clinical condition. As the drug falls under NCE, it is subjected for, Acute/Sub acute/Chronic

toxicity. It is approved in IAEC to continue the same. The Anti-inflammatory and Analgesic activity will be carried over for the above said drug. After obtaining the Pre Clinical results the drugs will be put into Clinical trial. The dosage will be 2g bid with honey two times after food for a period of 60 days.

2. Clinical Study Objectives:

2.1 Primary objective:

Clinical Evaluation of *OA-1 Churnam* & *xxx by* measuring the WOMAC Index.

2.2 Secondary objectives:

Evaluation of the safety of the drugs *OA-1Churnam* & *xxx*

3. Study Design:

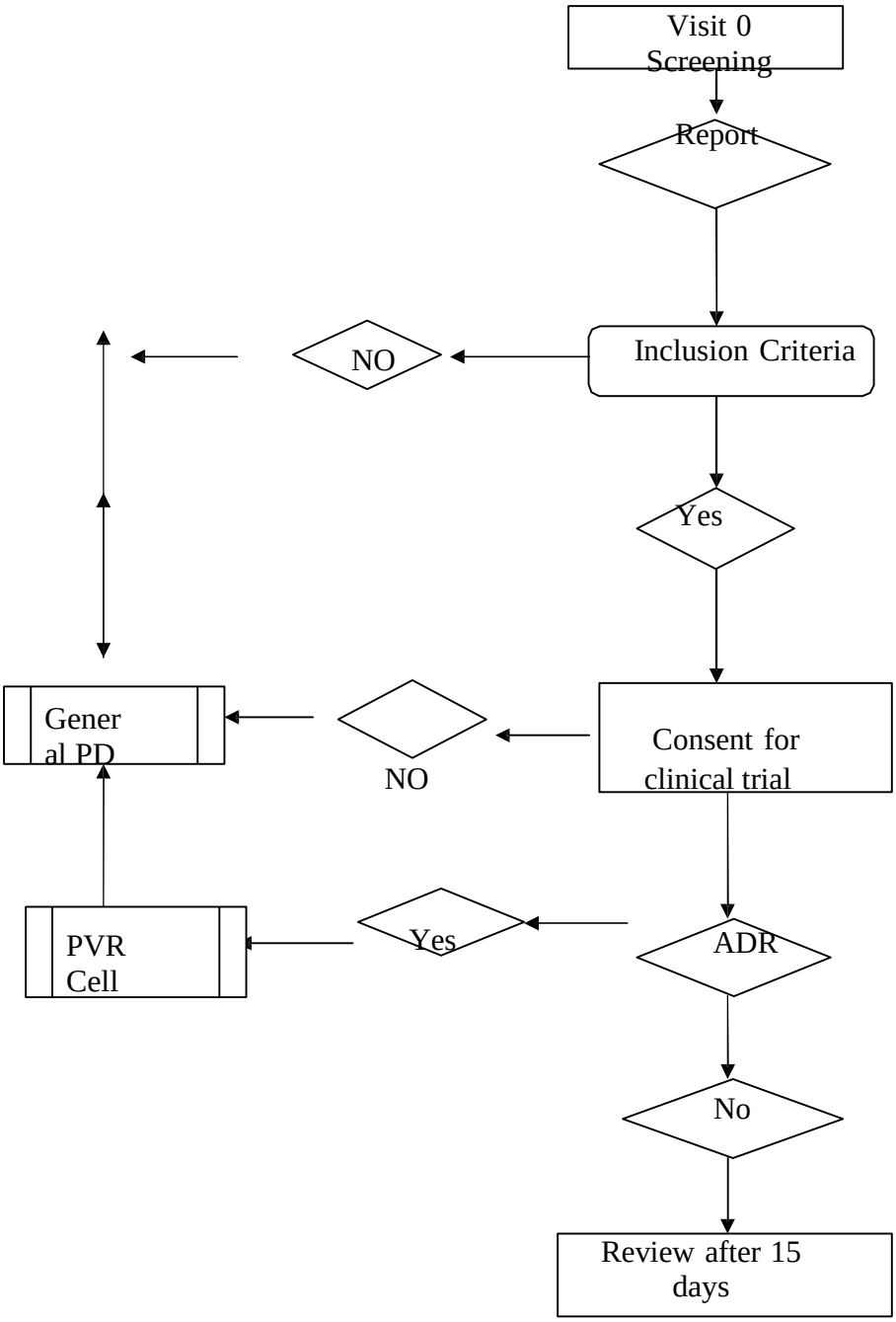
Type of study: Multi centric Open Clinical trial

Sample size : 40 subjects for each centre.

