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Research Article

Clinical Evaluation Of Siddha Mono-Herbal Formulation *Oorithal Thaamarai Chooranam*: A Prospective, Open-Labelled, Single-Armed, Non-Randomized, Phase-II Clinical Trial In The Management Of *Madhumegatthal Parutha Udal* (Diabetic Dyslipidemia)

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ABSTRACT

Background: Diabetes mellitus is a major metabolic disorder affecting millions worldwide, with the WHO predicting that by 2025, 75% of 300 million adults with diabetes will reside in developing countries. The Siddha Materia Medica, Plant Division, identifies *Oorithal Thaamarai Chooranam* (Hybanthus ennaspermus (L) F.Muell. whole plant powder) as a traditional remedy specifically indicated for *Madhumegatthal Parutha Udal* (Diabetic dyslipidemia). Previous studies confirm the drug's safety and its anti-diabetic, hepatoprotective, antioxidant and hypolipidemic properties.

Objective: This study aimed to evaluate the therapeutic efficacy of *Oorithal Thaamarai Chooranam* for managing *Madhumegatthal Parutha Udal* (Diabetic dyslipidemia).

Materials and Methods: Conducted as a prospective, open-label, non-randomized clinical trial over 18 months (November 2019 to April 2021) at Government Siddha Medical College, Tamil Nadu, 60 participants were recruited post-CTRI registration. The trial drug (25 mg/kg body weight) was administered orally twice daily for 90 days. Laboratory tests and assessments were conducted at baseline and after 30 days. No adverse effects was observed.

Results: Statistical analysis using SPSS showed a highly significant improvement in patients' diabetic dyslipidemia grades, with a calculated t-value of 41.974 and a p-value <0.01, indicating strong treatment efficacy as well as the null hypothesis had rejected concerning assessment parameters. There are significant differences between these parameters before and after treatment.

Conclusion: This clinical trial demonstrates that *Oorithal Thaamarai Chooranam* is a safe, effective and cost-efficient herbal formulation for treating diabetic dyslipidemia.

Keywords: Diabetic dyslipdemia, clinical trial, *parutha udal*, *oorithalthaamarai chooranam*,siddha medicine.

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INTRODUCTION

Diabetes mellitus is one of the most prevalent and serious metabolic diseases in the world which is predicted to increase dramatically (Hill *et al*, 2024). It is frequently associated with long-term complications with macro vascular and micro vascular origin (Banday *et al*, 2020). Atherosclerotic Cardiovascular Disease (ASCVD) is the commonest cause of death in the United States and Western world. Diabetes is a significant risk factor for ASCVD and it is the leading cause of mortality (Brown *et al*, 2024)

Diabetic patients are 2-4 times more likely to die from ASCVD as compared to non-diabetic patients (Bertoluci *et al*,2017). Dyslipidemia in diabetes is common and is characterized by hypertriglyceridemia (HTG) with decreased levels of high density lipoprotein (HDL) whilst low density lipoprotein (LDL) levels are usually not elevated there is a preponderance of small dense LDL particles which appear to be more atherogenic [Feingold *et al*, 2023). Furthermore there is an increase in apolipoprotein B levels and non-HDL–cholesterol levels. The two major sequelae of diabetic dyslipidemia are premature ASCVD from the elevated apolipoprotein B carrying particles and pancreatitis with severe HTG > 1000mg/dl (Yun ym *et al*, 2022).

Apart from classical risk factors like diabetic dyslipidemia, elevated HbA1c has now been identified as an independent risk factor for cardiovascular disease in subjects with or without diabetes. Estimated risk of cardiovascular disease has shown to be increased by 18% for each 1% increase in absolute HbA1c value in diabetic population (Kidwai *et al*, 2020).

