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A Prospective, Open-label, Non-randomised Clinical Trial to Evaluate the Safety and Efficacy of Cholecurb in the Treatment of Dyslipidemia

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ABSTRACT

Objectives: To evaluate the clinical efficacy and safety of Cholecurb Tablets in Dyslipidemia. **Materials and Methods:** A prospective, interventional clinical study was conducted on 55 patients, aged between 18-55 years, confirmed with dyslipidemia and who were willing to give informed consent. All patients received Cholecurb Tablets at a dose of two tablets four times in a day for four weeks. All patients were evaluated at baseline, 45 and 120 days for parameters of fasting plasma lipid profile. The Physician's global assessment and Patient's global assessment (at end of the study) on efficacy and tolerability were made on a scale of 1- 5, namely, Very Good = 5, Good = 4, Fair = 3, Poor = 2 and Very Poor = 1. **Observation and Results:** Cholecurb Tablets significantly improved all lipid outcomes at both 45 days and 120 days after onset of treatment. There were no significant differences in the laboratory findings at baseline, 45 days and 120 days. The global assessment of response by physicians showed that 72% of patients showed a good improvement while another 16% showed very good improvement in their condition by the end of 120 days of treatment. Similarly, 58% and 31% of the patients' global assessment indicated good and very good response at the end of treatment, respectively. These findings confirm the efficacy of Cholecurb Tablets in the study population during the study period. **Conclusion:** Cholecurb Tablets typically lowered LDL, TG, TC and elevated HDL, assessed at baseline, 45 days and 120 days. There were no clinically significant adverse events either reported or observed during the entire study period.

Key words: *Cholecurb Tablet, Dyslipidemia, cardiovascular diseases, metabolic disorders*

INTRODUCTION

Dyslipidemia is defined as abnormal levels of lipids in the bloodstream. Lipids are fatty substances, such as low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol and triglycerides (TG). Lipids are absorbed from the intestines and carried throughout the body via lipoproteins for energy, steroid production and bile acid formation. Major contributors to dyslipidemic pathways are cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides and high-density lipoprotein (HDL). An imbalance of any of these factors, either from organic or non-organic causes, can lead to dyslipidemia.

Dyslipidemia may not always cause symptoms but it can lead to or pose a significant risk for other disease conditions. Dysregulation of these lipids in blood, whether due to genetic predispositions or lifestyle factors, can lead to atherosclerosis, increase the risk of cardiovascular diseases (CVD) and other complications.

Dyslipidemia is classified into 2 types, primary and secondary. Primary dyslipidemia is inherited and caused by genetic mutations that affect lipid metabolism. Secondary dyslipidemia is acquired and caused by lifestyle factors or other medical conditions that alter lipid levels.

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The most common forms of dyslipidemia are:

1. High LDL cholesterol: LDL is considered 'bad cholesterol' because it can form plaques in the arteries and reduce blood flow.
2. Low HDL cholesterol: HDL is considered 'good cholesterol' because it can help remove LDL from the blood and protect against atherosclerosis.
3. High triglycerides: TGs are stored in fat cells and released as energy when needed. High triglycerides can also contribute to plaque formation and inflammation in the arteries.
4. High total cholesterol: It is the sum of LDL, HDL, and half of the triglyceride level. High total cholesterol can indicate an increased risk of heart disease and stroke.

Epidemiology

The incidence and mortality of dyslipidemia are challenging to measure directly, as dyslipidemia is usually asymptomatic and often coexists with other risk factors, such as hypertension, diabetes, obesity and smoking. Most studies use surrogate endpoints, such as cardiovascular events, to assess the impact of dyslipidemia on morbidity and mortality.[1] Dyslipidemia is a health concern affecting millions of people globally and the leading cause of death worldwide. The epidemiology of dyslipidemia is influenced by age, sex, ethnicity, genetic and environmental factors.[2] The global prevalence of dyslipidemia in adults is estimated to range from 20 to 80%.[3]

The epidemiology of dyslipidemia also reveals gender differences, as women tend to have higher HDL cholesterol and lower LDL cholesterol than men, but this advantage diminishes after menopause.[4]

The prevalence of dyslipidemia in children and adolescents is increasing, due to the rising rates of obesity, sedentary lifestyles and unhealthy diets. The median prevalence of childhood obesity-related hypertension was 38.6 % in Asia. For metabolic syndrome, the median prevalence was 25.8 % in Asia.[5] Dyslipidemia in childhood can persist into adulthood and increase the risk of premature cardiovascular disease. Dyslipidemia is a modifiable risk factor for cardiovascular disease, and prevention and management are essential to reduce the global burden of morbidity and mortality.