Duration of subject participation: 60 days.

Study period: 1 Year

3.1 Study design schematic:



4. Subject Selection:

4.1 Subject inclusion criteria:

1. Age between 45 years to 60 years
2. Patients with Primary Osteo arthritis (Knee joints) Single or Both
3. Symptoms of OA over a period of at least six months
4. Crepitations & Swelling felt over the affected Knee joints
5. Morning stiffness of the Knee joints
6. Involvement of Knee Joints with / without other major / minor joints
7. Difficulty in walking / climbing stairs
8. X-ray findings

4.2 Subject exclusion criteria

1. Age less than 45 years or more than 60 years
2. Patients with systemic conditions such as Gouty arthritis, Rheumatoid arthritis, Psoriatic arthritis, SLE. [will be excluded by the past medical history and the current medication]
3. Patients with Diabetes mellitus / Hypertension
4. Bed ridden patients
5. Patients using anti-inflammatory medicine other than Research drugs
6. Patients taking active Allopathy / Homeopathic Treatment
7. Low back ache with or without radiation to legs
8. Patients with metallic implants
9. Subjects having any deformity of Knee or Hip
10. History of bony or soft tissue injury to Knee joints

Study Drug(s):

1. OA-1 Churnam - 2g bid – Oral administration

2. xxx - External application

CRITERIA FOR WITHDRAWAL

During the course of the trial if any adverse condition develops which requires emergency treatment, such subject may be withdrawn from the trial and managed by the principal investigator accordingly and new subjects will be recruited for the study.

ROUTINE EXAMINATION AND ASSESSMENT

The full details of the history and physical examination of the patient will be recorded as per the Proforma. Clinical assessment will be made on 0 day, 15^{th}, 30^{th}, 45^{th} and 60^{th} day. Laboratory investigations will be recorded before and after treatment, followed by clinical follow up without drug during 3^{rd} & 4^{th} month.

CLINICAL ASSESSMENT

Clinical assessment will be made by the WOMAC index chart for OA-Knee joints as mentioned in the case record form. The results will be categorized according to the variation in the score before and after treatment.

Primary endpoints

1. The decrease in WOMAC Index Score and symptomatic relief as recorded in the proforma.

Secondary endpoints:

1. Evaluating safety parameters - LFT & RFT.

References:

1. Jackson BD, Wluka AE, Teichtahl AJ, et al. Reviewing knee Osteo arthritis – a biomechanical perspective. J Sci Med Sport. 2004; 7(3):347–357.
2. Wu CW, Kalunian KC. New developments in Osteo arthritis . Clin Geriatr Med. 2005;21(3):589–601.
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7. Zhang Y, Xu L, Nevitt MC, et al. Comparison of the prevalence of knee Osteo arthritis between the elderly Chinese population in Beijing and whites in the United States: The Beijing OA Study. Arthritis Rheum. 2001;44(9):2065–2071.
8. Du H, Chen SL, Bao CD, et al. Prevalence and risk factors of knee Osteo arthritis in Huang-Pu District, Shanghai, China. Rheumatol Int. 2005;25(8):585–590.
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CENTRAL COUNCIL FOR RESEARCH IN SIDDHA

Multicentric Open Clinical Study on *Azhal Keel Vayu* (Osteo arthritis – Knee joints) Case Report Form I – SCREENING PROFORMA

(Please tick wherever applicable)

1. Code No ____ Level of study OPD/IPD

2. Subject No ____

3. Name of the Patient _____

Address:

Phone no:

4. Gender Male Female

5. Age _____ Yrs

6. Date of Assessment_____

CRITERIA FOR INCLUSION: **Yes** **No**

1. Age between 45 years to 60 years
2. Patients with Primary Osteo arthritis (Knee joints) Single or Both
3. Symptoms of OA over a period of at least six months
4. Crepitations felt over the affected Knee joints
5. Morning stiffness of the Knee joints
6. Involvement of Knee Joints with / without other major / minor joints
7. Difficulty in walking / Climbing stairs
8. X-ray findings

CRITERIA FOR EXCLUSION:

9. Age less than 45 years or more than 60 years
10. Patients with systemic conditions such as Gouty arthritis, Rheumatoid arthritis, Psoriatic arthritis,SLE.
11. Patients with Diabetes mellitus / Hypertension
12. Bed ridden patients
13. Patients using anti-inflammatory medicine other than Research drugs
14. Patients taking active Allopathy / Homeopathic
15. Low back ache with or without radiation to legs
16. Patients with metallic implants
17. Subjects having any deformity of Knee or Hip
18. History of bony or soft tissue injury to Knee joints

A patient is eligible for admission if Serial number 1- 3 are Yes; among Serial number 4-8 at least two must be Yes and Serial number 9-18 are No.