This clinical trial was an attempt to reassess the association of glycemic control and lipid profile using HbA1c whiles taking into consideration some of the factors affecting its use. This study was also afford health care providers attending to diabetic patients, the needed information as to when to use HbA1c in clinical monitoring of glycation and diabetic dyslipidemia

Our Siddha ancestors elaborated the knowledge about *Madhumegam* which can be clinically correlated with the symptoms of Diabetes mellitus. Siddhar *Theraiyar* in the classical Siddha textbook *Therankarisal*, he has mentioned the classification about the diseases of the urinary system into two major categories of *Neerinaiperukkal noikal* (diseases with excessive urinary output) and *Neerinaiarukkal noikal* (diseases with decreased urinary output) (Shanmugavelu *et al,2010*).

According to another Siddha classical textbook, *Noi nadal Noi MudhalNaadal* Part-1, the diseases of urinary output was classified according to frequency,specific gravity and frothy urination. *Madhumegam* (Diabetes mellitus) comes under *Neerinaiperukkal noikal* (diseases with excessive urinary output), according to clinical symptoms, pulse and eight type of diagnostic tools of siddha has been made and also the severity of diseases (Saambasivam pillai *et al,1977*).

With this background, I have selected the disease *Madhumegatthal Parutha Udal* (Diabetic dyslipidemia) for this clinical trial. The purpose of the interventional study was to assess the trial drug's effectiveness on *Madhumegatthal Parutha Udal* (Diabetic dyslipidemia) by using clinical parameters to assess the condition's symptoms and prognosis. After a deep review of the Siddha literature, the following medicine had carefully chosen for the study as the trial medicine because of its easy availability and cost-effectiveness.

*Oorithal Thaamarai Chooranam*is a mono-herbal Siddha formulation mentioned in the classical Siddha literature "*GunapadamMooligaiMuthalPaakam – Mooligai Vaguppu* which the drug had been chosen to study its efficacy in the management of *Madhumegatthal Parutha Udal* (Diabetic dyslipidemia) (Murugesa muthaliyar *et al*,2006).

MATERIALS AND METHODS

Pre-Clinical Data: Toxicological (acute and sub-acute) and pharmacological studies (hypoglycemic, hypolipidemic and anti – oxidant) were done.

IEC & IAEC approval and Clinical trial registration: Firstly, the study received approval from the Institutional Ethical Committee (IEC) with the approval number GSMC-V-IEC/2019/BR I-1/09.04.2019. Animal studies approved by the Institutional Animal Ethics Committee (IAEC) of Arulmigu Kalasalingam College of Pharmacy, Krishnankoil, Srivilliputur under the approval number of AKCP/IAEC/38/20-21. Finally, before giving the intervention to the patients, the study was registered and got approval from the Clinical Trials Registry – India (CTRI) with the registration number CTRI/2021/01/030756.

Study design, place, duration and the trial drug: The study was a prospective, open-label, single-arm, non-randomized phase II clinical trial. Conducted over 18

months (November 1, 2019 – April 30, 2021) at the Government Siddha Medical College and Hospital, Palayamkottai, Tamil Nadu, India, it included 60 patients (30 outpatients and 30 inpatients). Participants received the trial drug, *Oorithal Thaamarai Chooranam*, at a dose of 25 mg/kg body weight, administered orally twice a day after food for 90 days, with water as an adjuvant.

Recruitment of the patients: Trial eligibility were based on cases presenting with symptoms fulfilling the inclusion criteria. The patient gave their consent in advance before beginning the investigation.

Conduct of the Study: The study included individuals who were either newly diagnosed with *Madhumegatthal Parutha Udal* (Diabetic dyslipidemia)or had a previous diagnosis, regardless of whether they were receiving treatment. Participants were required to provide written informed consent. Before administering the trial medication, the study's purpose was explained to them. Information on the patient's demographics, lifestyle, anthropometric measurements, and Siddha parameters was collected before beginning the treatment. A total of 60 patients, both male and female, aged 15 to 60, were selected for the study. These patients received the trial drug for the entire duration of the study, which lasted 90 days.