Pathophysiology

The role of a spectrum of inter-connected metabolic and cardiovascular disturbances elucidates the understanding of dyslipidemia pathophysiology. Dyslipidemia can cause inflammation, oxidative stress, cardiovascular diseases, and other metabolic dysfunctions by different mechanisms.

Inflammation: Dyslipidemia can activate inflammatory cells, such as macrophages and T cells, and inflammatory mediators, such as cytokines and chemokines which can infiltrate and damage the endothelium. It also modulates and impairs the function of endothelial progenitor cells (EPCs), which are involved in the repair and regeneration of the endothelium, compromising endothelial integrity and function.

Oxidative stress: LDL particles, when retained in arterial walls, undergo oxidative modifications. Oxidized LDL becomes pro-inflammatory and pro-atherogenic, increasing the production of reactive oxygen species (ROS), unstable molecules that damage cells and tissues by oxidizing components such as lipids, proteins, and deoxyribonucleic acid. Dyslipidemia can also decrease the levels of antioxidants, which can neutralize ROS and protect the cells and tissues from oxidative damage.

Cardiovascular diseases: Dyslipidemia can increase the risk of cardiovascular diseases, such as coronary artery disease, peripheral artery disease, stroke, and heart failure, by promoting atherosclerosis and its complications. Dyslipidemia can also affect the function of the heart and the blood vessels by impairing the production and availability of nitric oxide, a key regulator of vascular tone, blood pressure, and platelet aggregation. Dyslipidemia can induce endothelial dysfunction, impairment of the ability of the endothelium to maintain vascular homeostasis and to respond to physiological stimuli. Dyslipidemia can

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also affect the structure and function of the cardiac muscle, leading to cardiac hypertrophy, fibrosis, and arrhythmias.

Other metabolic dysfunctions: Additional effects exist on the metabolism of other organs and systems, such as the liver, pancreas, adipose tissue and skeletal muscle, by altering lipid and glucose metabolism, insulin sensitivity and inflammatory status. Dyslipidemia can also interact with other metabolic disorders, such as obesity, diabetes, metabolic syndrome, etc. and exacerbate complications.

Diagnosis:

Understanding the signs and symptoms of dyslipidemia is crucial for timely intervention and preventing associated complications. As dyslipidemia often progresses silently and does not cause any symptoms; fasting lipid profile, comprising of total cholesterol, LDL, HDL, and triglycerides, detected by a blood test remains a cornerstone for early detection and effective management. Broader clinical context, including past medical, family and social history; diet and other risk factors should be considered. The optimal lipid level varies depending on the individual's age, sex, and other risk factors. Generally recommended target levels for optimal Cardiovascular health are:

Total cholesterol

- Desirable: <200 mg/dL
- Borderline high: 200 mg/dL to 239 mg/dL
- High: ≥240 mg/dL

Low-density lipoprotein cholesterol

- Optimal: <100 mg/dL
- Near optimal/above optimal: 100 mg/dL to 129 mg/dL
- Borderline high: 130 mg/dL to 159 mg/dL
- High: 160 mg/dL to 189 mg/dL
- Very high: ≥190 mg/dL

High-density lipoprotein cholesterol

- Low: <40 mg/dL (men), <50 mg/dL (women)
- High: ≥60 mg/dL

Triglycerides

- Normal: <150 mg/dL
- Borderline high: 150 mg/dL to 199 mg/dL
- High: 200 mg/dL to 499 mg/dL
- Very high: ≥500 mg/dL

Conventional Treatment

Preventing dyslipidemia is essential to reduce the risk of cardiovascular complications and improve the quality of life. Treatment strategies work to mitigate risks by targeting specific lipid abnormalities, emphasizing lifestyle modifications and considering comorbidities to individualize care. Given the multifaceted nature of dyslipidemia management, a multidisciplinary approach is essential for comprehensive patient care. Treating dyslipidemia depends on the type and severity of the condition and the presence of other risk factors such as diabetes, hypertension, obesity, or smoking. The main goals of treatment are to lower LDL cholesterol, raise HDL cholesterol and reduce triglycerides.