Date: Signature of Investigator /Co Investigator

CENTRAL COUNCIL FOR RESEARCH IN SIDDHA

Multicentric Open Clinical Study on *Azhal Keel Vayu* (Osteo arthritis – Knee joints) Case Report Form II - HISTORY PROFORMA

(Please tick wherever applicable)

1. Code No ____ Level of study OPD/IPD
2. Subject No ____
3. Name of the Patient_____

   Address:

   Phone no:

4. Gender Male Female

5. Age _____Yrs

6. Date of Assessment_____

7. Educational status:

Illiterate Read & Write Middle school High school College

Others (Specify)

8. Occupation:

a) Desk work b) Field work

c) Field work with physical Labour

d) Field work with intellectual acumen

e) Constant sitting /standing for long hour f) Home Maker

g) Others, please specify:

9. Family income per month in Rupees

10. Total family members

11. Marital status Single Married Separated Widow Widower

12. History of Present illness:

Onset of the disease: Acute Insidious

Duration of the disease [in months] _____

Factors aggravating the disease / Chief complaints _____

Factors relieving / Chief complaints _____

History of Past illness, related with present illness: Yes / No

if yes, specify_____

13. History of Past illness

History of trauma / Injury Yes / No

If yes, specify_____

Undergone treatment before Yes / No

14. a) Personal history

Diet: Veg / Non veg

Addiction: Smoking / Alcohol / Tobacco chewing

b) Udaliyal (Prakriti)

S.No	Vali		Azhal		Iyam	
1.	Lean Built		Medium built		Stout/Well built	
2.	Less Strength		Medium Strength		Good Strength	
3.	Dry Body		Excessive sweating		Oily Body	
4	Dry and Dark skin		Pinkish or yellowish		Fair, Soft & smooth skin	
5.	Scanty and Brown hair		Early graying and		Black and thick hair	
6	Fickle minded		Short tempered		Steady and patient	
7	Irregular appetite and thirst		Excessive appetite and thirst		Normal appetite and thirst	
8	Constipate tendency		Frequent and large		Normal steady bowel	
9	Disturbed Sleep		Average sleep		Sound deep sleep	

Vali Azhal Iyam Thontham

Chief complaints with duration:

15. Pain:

Name of joints

Increased by exertion	Yes	No
Relieved by taking rest	Yes	No
Pain at rest	Yes	No
Radiating to other parts	Yes	No

16. Stiffness:

Name of joints involved: Duration:

Morning stiffness	Yes	No
Lasting for an hour or so	Yes	No

17. Swelling:

Name of joints involved:

Duration:

18. Restricted movements:

Name of joints involved:

Duration:

Crepitus: Yes / No

Duration:

19. Variation in pain

Climate

Season

Day / Night

Rest / Movement

Walking /

Exertion Other

relations any

20. General examination of the patient:

a) Febrile / Afebrile

: b) Height

: c) W e i g h t

:

d) Pallor : Present

Absent e) Icterus : Present

Absent f) Oedema : Present

Absent g) Clubbing : Present

Absent h) Cyanosis : Present

Absent i) Lymphadenopathy : Present

Absent j) Pigmentation : Present

Absent k) Deformity : Present

Absent l) Pulse rate __

m) Respiratory rate _____

n) Blood pressure _____

21. Systemic examination of the patient

a) Gastro intestinal system : Normal Abnormal

If abnormal, specify_____

b) Cardio vascular system : Normal Abnormal

If abnormal, specify_____

c) Respiratory system : Normal Abnormal

If abnormal, specify_____

d) Central nervous system : Normal Abnormal

If abnormal, specify_____

e) Genito urinary system : Normal Abnormal

If abnormal, specify_____

f) Reticulo endothelial system : Normal Abnormal

If abnormal, specify_____

22. Seven Udal Thaathukkal

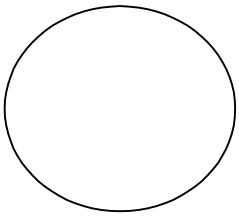
Saaram :
Senneer :
Oon :
Kozhuppu :
Enbu :
Moolai :
Sukkilam / Suronitham :