Selection of the Patients: On screening, the patients presenting with symptoms that met the inclusion criteria at the outpatient department of the Post Graduate, Department of *Pothu Maruthuvam* at GSMC, Palayamkottai, underwent a screening test, with results documented on a screening proforma. On screening, the patients had the specification points in exclusion criteria were not included. Information such as personal history, family history, occupation, habits, clinical symptoms, medical history, and the duration of illness was recorded for all patients. Among 60 patients, 30 were treated in outpatient department and the other 30 patients were admitted and treated in inpatient department, during the study period.

a) Inclusion Criteria:

1.Age between 40 and 59 years

2.Type-II Diabetes mellitus
If yes in any of three, FBS - > 126 mg/dl or PPBS - > 200mg/dl or HbA1c > 6.5 and<10 (ADA 2017).

3.Total cholesterol - >199 mg/dl or LDL - >159 mg/ dl or Triglycerides - >150 mg/dl or HDL level - < 60 mg /dl

4.Willing to give blood sample for the Lab investigations.

b) Exclusion Criteria

1. Age below 40 and above 60
2. If yes in any one of three

FBS - < 125 mg/dl or PPBS - <199mg/dl or HbA1c< 6.5 lipid profile has values of, Total cholesterol <199 mg/dl or LDL<159 mg/ dl or Triglycerides <150 mg/dl

3. Type-I Diabetes mellitus
4. Secondary hypertension
5. Pregnant woman
6. Lactating mother
7. Chronic kidney disease / Renal failure
8. Corticosteroid therapy
9. Chronic active viral hepatitis/cirrhosis/ascites.

c) Withdrawal Criteria

Patients were withdrawn from the study if they developed an intolerance to the drug, experienced adverse reactions during the trial, demonstrated poor compliance or defaulted, became unwilling to continue, or developed any serious illness.

Adverse Effect / Serious Effect Management: During the trial, no patients experienced adverse reactions. If any adverse reaction had occurred, the patient would be withdrawn from the trial immediately, and receive appropriate management at the OPD of Government Siddha Medical College and Hospital, Palayamkottai, and the incident would be reported to the pharmacovigilance committee.

Diagnosis: The diagnostic procedures included in this study comprised tests and assessments for clinical evaluation and routine investigations specific to Diabetic dyslipidemia.

a) Clinical Assessment: Evaluation visits were conducted at baseline and after 90 days. Treatment efficacy was assessed by measuring changes in signs and symptoms.

b) Routine Investigations: Investigations conducted before treatment and on the 90th day included:

1. Blood analysis: Hb (gm/dl), total WBC count (cells/cu mm), DC (polymorphs, lymphocytes, eosinophils, monocytes, basophils), total RBC count (million cells/cu mm), ESR (mm/hour), fasting blood glucose (mg/dl), postprandial glucose (mg/dl), blood urea (mg/dl) and blood creatinine (mg/dl)
2. Urine analysis: sugar, albumin, deposits.
3. HbA1c, Lipid profile.

c) Specific Investigations: The prognosis is deemed good after treatment if the value of HbA1c decreases below 5.7% from the time of admission and FBS - < 125 mg/dl or PPBS - <199mg/dl or HbA1c < 6.5 lipid profile has values of Total cholesterol <199 mg/dl or LDL<159 mg/ dl or Triglycerides <150 mg/dl . It is considered moderate if the HbA1c value ranges between 5.7% to 6.4%. The prognosis is regarded as poor if there is no change in the HbA1c value or if it increases more than 6.5%.

Data collection: The necessary information from each patient was collected using a variety of forms, including screening and selection proforma, history taking proforma on enrollment, clinical assessment proforma, laboratory investigation proforma, informed consent form in English and Tamil, withdrawal form, patient information sheet, advice form, adverse drug reaction form, drug compliance form, and discharge proforma.