The prevention strategies include

- Dietary Modification
- Physical Activity
- Weight Management
- Smoking Cessation

The first-line treatment for dyslipidemia is statins that inhibit 3-hydroxy-3methyl glutaryl-(HMG) coenzyme A reductase. For secondary prevention, another agent is added to inhibit the absorption of cholesterol, target proprotein convertase subtilisin/kexin type 9 (PCSK9), inhibit adenosine triphosphate citrate lyase, decrease bile acid reabsorption and activate peroxisome proliferator-activated receptor. Many new medications are being researched to help lower cholesterol levels and prevent cardiovascular events.

Patients with dyslipidemia do not have access to a remedy that cures the metabolic defect to stop the recurrence of dyslipidemia. Current therapeutics

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possess certain drawbacks, including the frustration of the patients due to the intolerance, non-adherence, ineffectiveness of drugs and possible side-effects. Incidence of cataracts or cognitive dysfunction and others presented in the literature (e.g. proteinuria and haematuria) have been never confirmed to have a causal link.[6]

Not all the glitter is gold. Although pleiotropic effects of statins may be a cause for enthusiasm, there are many adverse effects that, for the most part, are unappreciated and need to be highlighted. These adverse effects include myopathy, new-onset type 2 diabetes, renal and hepatic dysfunction (hepatic transaminase elevations).[7] Statins may cause neuro-muscular side-effects, representing about two-third of all adverse events. Muscle-related adverse events include cramps, myalgia, weakness, immune-mediated necrotizing myopathy and, more rarely, rhabdomyolysis. Moreover, they may lead to peripheral neuropathy and induce or unmask a preexisting neuromuscular junction dysfunction.[8]

There is a lack of an effective and long-term treatment plan in the fight against dyslipidemia. There is a great need for the continuous development of new, safe, and effective treatment of dyslipidemia. Among the many active compounds that have been studied for the treatment of dyslipidemia, extracts from plants and specific phyto-chemicals from natural resources have been of great interest in recent decades. Several studies evaluating dyslipidemia therapy based on natural sources revealed potential activity, especially in reduction of total cholesterol, low-density lipoprotein (LDL) cholesterol and triglycerides. Natural substances, in comparison with medicament, do not cause such adverse effects, which is the positive side of their use.

In the present study, Cholecurb Tablets, manufactured by Charak Pharma Pvt. Ltd. was studied for its efficacy and safety in patients with leucorrhoea.

Materials and Methods

Study Design

Prospective, non-randomised, open-label clinical trial.

Study Objectives

The main objective of the study was to evaluate the clinical efficacy of Cholecurb Tablets in Dyslipidemia. Further, the study also observed the clinical safety of Cholecurb Tablets in Dyslipidemia.

Inclusion Criteria

Participants, aged 18 to 55 years and visiting the outpatient department, diagnosed with dyslipidemia; Patients willing to provide informed consent; comply with study requirements, attending study visits and adhering to treatment protocols; having adequate understanding of the study procedures and ability to communicate effectively with study staff; to be available for the duration of the study period were enrolled in the study.

Exclusion Criteria

Individuals with significant comorbidities that could confound the study results, such as severe liver disease, respiratory disease, renal failure, or active malignancy; individuals on medications that could significantly affect lipid levels or metabolism; pregnant or breastfeeding individuals, as hormonal changes during these periods can affect lipid levels; individuals with active substance abuse, as this could affect compliance and confound results; individuals with uncontrolled hypertension, as it could impact lipid metabolism and complicate interpretation of results; individuals who have undergone recent lipid-lowering procedures such as bariatric surgery, as these could confound results; individuals who are unlikely to comply with study protocols or follow-up visits were excluded. Individuals with any other condition or circumstance that, in the judgment of the investigator, would make the participant unsuitable for participation in the study were excluded. Patients could be withdrawn from the study at their own request or if they experience intolerable adverse events, show insufficient therapeutic effect, or needed deviations from the protocol at the discretion of the investigator.

Study Design

A non-randomized phase 4, prospective open label

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clinical trial in 55 patients diagnosed with dyslipidemia was planned following required GCP guidelines. After careful selection in terms of the eligibility criteria, screened subjects willing to enroll after explaining the clinical study procedure were requested to sign the Patient Consent Form. At baseline visit (0 day), Patient information sheet was provided to each subject in their language of preference. Case record form (CRF) was filled by the attending physician with complete medical history and required personal details of the subject at the start of the study. A thorough physical examination and necessary laboratory investigations were carried out before (0 day) and during (45 days) drug administration and after completion of treatment (120 days).

Safety and efficacy evaluation of patients' clinical response to treatment was monitored from baseline till end of 120 days. All data were carefully entered in the Case Record Form provided. Side-effects were closely monitored in all patients. All adverse events were recorded by the investigator, and rated for severity and relationship to the study medication.

Clinical assessments

The patients were evaluated at baseline, 45 days and 120 days after onset of treatment. Efficacy was evaluated on the basis of fasting plasma total cholesterol (TC), triglycerides (TG), low density lipid cholesterol (LDL-C), high density lipid cholesterol (HDL-C), LDL-C to HDL-C ratio. The Physician global assessment and Patient's global assessment (at end of the study) on efficacy and tolerability were made on a scale of 1- 5, namely, Very Good = 5, Good = 4, Fair = 3, Poor = 2 and Very Poor = 1.

Intervention

Cholecurb Tablets, manufactured by Charak Pharma Pvt. Ltd. was studied for its efficacy and safety in patients with dyslipidemia, in a dose of two tablets four times in a day for 120 days. Cholecurb Tablets contain *Pterocarpus marsupium, Plumbago zeylanica, Bauhinia variegata, Emblica officinalis, Terminalia belerica, Terminalia chebula, Allium sativum, Cyperus rotundus, Curcuma longa, Zingiber officinale and Piper longum.*

OBSERVATION

All 55 patients enrolled in the trial completed the study. Table 1 shows Demographic data of Patients who participated in our study before intervention. Table 2 shows lipid parameters at baseline, 45 days and 120 days from onset of treatment. After 120 days of treatment with Cholecurb Tablets, there was a reduction in reduction in TC, TG, LDL-C and non-HDL-C, without reduction in HDL. Table 3A and 3B shows laboratory findings of patients before and after treatment. Treatment with the Cholecurb Tablets did not lead to any abnormalities in the laboratory investigations as compared to the baseline values. Table 3C shows physical examination of patients before and after treatment. Patients tolerated the Cholecurb Tablets without any adverse events that needed discontinuation. Table 4 and 5 shows Global assessment of response by Physicians and Patients respectively after 120 days of treatment with Cholecurb Tablets.

Table 1: Demographic Data of Patients at Baseline

Age (year)	58.47 ± 8.81
Male/Female (n)	14 (25.5)/41 (74.5)
Smoking (n)	7 (12.7)
Alcohol (n)	5 (9.1)
Lipid-lowering drugs (n)	0
Tea (n)	18 (32.7)
Medical history (n)	44 (80.0)
Hypertension (n)	23 (41.8)
Diabetes (n)	8 (14.5)
Heart disease (n)	7(12.7)
BMI (kg/m2)	26.17 (25.43 to 26.91)
SBP (mmHg)	132.09 (127.47 to 136.71)
DBP (mmHg)	85.07 (82.15 to 87.99)

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Waist-to-hip ratio (%)	93.54 (92.09 to 94.99)
Milk, dairy, and soy nut products (times/day)	0.80 (0.58 to 1.03)
Animal food (times/day)	1.22 (0.95 to 1.48)
Plant foods (times/day)	7.37 (6.58 to 8.16)
Cereals and potatoes (times/day)	3.70 (3.35 to 4.05)
Vegetables and fruits (times/day)	3.67 (3.07 to 4.26)
Metabolic levels (kcal/day)	2132.78 (1880.76 to 2384.79)

Table 2: Lipid Parameters at Baseline, 45 days and 120 days from onset of treatment

Parameters	Baseline (mmol/L)	45 days (mmol/L)	Absolute change from baseline to 45 days (mmol/L)	% change from baseline to 45 days	120 days (mmol/L)	Absolute change from baseline to 120 days (mmol/L)	% change from baseline to 120 days
TC	5.99 (5.77 to 6.20)	5.06 (4.87 to 5.26) ***	−0.93 (−1.14 to −0.70)	−14.75 (−18.04 to −11.46)	5.14 (4.92 to 5.37) ***	−0.85 (−1.03 to −0.65)	−13.75 (−16.81 to −10.69)
TG	2.66 (2.36 to 2.96)	2.08 (1.78 to 2.39) ***	−0.58 (−0.84 to −0.31)	−17.56 (−28.64 to −6.48)	2.07 (1.83 to 2.30) ***	−0.59 (−0.85 to −0.33)	−16.10 (−27.19 to −5.01)
LDL-C	3.66 (3.49 to 3.84)	3.09 (2.92 to 3.26) ***	−0.57 (−0.72 to −0.43)	−15.20 (−18.89 to −11.50)	3.26 (3.06 to 3.46) ***	−0.40 (−0.54 to −0.27)	−10.99 (−14.72 to −7.25)
non-HDL-C	4.54 (4.32 to 4.75)	3.58 (3.37 to 3.79) ***	−0.96 (−1.17 to −0.75)	−20.49 (−24.74 to −16.23)	3.61 (3.38 to 3.83) ***	−0.93 (−1.13 to −0.74)	−20.18 (−24.26 to −16.09)
HDL-C	1.45 (1.37 to 1.53)	1.49 (1.41 to 1.57) *	0.04 (0.01 to 0.07)	3.28 (0.87 to 5.68)	1.54 (1.46 to 1.62) ***	0.09 (0.05 to 0.13)	7.03 (4.30 to 9.76)
LDL-C to HDL-C ratio	2.63 (2.45 to 2.82)	2.17 (1.99 to 2.35) ***	−0.46 (−0.55 to −0.37)	−17.74 (−21.18 to −14.30)	2.20 (2.02 to 2.38) ***	−0.43 (−0.53 to −0.33)	−16.31 (−20.09 to −12.53)

The difference is considered statistically significant when $p < 0.05$, denoted as * and when $p < 0.001$, denoted as ***

Table 3A: Laboratory Investigations

Coagulation Parameters	Baseline	45-days	Absolute change from baseline to 45-days	120-days	Absolute change from baseline to 120-days
Prothrombin Time (PT)	10.35 (10.13 to 10.57)	11.63 (10.95 to 12.31)	1.29 (0.63 to 1.94)	12.28 (11.83 to 12.72)	1.89 (1.42 to 2.36)
International normalized ratio	0.88 (0.85 to 0.91)	0.88 (0.86 to 0.90)	0.00 (-0.03 to 0.02)	0.89 (0.87 to 0.91)	0.01 (-0.03 to 0.05)
Activated partial PT	30.91 (29.50 to 32.31)	31.53 (30.56 to 32.51)	0.63 (-0.84 to 2.09)	32.29 (31.39 to 33.19)	1.39 (0.11 to 2.67)
Fibrinogen, g/L	2.99 (2.83 to 3.15)	2.97 (2.47 to 3.46)	-0.02 (-0.52 to 0.48)	2.79 (2.65 to 2.92)	-0.18 (-0.34 to -0.02)

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Table 3B: Laboratory Investigations

Parameters		Baseline	45-days	120-days
Liver function	Total bilirubin, µmol/L	17.79 (15.39 to 20.19)	18.16 (16.23 to 20.08)	16.18 (14.31 to 18.05)
	Direct bilirubin, µmol/L	3.53 (3.12 to 3.94)	4.42 (4.04 to 4.80)	4.14 (3.77 to 4.51)
	Indirect bilirubin, µmol/L	14.26 (12.07 to 16.45)	13.74 (12.12 to 15.35)	12.04 (10.46 to 13.62)
	Alanine aminotransferase, U/L	24.88 (20.75 to 29.01)	26.71 (23.25 to 30.17)	24.81 (21.29 to 28.33)
	Aspartate aminotransferase, U/L	26.35 (22.11 to 30.58)	26.04 (23.93 to 28.14)	25.74 (23.48 to 28.01)
	AST/ALT	1.21 (1.09 to 1.34)	1.08 (0.99 to 1.17)	1.18 (1.08 to 1.28)
	Alkaline phosphatase, U/L	77.87 (70.02 to 85.73)	72.84 (66.22 to 79.46)	91.71 (84.76 to 98.65)
	Total protein, g/L	81.13 (80.26 to 82.00)	75.28 (72.66 to 77.89)	78.58 (77.71 to 79.45)
	Albumin, g/L	51.75 (51.21 to 52.28)	47.21 (46.57 to 47.86)	48.73 (48.15 to 49.32)
	Globulin, g/L	29.38 (28.56 to 30.20)	29.37 (28.57 to 30.17)	29.84 (29.02 to 30.65)
	ALB/GLB	1.78 (1.73 to 1.84)	1.63 (1.57 to 1.68)	1.65 (1.59 to 1.70)
Renal function	Urea, mmol/L	6.28 (5.72 to 6.85)	5.17 (4.73 to 5.62)	5.05 (4.67 to 5.43)
	Uric acid, µmol/L	293.48 (266.70 to 320.27)	274.17 (252.22 to 296.11)	267.74 (244.66 to 290.82)
Blood glucose	Fasting glucose, mmol/L	5.58 (5.14 to 6.02)	5.28 (4.86 to 5.70)	5.47 (5.00 to 5.94)
Blood routine	White blood cell,10^9/L	6.18 (5.77 to 6.58)	6.30 (5.86 to 6.73)	6.07 (5.64 to 6.51)
	Absolute neutrophil count,10^9/L	3.54 (3.20 to 3.87)	3.68 (3.32 to 4.03)	3.44 (3.10 to 3.77)
	Neutrophil percentage, %	56.40 (54.26 to 58.53)	57.39 (55.26 to 59.52)	55.68 (53.70 to 57.65)
	Absolute lymphocyte,10^9/L	2.17 (2.01 to 2.32)	2.15 (2.02 to 2.29)	2.18 (2.04 to 2.33)
	Lymphocyte percentage, %	35.93 (33.80 to 38.06)	35.27 (33.15 to 37.40)	36.83 (34.82 to 38.83)
	Absolute monocyte count,10^9/L	0.34 (0.30 to 0.37)	0.34 (0.31 to 0.37)	0.32 (0.29 to 0.35)
	Percentage of monocytes, %	5.46 (5.07 to 5.86)	5.38 (5.04 to 5.71)	5.36 (4.98 to 5.73)
	Eosinophil count,10^9/L	0.11 (0.08 to 0.14)	0.10 (0.08 to 0.12)	0.11 (0.08 to 0.13)
	Hemoglobin, g/L	144.85 (140.80 to 148.91)	145.51 (141.79 to 149.23)	149.40 (145.80 to 153.00)
	Red blood cell count,10^12/L	4.66 (4.54 to 4.78)	4.69 (4.58 to 4.80)	4.79 (4.68 to 4.90)
	Hematocrit, %	43.63 (42.48 to 44.79)	43.87 (42.81 to 44.94)	44.90 (43.87 to 45.92)
	Mean corpuscular volume, fL	93.79 (92.45 to 95.13)	93.77 (92.54 to 94.99)	93.82 (92.65 to 94.99)
	Platelet,10^9/L	226.40 (209.80 to 243.00)	234.31 (216.46 to 252.16)	227.24 (210.03 to 244.44)

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Table 3C: Physical Examination

Parameters	Baseline	45-days	120-days
BMI, kg/m2	26.17 (25.43 to 26.91)	26.27 (25.53 to 27.02)	26.38 (25.65 to 27.12)
SBP, mmHg	132.09 (127.47 to 136.71)	130.16 (125.95 to 134.38)	133.47 (129.23 to 137.71)
DBP, mmHg	85.07 (82.15 to 87.99)	84.56 (82.08 to 87.05)	84.89 (82.44 to 87.34)
Waist-hip ratio	93.54 (92.09 to 94.99)	91.49 (90.05 to 92.93)	90.77 (89.06 to 92.48)

Table 4: Global assessment of response by Physicians after 120 days of treatment.

Assessment by Physicians	Very Poor	Poor	Fair	Good	Very Good
Efficacy	0	0	6	40	9
Tolerability	0	0	2	46	7

Table 5: Global assessment of response by Patients after 120 days of treatment.

Assessment by Physicians	Very Poor	Poor	Fair	Good	Very Good
Efficacy	0	2	10	24	19
Tolerability	0	2	4	32	17

RESULTS

Cholecurb Tablets could significantly improve all lipid outcomes (TC, TG, LDL-C, HDL-C, non-HDL-C, and LDL-C to HDL-C ratio) at both 45 days and 120 days after onset of treatment.

The absolute change at 45 days intervention for TC, TG, LDL-C, non-HDL-C, HDL-C and LDL-C to HDL-C ratio was −0.93 (−1.14 to −0.70), −0.58 (−0.84 to −0.31), −0.57 (−0.72 to −0.43), −0.96 (−1.17 to −0.75), 0.04 (0.01 to 0.07) and −0.46 (−0.55 to −0.37), respectively. The absolute change at 120 days intervention for TC, TG, LDL-C, non-HDL-C, HDL-C and LDL-C to HDL-C ratio was −0.85 (−1.03 to −0.65), −0.59 (−0.85 to −0.33), −0.40 (−0.54 to −0.27), −0.93 (−1.13 to −0.74), 0.09 (0.05 to 0.13) and −0.43 (−0.53 to −0.33), respectively.

The absolute percentage change at 45 days intervention for TC, TG, LDL-C, non-HDL-C, HDL-C and LDL-C to HDL-C ratio was −14.75 (−18.04 to −11.46), −17.56 (−28.64 to −6.48), −15.20 (−18.89 to −11.50), −20.49 (−24.74 to −16.23), 3.28 (0.87 to 5.68) and −17.74 (−21.18 to −14.30), respectively. The absolute percentage change at 120 days intervention for TC, TG, LDL-C, non-HDL-C, HDL-C and LDL-C to HDL-C ratio was −13.75 (−16.81 to −10.69), −16.10 (−27.19 to −5.01), −10.99 (−14.72 to −7.25), −20.18 (−24.26 to −16.09), 7.03 (4.30 to 9.76) and −16.31 (−20.09 to −12.53), respectively.

There were no significant differences in the laboratory findings and physical examination parameters at baseline, 45 days and 120 days.

The global assessment of response by physicians showed that 72% of patients showed a good improvement while another 16% showed very good improvement in their condition by the end of 120 days of treatment. Similarly, 58% and 31% of the patients' global assessment indicated good and very good response at the end of treatment, respectively. These findings confirm the efficacy of Cholecurb Tablets in the study population during the study period.

DISCUSSION

Lipid disorders involving derangements in serum cholesterol and triglycerides are commonly encountered in clinical practice and often have implications for cardiovascular risk and overall health. Recent advances in knowledge, recommendations and treatment options have necessitated an updated approach to these disorders. Older classification schemes have outlived their usefulness, yielding to an approach based on the primary lipid disturbance identified on a routine lipid panel as a practical starting point. Although dyslipidemias are monogenic but most individuals with lipid disorders have polygenic predisposition with secondary factors such as obesity and type 2 diabetes. In cardiovascular disease,

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elevated low-density lipoprotein cholesterol is important causal factor with recent studies establishing elevated triglycerides as another risk factor.[9] The ongoing development of new agents, especially from natural plant/phyto source will provide additional management options, which in turn motivates discussion on how best to incorporate them into current treatment algorithms.

Diverse approaches are recommended to manage dyslipidemia such as lifestyle modifications, diet intervention and pharmacotherapy. Despite the worldwide use of lipid-lowering agents, their long-term efficacy is still questionable. Consequences of these drugs are arguable, due to their numerous adverse effects. The management of dyslipidemia mostly involves a constant decrease in lipid level using different remedial drugs like statin, fibrate, bile acid sequestrates and niacin.[10] Lipid-lowering medications are associated with various adverse effects such as myopathy, impaired liver function, neuropathy and declined mental status. Also increased risk of diabetes has been reported to be associated with the use of lipid-lowering medications. Traditional herbal medicine represents an alternative and complementary approach for managing dyslipidemia because of its low toxicity and beneficial effects, such as anti-inflammatory and antioxidant effects.[11] Recently, there is a tremendous awareness in patients and physicians to manage lipid profile with natural extracts. Large number of studies performed on the efficacy and safety of natural products, showed significant reduction in the lipid profile and thus, reduction of the risk of CVD.[12]

The flavonoid phytoconstituents of Pterocarpus marsupium mainly marsupin, pterosupin, and liquiritigenin are proven to have anti-hyperlipidemic effect. The extract is able to reduce serum triglyceride, total cholesterol, low-density lipoproteins and low-density lipoproteins -cholesterol without any significant effect on the level of HDL cholesterol. Marsupin is the active constituent of Pterocarpus marsupium and has been reported to downregulate the adipogenesis related transcriptional factors PPAR-γ, C/EBP-α, and SREBP-1 and to inhibit adipocyte differentiation during the early stage. Pterocarpus marsupium is also shown to increase lipolysis and triglyceride hydrolysis to diminish fat stores, thereby combating obesity. Marsupin and other phytoconstituents of Pterocarpus marsupium have been shown to act in the gut lumen by forming a covalent bond with the active serine site of gastric and pancreatic lipases by forming the covalent bond, thus inhibiting these lipases from hydrolyzing the ingested fat into absorbable free fatty acids and monoglycerides. It has been suggested that Pterocarpus marsupium suppresses adiposity and affects the expression of lipid metabolism genes, especially hepatic expression of the lipid catabolism genes, acyl coenzyme A oxidase 1, palmitoyl, acyl coenzyme-A dehydrogenase, c-4 to c-12 straight chain, and peroxisome proliferator-activated receptor alpha.[13]

Plumbago zeylanica roots ameliorate the hyperlipidemic condition leading to atherosclerosis. It significantly increases fecal cholesterol excretion indicating a reduction in intestinal cholesterol absorption. Additionally, it lowers the activity of lipogenic enzymes like HMGCoA reductase in the liver, thus decreasing the cholesterogenesis. Also, it significantly reduces the total lipid content in the liver. Moreover, it demonstrates a potential antioxidant capacity.[14] Extract of B. variegate is pre-clinically proven to significantly reduce Total cholesterol (TC), Triglycerides (TG) and elevate High density lipoprotein (HDL).[15]

In a randomized, double blind, placebo controlled, multicenter clinical trial, Emblica officinalis extract significantly lowered the major lipids such as total cholesterol (TC), triglyceride (TG), low density lipoprotein cholesterol (LDL-C) and very low density lipoprotein cholesterol (VLDL-C) with 12 weeks of treatment in patients with dyslipidemia. Additionally, there was a 39% reduction in atherogenic index of the plasma.[16]

Curcumin is a bioactive phytochemical with well-known antioxidant, anti-inflammatory, and cardio-protective properties. A study investigated the

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hypolipidemic activity of curcumin in obese individuals. Curcuminoid supplementation significantly reduced serum triglycerides.[17] Based on studies, turmeric and its bioactive component, curcumin, due to their anti-inflammatory and antioxidant properties, have antidiabetic effects through increasing insulin release, antihyperlipidemic effects by increasing fatty acid uptake, anti-obesity effects by decreasing lipogenesis, and antihypertensive effects by increasing nitric oxide.[18] Ginger supplementation decreases TG in obese and diabetic subjects more efficiently.[19]

CONCLUSION

The present interventional study indicates that Cholecurb Tablets are effective and safe in controlling dyslipidemia. There were no clinically significant adverse events either reported or observed during the entire study period. The overall compliance with the treatment was good and no treatment discontinuations were reported. Cholecurb Tablets typically lowers LDL, TG, TC and elevates HDL. Cholecurb Tablets aim at reversing dyslipidemia with an alternative approach to disconnect with other risk factors, such as hypertension, diabetes, obesity, etc.

Cost of Study

All medications required during the 120 days of trial were provided by the sponsor. Charak Pharma Pvt. Ltd. reserves all rights over any publications of the study during the course and post completion.

Conflict of Interest

To avoid any conflict of interest, study was carried out under the unbiased supervision of Laxmi Clinic HCP who are not associated with the sponsors.

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