23. Enn Vagai Thervu

Naadi :
Sparisam :
Naa :
Niram :
Mozhi :
Vizhi :
Malam :
Moothiram :

a) Neerkuri
   Niram
   Nirai
   Mana
   m
   Enjal

b) Neikuri



Date: Signature of Investigator/Co Investigator

CENTRAL COUNCIL FOR RESEARCH IN SIDDHA

Multicentric Open Clinical Study on *Azhal Keel Vayu*(Osteo arthritis – Knee joints) Case Report Form III - LABORATORY INVESTIGATIONS

1. Code No ____ Level of study OPD/IPD
2. Subject No ____
3. Name of the Patient_____

   Address:

   Phone no:
4. Gender Male Female
5. Age _____Yrs

S.No	Parameters	Status	Before Treatment	After Treatment	Follow up	
					1 M	2 M
VITAL BLOOD PARAMETERS						
1.	R.A Factor	Positive				
		Negative				
2.	Uric acid					
3.	A.S.L.O. Titer	Positive				
		Negative				
4.	C.R.P	Positive				
		Negative				
5.	LFT					
6.	RFT					

URINE

1.	Albumin					
2.	Sugar	Fasting				
		PP				
3.	Deposits					

STOOLS

1.	Ova				
2.	Cysts				
3.	Occult blood				

Other Blood Parameters

1.	TC				
2.	DC				
3.	Hb gms/%				
4.	ESR 30 mts 60 mts				
5.	Blood Sugar – Fasting				
	PP				
6.	S. Cholesterol				
7.	B. Urea				
8.	S. Creatinine				
9.	VDRL				

X-Ray Findings:

Any other investigations_____

Date: Signature of Investigator/Co Investigator

CENTRAL COUNCIL FOR RESEARCH IN SIDDHA

Multicentric Open Clinical Study on *Azhal Keel Vayu* (Osteo arthritis – Knee joints) *CASE RECORD FORM IV – CLINICAL ASSESSMENT*

1. Code No ____ Level of study OPD/IPD

2. Subject No ____

3. Name of the Patient_____

Address:

Phone no:

4. Gender Male Female

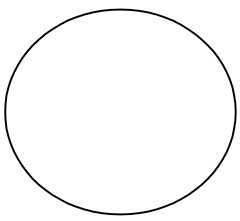
5. Age _____Yrs

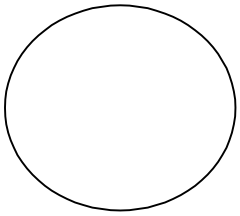
MEASUREMENT OF THE JOINTS

Joints	Side	Swelling (cms)	
		Before treatment (Date:)	After treatment (Date:)
Knee	Right		
	Left		

Note: Swelling is measured by means of a Non Elastic inch tape.

NEIKURI **Before treatment** **After treatment**





WOMAC OSTEO ARTHRITIS INDEX (Please tick wherever applicable)

Symptoms	**Before Treatment** (Date:)					**After Treatment** (Date:)				
	0	1	2	3	4	0	1	2	3	4
Pain										
(1) Walking										
(2) Stair climbing										
(3) Nocturnal										
(4) Rest										
(5) Weight bearing										
Stiffness:										
(1) Morning stiffness										
(2) Stiffness occurring later in the day										
Physical function:										
(1) Descending stairs										
(2) Ascending stairs										
(3) Rising from sitting										
(4) Standing										
(5) Bending to floor										
(6) Walking on flat										
(7) Getting in or out of car										
(8) Going shopping										
(9) Putting on socks										
(10) Rising from bed										
(11) Taking off socks										
(12) Lying in bed										
(13) Getting in or out of bath										
(14) Sitting										
(15) Getting on or off toilet										
(16) Heavy domestic duties										
(17) Light domestic duties										
Total										

Points – Response: 0 –None; 1 –Slight; 2- Moderate; 3- Severe; 4- Extreme

Date:

Signature of Investigator/Co Investigator

WOMAC OSTEO ARTHRITIS INDEX (Please tick wherever applicable)