Data Management: After enrolling the patients for the study, a distinct file was maintained for each patient, housing all requisite forms. Study numbers and patient identity numbers were recorded at the top of each file for streamlined identification purposes. During the study

period, whenever study patients visited the outpatient department (OPD) or were admitted to the inpatient department (IPD), necessary entries were diligently made in the assessment form, with screening forms filled out separately. Monitoring of data recordings and any potential adverse events was conducted by the Head of Department (HOD) and the pharmacovigilance committee. Furthermore, all forms underwent thorough scrutiny by the Research Officer (Statistics) to detect logical errors and ensure completeness of data, thereby mitigating any potential bias. No alterations to the results were permitted to maintain the integrity of the reports.

ASSESSMENT OF OUTCOME

a) Primary outcome – assessment: The primary outcome was evaluated by comparing the reduction of identifiedHbA1c values and comparing various parameters before and after treatment, including fasting and post prandial blood glucose (mg/dl), Lipid profile during clinical assessment before and after treatment.

b) Secondary outcome – assessment: The secondary outcome primarily involved evaluating the pre and post-treatment in case of Body Mass Index(BMI).

Statistical Analysis of Data: The significance of the difference in mean scores between the baseline and final screening was assessed through both the paired "t" test and the Pearson Correlation test. All analyses were conducted using the software SPSS 20.0 (IBM). All the derived data from the analysis were presented as means and standard deviations. A probability value below 0.05 was deemed statistically significant.

OBSERVATIONS

The study population possessed a wide range of demographic and clinical characteristics such as , Participants varied in age as shown in Table 1 and gender in Table 2,multiple religious backgrounds in Table 3 and educational levels in Table 4.Occasionally, occupation and socio-economic levels shown in Table 5 and Table 6. Dietary habits, duration of illness and BMI of participants as detailed in Table 7,8 and 9. Family history and clinical manifestations among study population provided in Table 10 and 11.

Table 1. Age distribution among study population

Sl. No.	Age group (In years)	Out Patients		In Patients	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	40	02	6.67%	01	3.33%
2.	41-50	10	33.33%	05	16.67%
3.	51-60	18	60%	24	80%

Table 2. Gender distribution among study population

	Sex	Out Patients		In Patients	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Male	18	60%	12	40%
2.	Female	12	40%	18	60%

Table 3. Religion distribution among study population

Sl. No.	Religion	Out Patients		In Patients	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Hindu	23	76.67%	27	90%
2.	Christian	3	10%	3	10%
3.	Muslim	4	13.33%	-	-

Table 4.Educational status distribution among study population

Sl. No.	Educational Status	Out Patients		In Patients	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Illiterate	10	33.33%	15	50%
2.	Read & Write	5	16.67%	-	-
3.	Primary	5	16.67%	5	16.67%
4.	Middle School	-	-	-	-
5.	High School	5	16.67%	5	16.67%
6.	College	5	16.67%	5	16.67%
7.	Others	-	-	-	-

Table 5. Occupational status distribution among study population

Sl. No.	Occupation	Out Patients		In Patients	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Business	2	6.67%	5	16.67%
2.	Agricultural Labours	2	6.67%	-	-
3.	House wife	3	10%	5	16.67%
4.	Cook	3	10%	2	6.67%
5.	Painter	5	16.67%	-	-
6.	Policeman/Army	-	-	-	-
7.	Office worker	2	6.67%	3	10%
8.	Coolie Worker	10	33.33%	10	33.33%
9.	Driver	3	10%	5	16.67
10.	Welding worker	-	-	-	-

Table 6. Socio-economic status distribution among study population

Sl. No.	Socio-Economical Status	Out Patients		In Patients	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Upper High	-	-	-	-
2.	High	2	6.67%	1	3.33%
3.	Upper Middle	2	6.67%	3	10%
4.	Lower Middle	6	20%	6	20%
5.	Poor	10	33.33%	10	33.33%
6.	Very Poor or Below Poverty Line	10	33.33%	10	33.33%

Table 7. Dietary habits distribution among study population

Sl. No.	Personal History	Out Patients		In Patients	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Vegetarian	5	16.67%	6	20%
	Non Veg	-	-	-	-
	Mixed Diet	25	83.33%	24	80%

Table 8. Duration of the illness distribution among study population

Sl. No.	Duration of illness	Out Patients		In Patients	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	6 months -2 Years	15	50%	12	40%
2.	2Years - 4 Years	07	23.33%	11	36.67%
3.	4 Years - 6 Years	08	26.67%	07	23.33%

Table 9. BMI distribution among study population

Sl. No.	Body Mass Index in kg/m^2	Out Patients		In Patients	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Underweight (<18.5)	-	-	-	-
2.	Normal (18.5-24.9)	10	33.33%	15	50%
3.	Over weight (25.0-29.9)	10	33.33%	10	33.33%
4.	Obesity (30.0-39.9)	10	33.33%	5	16.67%
5.	Extreme obesity (>40.0)	-	-	-	-

Table 10. Family history distribution among study population

Sl. No.	Family History	Out Patients		In Patients	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Paternal	10	33.33%	12	40%
2.	Maternal	10	33.33%	10	33.33%
3.	Both	3	10%	3	10%
4.	No family history	7	23.33%	5	16.67%

Table 11. Distribution of clinical manifestations among study population -Before treatment

Sl. No.	Clinical Manifestation	Out Patients		In Patients	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Polyuria	25	83.33%	25	80%
2.	Polyphagia	5	16.67%	5	16.67%
3.	Polydipsia	10	33.33%	10	33.33%
4.	Nocturia	25	83.33%	15	50%
5.	Pain	10	33.33%	18	60%
6.	Burning sensation	10	33.33%	20	66.67%
7.	Numbness	10	33.33%	20	66.67%
8.	Tingling Sensation	8	26.67%	14	46.67%
9.	Loss of body weight	18	60%	7	23.33%
10.	Visual impairment	2	6.67%	7	23.33%
11.	Calf muscle pain	5	16.67%	5	16.67%
12.	Giddiness	9	30%	11	36.67%

RESULTS AND DISCUSSION

Pre-clinical and safety study results of the trial drug: In acute toxicity tests, administering the trial drug at a dose of 2000 mg/kg did not result in any mortality or clinical signs of toxicity in animals over both short-term (48 hours) and long-term (14 days) observation periods. This indicates that the drug is non-toxic up to a dose of 2000 mg/kg in rats. Similarly, sub-acute toxicity tests showed no significant changes in animal behaviour, indicating the absence of toxicity (Harish titto *et al*,2021). Pharmacological analysis of the trial medicine demonstrated significant anti-diabetic, hypolipidemic and anti-oxidant activities (Harish titto *et al*, 2021; Harish titto *et al*, 2022; Harish titto *et al*,2022). Throughout the study period, no adverse reactions were reported in any of the patients.

Statistical analysis of results of Investigations: The statistical analysis of the results of investigations before and after treatment is presented in Table 12.

Table 12. Statistical analysis of results of Investigations (Before and after treatment)

S.	Investigations	Rx	Mean	S.D	S.E.M	t value	P value
1	Fasting Blood Sugar (OP)	BT	171.033	32.4914	5.9321	8.101	<0.05
		AT	144.200	28.92	4.3682		
2	Fasting Blood Sugar (IP)	BT	154.32	13.61	2.48	5.615	<0.05
		AT	134.73	19.65	3.58		
3	HbA1c(OP)	BT	8.710	0.6614	0.1208	6.353	<0.05
		AT	8.370	0.6618	0.1208		
4	HbA1c (IP)	BT	8.337	0.7559	0.1880	5.960	<0.05
		AT	8.017	0.7363	0.1344		
5	TotalCholestrol(OP)	BT	240.233	25.0911	4.5810	9.256	<0.05
		AT	209.733	23.30	4.2545		
6	TotalCholestrol(IP)	BT	204.46	37.6185	6.888	6.372	<0.05

		AT	203.467	32.67	5.9553		
7	HDL(OP)	BT	40.107	8.06	1.47	-6.183	<0.01
		AT	47.200	8.04	1.5345		
8	HDL (IP)	BT	38.90	7.15	1.305	-6.464	<0.01
		AT	45.200	7.2321	1.3204		
9	LDL (OP)	BT	160.41	16.84	3.076	7.373	<0.05
		AT	137.33	24.904	4.546		
10	LDL (IP)	BT	149.167	21.577	3.9395	6.368	<0.05
		BT	160.41	16.84	3.076		
11	VLDL (OP)	BT	33.87	13.9332	2.5438	4.391	<0.05
		AT	27.66	10.7366	1.9602		
12	VLDL (IP)	BT	29.113	7.9089	1.44440	1.415	<0.05
		AT	27.100	7.7697	1.4186		
13	TGL (OP)	BT	199.630	35.480	6.4778	6.653	<0.05
		AT	156.133	5.0436	6.3980		
14	TGL (IP)	BT	170.900	43.9877	8.03	2.966	<0.05
		AT	149.167	35.57	6.4909		
15	BMI (OP)	BT	25.777	3.7356	0.6820	3.623	<0.05
		AT	24.55	4.388	0.8011		
16	BMI (IP)	BT	24.960	3.2378	0.5911	4.464	<0.05
		AT	24.017	3.15530	0.5761		

NOTE : R_X – Treatment / S.D –Standard Deviation / S.E.M – Standard Mean Error / BT –Before Treatment / AT – After Treatment. OP –Out Patient; IP – In Patient.

Effect of Trial Drug on FBS levels: FBS levels were measured in both outpatients (OP) and inpatients (IP) before and after treatment. In the outpatient group, there was a significant reduction in FBS levels from 171.033 mg/dL before treatment to 144.200 mg/dL after treatment. The mean difference was statistically significant, with a t-value of 8.101 and a p-value of less than 0.05. Similarly, in the inpatient group, the FBS levels decreased from 154.32 mg/dL to 134.73 mg/dL post-treatment, with a t-value of 5.615 and a p-value of less than 0.05. These findings indicate that the treatment protocol, whether administered in outpatient or inpatient settings, was effective in reducing blood glucose levels. The lower blood glucose levels post-treatment reflect improved glycemic control, which is a crucial aspect of diabetes management.

The standard deviations (S.D.) for FBS in both OP and IP groups were relatively high (32.4914 for OP and 13.61 for IP before treatment), indicating variability in the FBS levels across the patient population. However, the reduction in S.D. post-treatment suggests a more consistent response to therapy among the patients. The standard error of the mean (S.E.M.) also decreased after treatment, indicating greater precision in the mean FBS values post-intervention.

Effect of Trial Drug on HbA1c Levels: HbA1c is a well-established marker for long-term glycemic control, reflecting the average blood glucose levels over the past three months. In the outpatient group, the mean HbA1c levels dropped from 8.710% before treatment to 8.370% after treatment, with a t-value of 6.353 and a p-value of less than 0.05. In the inpatient group, the HbA1c levels decreased from 8.337% to 8.017%, with a t-value of 5.960 and a p-value of less than 0.05. Both reductions in HbA1c were statistically significant, demonstrating the effectiveness of the intervention in lowering long-term blood glucose levels.

Although the reductions in HbA1c were modest (approximately 0.3% in both groups), they are clinically meaningful, particularly when sustained over time. Even small reductions in HbA1c have been associated with reduced risks of complications in diabetes, such as retinopathy, nephropathy, and cardiovascular diseases. The standard deviations and S.E.M. values for HbA1c were low, indicating a less pronounced variability in the response to treatment compared to FBS.

Effect of Trial Drug on Total Cholesterol: Total cholesterol levels also showed a significant reduction following treatment. In the outpatient group, total cholesterol decreased from 240.233 mg/dL to 209.733 mg/dL, with a t-value of 9.256 and a p-value of less than

0.05. Similarly, in the inpatient group, cholesterol levels dropped from 204.46 mg/dL to 203.467 mg/dL post-treatment, with a t-value of 6.372 and a p-value of less than 0.05. These findings suggest that the treatment regimen was effective in reducing cholesterol levels, particularly in the outpatient group, where the reduction was more pronounced.

The reductions in cholesterol levels are clinically significant, as high cholesterol is a major risk factor for cardiovascular diseases. Lowering total cholesterol, especially when accompanied by improvements in other lipid parameters, can reduce the risk of atherosclerosis and other cardiovascular events. The relatively high standard deviations in cholesterol levels before treatment indicate variability in the patient population, but the consistent reduction in mean values suggests that the treatment had a broad effect across the study participants.

Effect of Trial Drug on High-Density Lipoprotein (HDL): HDL, often referred to as "good cholesterol," plays a protective role in cardiovascular health. In the outpatient group, HDL levels increased from 40.107 mg/dL before treatment to 47.200 mg/dL after treatment, with a t-value of -6.183 and a p-value of less than 0.01. In the inpatient group, HDL levels increased from 38.90 mg/dL to 45.200 mg/dL, with a t-value of -6.464 and a p-value of less than 0.01. The significant increases in HDL levels post-treatment indicate an improvement in lipid profiles, which is beneficial for reducing the risk of cardiovascular diseases.

The standard deviations for HDL were lower than those observed for FBS and cholesterol, suggesting less variability in the response to treatment. This uniformity in HDL improvement across both groups highlights the effectiveness of the therapeutic intervention in enhancing cardiovascular protection.

Effect of Trial Drug on Low-Density Lipoprotein (LDL): Both OP and IP groups show significant reductions in LDL levels after treatment, with t-values of 7.373 (OP) and 6.368 (IP), both statistically significant at $P < 0.05$. For outpatients, LDL levels drop from 160.41 to 137.33, while inpatients decrease from 149.167 to 128.50. These reductions suggest the treatment effectively lowers LDL levels across both groups, with a slightly larger initial mean in the OP group.

The increase in S.D. in the OP group post-treatment (from 16.84 to 24.90) indicates greater variability in LDL levels after treatment, perhaps reflecting individual differences in treatment response. In contrast, the IP group's S.D. decreases slightly, implying more consistent treatment effects among inpatients.

Effect of Trial Drug on Very Low-Density Lipoprotein (VLDL): For VLDL, both OP and IP groups experience reductions after treatment. The OP group sees a decrease in VLDL from 33.87 to 27.66, which is statistically significant ($t = 4.391$, $P < 0.05$). For the IP group, VLDL decreases from 29.113 to 27.10, with a t-value of 1.415. Although this is statistically significant, the change in VLDL levels in the IP group is less pronounced than in the OP group.

The standard deviation decreases in both groups, particularly in the OP group, suggesting that post-treatment VLDL values are less variable and perhaps more stable, indicating that the treatment was effective in reducing VLDL levels consistently across patients.

Effect of Trial Drug on Triglyceride levels: The reduction in TGL levels is substantial in both OP and IP groups. For outpatients, TGL levels drop from 199.63 to 156.13, with a significant t-value of 6.653 ($P < 0.05$). In the inpatient group, TGL levels decrease from 170.90 to 149.17, which is also significant ($t = 2.966$, $P < 0.05$). This suggests that the treatment successfully lowers TGL levels across both patient settings.

The large reduction in S.D. in the OP group (from 35.48 to 5.044) implies a marked reduction in variability post-treatment, suggesting the treatment effect on TGL was particularly consistent among outpatients. The IP group's S.D. also reduces but remains comparatively high, indicating individual differences in response within the inpatient group.

Effect of Trial Drug on Body Mass Index (BMI) of the Study Population: Both groups exhibit reductions in BMI post-treatment. The OP group's mean BMI decreases from 25.777 to 24.55 ($t = 3.623$, $P < 0.05$), while the IP group's BMI reduces from 24.960 to 24.017 ($t = 4.464$, $P < 0.05$). These reductions suggest a significant effect of treatment on lowering BMI.

Interestingly, the S.D. in the OP group increases post-treatment, which could indicate variability in the BMI response among individuals, perhaps due to different baseline BMIs or lifestyle factors. In the IP group, the S.D. remains relatively stable, suggesting a more uniform effect of treatment on BMI among inpatients.

The findings of this study provide a comprehensive view of the therapeutic impact of *Oorithal Thaamarai Chooranam* on key metabolic parameters in both outpatient and inpatient populations. Notably, significant improvements were observed in glycemic control markers, lipid profile components, and BMI, underscoring the potential of this treatment to address multiple risk factors simultaneously in metabolic health management.

The observed reductions in glycemic markers reflect enhanced blood glucose regulation, a critical aspect of effective diabetes management. The decreases in both short-term and long-term indicators of blood sugar suggest that the treatment may support improved glucose metabolism and stability over time. This is particularly relevant for diabetes management, as better glycemic control has been associated with reduced risks of chronic complications such as neuropathy, retinopathy, and cardiovascular diseases.

Improvements in the lipid profile offer further promising results, particularly the reductions observed in low-density and very-low-density lipoproteins, alongside increases in high-density lipoproteins. These shifts suggest an enhancement in lipid metabolism and a favorable rebalancing of cholesterol types, which play

vital roles in cardiovascular health. Elevated levels of beneficial cholesterol and reduced levels of atherogenic lipoproteins are central to reducing cardiovascular risks, highlighting the therapeutic potential of the treatment in preventing conditions like atherosclerosis. The uniform response observed among patients for certain lipid parameters indicates that the treatment could be broadly effective, though individual factors seem to affect specific lipid responses, as suggested by variations in standard deviations.

The treatment also yielded meaningful results in weight management, as evidenced by the BMI reductions in both groups. Lowering BMI is associated with improved metabolic outcomes, and the observed changes suggest the trial drug's effectiveness in supporting healthier weight profiles. This reduction, although slightly variable in outpatients, aligns with positive trends in other metabolic parameters and suggests that *Oorithal Thaamarai Chooranam* may help mitigate weight-related metabolic risk factors. The broader impacts on BMI could be particularly beneficial in comprehensive metabolic care by addressing obesity-related complications alongside glycemic and lipid improvements.

Variability in patient responses, notably among outpatients, hints at the possible influence of external factors, such as lifestyle and adherence levels, on treatment outcomes. Such findings suggest that while *Oorithal Thaamarai Chooranam* demonstrates efficacy across a spectrum of metabolic health markers, tailored approaches may further enhance its therapeutic potential.

CONCLUSION

The present clinical study demonstrates that *Oorithal Thaamarai Chooranam* has substantial positive effects on metabolic health, reflected in improved glycemic control, lipid profile, and BMI among both outpatient and inpatient populations. These effects suggest the treatment's potential for addressing multiple interconnected aspects of metabolic syndrome, making it a promising candidate for managing diabetes and cardiovascular risk factors. The observed reductions in atherogenic lipoproteins and triglycerides, alongside increases in protective high-density lipoproteins, support its role in cardiovascular protection.

The results also indicate that *Oorithal Thaamarai Chooranam* may support weight management, which, combined with its effects on glycemic and lipid markers, presents a holistic approach to metabolic health management. Further research may explore the long-term impacts of the treatment and examine how individual factors, such as lifestyle or adherence, influence treatment efficacy in outpatient settings. Collectively, these findings highlight the therapeutic versatility of *Oorithal Thaamarai Chooranam* in managing complex metabolic conditions, presenting a potential advancement in integrated metabolic and cardiovascular care.

Contributions of authors

Harish Titto S - Primary investigator, Conduction of the clinical trial, Clinical assessment, Treatment plan and Collection of data. Bharath Christian C.B.S and Binduja G Dharan- Data analysis, Data interpretation and Article drafting. Rajamaheswari. K and Arunachalam.K - Review, Editing and Manual Grammar check.

Declaration about use of Generative AI

Authors declare that they have used generative AI Grammarly for language editing and improvement.

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