Symptoms	**Follow**									
	1 Month (Date:					**2 Month** (Date:				)
	0	1	2	3	4	0	1	2	3	4
Pain										
(1) Walking										
(2) Stair climbing										
(3) Nocturnal										
(4) Rest										
(5) Weight bearing										
Stiffness:										
(1) Morning stiffness										
(2) Stiffness occurring later in the day										
Physical function:										
(1) Descending stairs										
(2) Ascending stairs										
(3) Rising from sitting										
(4) Standing										
(5) Bending to floor										
(6) Walking on flat										
(7) Getting in or out of car										
(8) Going shopping										
(9) Putting on socks										
(10) Rising from bed										
(11) Taking off socks										
(12) Lying in bed										
(13) Getting in or out of bath										
(14) Sitting										
(15) Getting on or off toilet										
(16) Heavy domestic duties										
(17) Light domestic duties										
Total										

Points – Response: 0 –None; 1 –Slight; 2- Moderate; 3- Severe; 4- Extreme

Date: Signature of Investigator/Co Investigator

Clinical Assessment

	Assessment	**Before Treatment** (Date:)	**After treatment** (Date:)
1.	Pain score		
2.	Stiffness score		
3.	Physical function		
4.	Joint measurement for Swelling		

Follow up

	Assessment	**1 Month** (Date:)	**2 Month** (Date:)
1.	Pain score		
2.	Stiffness score		
3.	Physical function		
4.	Joint measurement for Swelling		

Date: Signature of Investigator /Co Investigator

CENTRAL COUNCIL FOR RESEARCH IN SIDDHA

Multicentric Open Clinical Study on *Azhal Keel Vayu* (Osteo arthritis – Knee joints) Patient Information Sheet

Study investigators: Site of investigation:

Contact number:

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. 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?

This study is done to assess the efficacy of ***OA-1 Churnam & xxx*** in the treatment of Azhal Keel Vayu (Osteo Arthritis – Knee joints). A total of 40 patients suffering with Azhal Keel Vayu like you 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 strictly. If you are eligible for the study you are expected to visit the hospital every15 days. The study will take approximately four months to complete. Before you start treatment, during the first visit to the clinic, you will undergo a complete physical examination, Blood and urine samples, X-Ray Investigation will also be taken. This is to make sure that you are eligible for the study.

What happens at the end of the study?

The trial treatment will be stopped at the end of 60 days. You will be referred to the General OPD.

Are there any risk?

If the trial drug cause any adverse effect it has to be reported to the doctor.

What are the alternatives?

Your doctor will be pleased to explain to you the available alternative treatment.

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.

What is the cost of the study?

All medications 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 asked to sign a consent form saying that you have been given information sheet about the study and you voluntarily agree to take part. It is important to follow all instruction 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 to 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.

Is there any other additional information regarding this trial?

If you have any questions regarding the research study related or if you need emergency medical treatment while you 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

CENTRAL COUNCIL FOR RESEARCH IN

SIDDHA Multicentric Open Clinical Study on

***Azhal Keel Vayu* (Osteo arthritis – Knee joints)**

DRUG COMPLIANCE FORM – 1st visit

1. Center: _____ _
2. S.No. of the patient: _____
3. Name of the patient: _____ _
4. Sex:Male ☐ Female ☐

Instructions:

1. Please take 2 gm of the medicine twice a day after food.
2. Please come for the next visit on _____

Day	Date	Morning		Evening	
		Please after taking the medicine.	Time	Please after taking the medicine	Time
1.					
2.					
3.					
4.					
5.					
6.					
7.					
8.					
9.					
10.					
11.					
12.					
13.					
14.					
15.					

Date _____
:

Signature / Thumb impression of patient

CENTRAL COUNCIL FOR RESEARCH IN

SIDDHA Multicentric Open Clinical Study on

***Azhal Keel Vayu* (Osteo arthritis – Knee joints)**

FORM V - PATIENT CONSENT FORM

I ----------S/o-H/o---------

Aged ---------years residing at----------

---------- agree and exercising my free power of choice, hereby give my consent to be included as a subject in the clinical trial of ***Azhal Keel Vayu* (Osteo arthritis – Knee joints)** which is to be conducted at CCRS centre

I understand that I may be treated with Herbal /Metal / Herbo - mineral preparation of Siddha system of medicines for the disease. I am suffering from ----------

----------I have been informed to my satisfaction by the attending physician about the purpose of clinical trial, the nature of drug treatment and follow up including the laboratory investigations to monitor and safe guard my body function. The consent, which I am giving to participate, is out of my own interest with my knowledge and full consciousness and after studying the patient information sheet given to me by the investigator and after full clarification of all my doubts. I also state that the consent is not given out of any undue influence or any other measures.

Signature / Thumb impression of the patient.

Date: Signature of Investigator/Co Investigator: