International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2019): 7.583

Hypolipaedemic Activity of *Cìraka Cūranam* against Atherogenic Diet Induced Hyperlipaedemia in Wistar Albino Rats

Sujeethasai K[1*], Manoharan A[2], Madhavan S**

[1]-PG Scholar, Government Siddha Medical College & Hospital, Palayamkottai-627002, Tirunelveli, Tamil Nadu, India
[2] - Professor & HOD, Dept. of *Pothu Maruthuvam*, Government Siddha Medical College & Hospital, Palayamkottai-627002, Tirunelveli, Tamil Nadu, India
[3]-MD (General Medicine), Associate Professor in Allopathy Medicine, Government Siddha Medical College & Hospital, Palayamkottai-627002, Tirunelveli, Tamil Nadu, India
*- Author - saai.kethees[at]gmail.com
**- Corresponding author - drmanoharan25[at]gmail.com

Abstract: ***Background*: Hypercholesterolemia is a common in global clinical challenge. The high blood cholesterol level has more in coronary heart disease, peripheral vascular disease, diabetes related metabolic syndrome, stroke and hypertension. Hypolipaedemic activity of herbs may contribute to prevent and control of the disease. *Aim*: To evaluate the hypolipaedemic activity of hydroalcoholic extract of Cìraka cūraṇam against atherogenic diet induced hyperlipaedemia in wistar albino rats. *Study design*: Observational in-vivo study. *Place and duration of study*: Animal bred house, Dept. of Pharmacology, Arulmigu Kalasalingam College of Pharmacy, Krishnankoil, Srivilliputtur, Tamilnadu. *Materials and methods*: Adult male wistar albino rats considering weigh of 150-200gm and atherogenic diet induced animal were selected, and albino rats divided into five groups. After the completion of experimental study, the blood was taken from the rats under mild anesthetic state by retro orbital sinus puncture. The lipid extract was taken for the estimation of lipid parameters. The serum and liver were evaluated for serum total cholesterol, triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL) by standard enzymatic calorimetric methods. The data were statistically analyzed by one-way ANOVA followed by Dennett's t-test, and significant Pvalue was considered as < 0.05. *Results*: Cìraka cūraṇam has significantly reduced in hyperlipidemia state.***

Keywords: Hypertension, Hypolipaedemic activity, *Cìraka cūraṇam,* Atherogenic diet, Wistar albino rats

1. Introduction

Human body needs cholesterol tobuild healthy cells, but high level of cholesterol can increase the risk of heart diseases. The heart has to strain much harder to pump blood due to atherosclerosis, as a result the blood pressure (BP) becomes abnormally high. [3]High cholesterol can be inherited, but often get from unhealthy diet and lifestyle patterns.[7, 12] The cumin seeds (*Cuminum cyminum* Linn.) is more contained in flavonoids which have anti-oxidant activity and oxidized level of LDL.[5, 11] It has significant inhibitory effects on lipid peroxidation.[2, 10]. The present study was to evaluate the hypolipaedemic activity of *CC (Cìraka cūraṇam)* against atherogenic diet induced wistar albino rats.

2. Aim

To evaluate the hypolipaedemic activity of hydro alcoholic extract of *Cìraka cūraṇam* against atherogenic diet induced hyperlipaedemia in wistar albino rats.

3. Materials and Methods

3.1 Study population-30Wistar Albino rats

3.2 Study design - In-vivo Observational Study

3.3 Study period - 27 days

3.4 Study place - Animal bred house, Dept. of Pharmacology, Arulmigu Kalasalingam College of Pharmacy, Krishnankoil, Srivilliputtur.

3.5 Study procedure

3.5.1 Animals
Wistar albino adult male rats considering weigh of 150-200gm were selected. The polypropylene cages maintained with temperature 27°C ±1°C and 12 hrs light and dark cycle. The animals were allowed to adapt to the atmosphere for seven days and supplied with a standard pellet diet (Sai Durga Foods, Bangalore) and water *ad libitum*. The experimental protocol possesses the approval IAEC bearing no: AKCP/ IEAC/33/20-21.

3.5.2 Chemicals
Atorvastatin was used in control study and diagnostic kits were purchased from Merck Diagnostics India Ltd, The anesthetic ether, ethyl acetate, and ethanol were purchased from SD Fine Chemicals, Mumbai.

3.5.3 Atherogenic diet
Experimental hyperlipidemic diet: Experimental diet contains of well-pulverized mixture of cholesterol - 400 mg/kg, cholic acid - 50 mg/kg, and coconut oil. This mixture is finished into paste-like molds and is fed to the rats.

3.5.4 Treatment with atherogenic diet
The prepared atherogenic diet was used in place of normal pellet diet to all the groups except control. Rats were exposed to atherogenic diet and water *ad libitum* for 20 days

and were used to study the effect of *CC* against experimental hyperlipidemia.

3.5.5 Pharmacological evaluation

All animals were starved for 18 hours and provided water *ad libitum* before the experiment. The rats were divided into five groups and allocated six rats in each group.

Table 1: The study design of trial drug *CC*

Group	Treatment	Dose
I	Normal Control	2% *CC*
II	Hyperlipaedemic Control group	Atherogenic diet
III	Standard group	Atorvastatin (10 mg/kg)
IV	Test group I	*CC* (200 mg/kg)
V	Test group II	*CC* (400 mg/kg)

As per table no: 01, all the groups except the normal control group administered received atherogenic diet. After inducing the hyperlipidemia, the particular treatment was continued for 7 days. The standard pellet diet and water *adlibitum* were given to the rats.

3.5.6 Collection of blood

The following day after the completion of experimental study, the blood was taken from the rats under mild anesthetic state by retro orbital sinus puncture. The blood samples were collected and centrifuged (2500 rpm) for 10 minutes. The separated serum samples were used for various biochemical analyses. Then animals were paralyzed and the liver, heart and kidney were taken for histopathological study.

3.5.7 Liver lipid extraction

The liver was standardized in cold 0.15M KCl and extracted with CHCl3: CH3OH (2% *v/v*). This lipid extract was taken for the estimation of lipid parameters.

3.5.8 Bio chemical analysis

The serum and liver were evaluated for serum total cholesterol, triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL) by standard enzymatic calorimetric methods.

3.5.9 Statistical analysis

All the values were stated as mean ± standard error of mean. The data were statistically analyzed by one-way ANOVA followed by Dennett's t-test, and significant P value was considered as < 0.05.

4. Results

4.1 The effect of *CC* on Blood lipid profile of atherogenic induced hyperlipidemic rats.

Table 2: The effect of *CC* on Serum lipid profile

Group	Treatment	TC	TG	LDL	HDL	VLDL
I	Normal Control	83.86±1.02	78.01±1.01	26.00±1.06	36.11±1.08	19.32±1.12
II	Hyperlipaedemic Control	169.17±1.10	154.10±1.01	55.10±1.10	20.07±1.02	39.62±1.11
III	*CC* 200mg/kg	86.32±1.38*	84.69±2.14*	36.05±1.20*	31.03±0.13*	21.03±0.62*
IV	*CC*400mg/kg	80.35±1.0 *	82.83±0.72*	28.33±1.16*	36.25±1.07*	17.07±1.12*
V	Atovastatin10mg/kg	79.5±1.16**	76.22±1.01**	24.63±2.40*	39.33±1.30*	16.19±1.02**

All the values were denoted as mean±SEM. All the data were statistically evaluated by one-way ANOVA followed by Dunnett's test and values $p<0.5$ were considered to the significant.*p<0.001; and **p<0.01 for control.

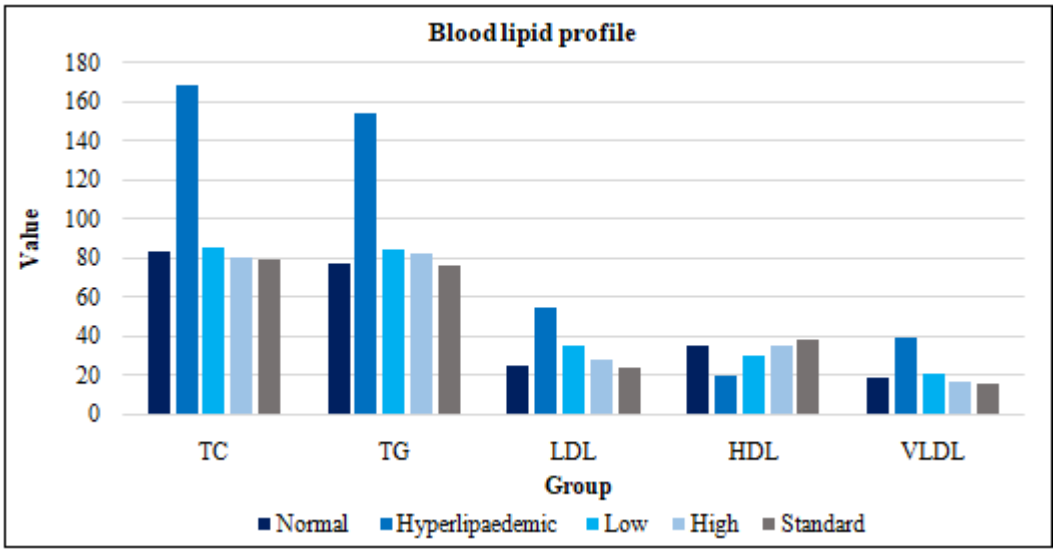

Figure 1: Effect of *CC* on Blood lipid profile

As per table no: 02 and figure no: 01, total cholesterol levels in the hyperlipidemia induced group have significantly increased compared to normal rats. The values have risen to 169.17 ± 1.10 mg/dl compared to Group I (normal rat group), in which values lie in the range 83.86 ± 1.02 mg/dl. This indicates hypercholesterolemia. In the treatment group treated with *CC* (200 mg/kg) and *CC*(400 mg/kg), the values are reduced to 86.32 ± 1.38 (P <0.001) and 80.35 ±1.0 mg/dl

($P < 0.01$), respectively. There is a significant reduction in total cholesterol values in *CC* treatment group. On the other hand, atorvastatin also has significantly reduced serum total cholesterol levels to 79.5 ± 1.16 mg/dl ($P < 0.001$).

The TG levels have reached as 154.10±1.01mg/dl in hyperlipidemia induced group compared to normal rats where the values are 78.01±1.01mg/dl. This indicates triglyceridemia. In the group treated with *CC* (200 mg/kg) and (400 mg/kg), the values are significantly reduced to 84.69±2.14*mg/dl ($P < 0.01$) and 82.83±0.72mg/dl ($P < 0.01$), respectively. In the atorvastatin treated group, the values are reduced to 76.22±1.01mg/dl ($P < 0.001$) [Table No: 02 and Figure No: 01].

LDL-cholesterol in atherogenic induced group has significantly increased to 55.10±1.10mg/dl compared to normal rat group, 26.000±1.06mg/dl. In the group treated with *CC* (200 mg/kg) and (400 mg/kg), the values were reduced to 36.05±1.20and 28.33±1.16 mg/dl ($P < 0.001$), respectively. There is a significant reduction in LDL-cholesterol values in *CC* treatment group. atorvastatin has significantly reduced LDL-cholesterol level to 24.63±2.40mg/dl ($P < 0.001$) [Table No: 02 and Figure No: 01].

HDL-cholesterol in atherogenic induced group has significantly decreased compared to normal rats. The values have reduced to 20.07±1.02mg/dl compared to normal rat group, 36.11±1.08mg/dl. In the group treated with *CC* (200 mg/kg) and (400 mg/kg), the values were 31.03±0.13 ($P < 0.01$) and 36.25±1.07mg/dl ($P < 0.01$), respectively. In atorvastatin treated group, the values were 39.33±1.30mg/dl ($P < 0.001$) [Table No: 02 and Figure No: 01].

VLDL-cholesterol in atherogenic induced group has significantly increased to 39.62±1.11mg/dl compared to normal rat group, 19.32±1.12mg/dl. In the group treated with *CC* (200 mg/kg, 400 mg/kg), the values are reduced to 21.03±0.62 ($P < 0.01$) and 17.07±1.12mg/dl ($P < 0.01$), respectively. There is a significant reduction in *CC* treatment group. Atorvastatin has significantly reduced VLDL-cholesterol level to 16.19±1.02mg/dl ($P < 0.001$) [Table No: 02 and Figure No: 01].

4.2 Effect of *CC* on liver lipid profile of atherogenic induced hyperlipidemic rats.

Table 3: The effect of *CC* on liver lipid profile

Group	Treatment	TC	TG	LDL	HDL	VLDL
I	Normal Control	83.70±0.12	91.70±1.27	24.17±1.24	40.07±0.10	19.99±1.18
II	Hypolipidaemic Control	184.10±1.12	184.02±1.10	53.25±2.16	21.10±1.2	41.01±0.17
III	*CC*200mg/kg	90.15±0.06*	99.15±1.21*	38.12±1.05*	32.9±0.9*	27.02±0.10*
IV	*CC* 400mg/kg	84.3±0.68*	82.12±1.12*	26.3±1.02*	36.05±1.4*	19.88±1.00*
V	Atorovastatin (10mg/kg/day)	82.05±1.60*	79.25±1.01*	24.90±1.15*	41.1±1.23*	18.78±0.05*

All the values were denoted as mean±SEM. All the data were statistically evaluated by one-way ANOVA followed by Dunnett's test and values $p<0.5$ were considered to the significant.*p<0.001; and **p<0.01 for control.

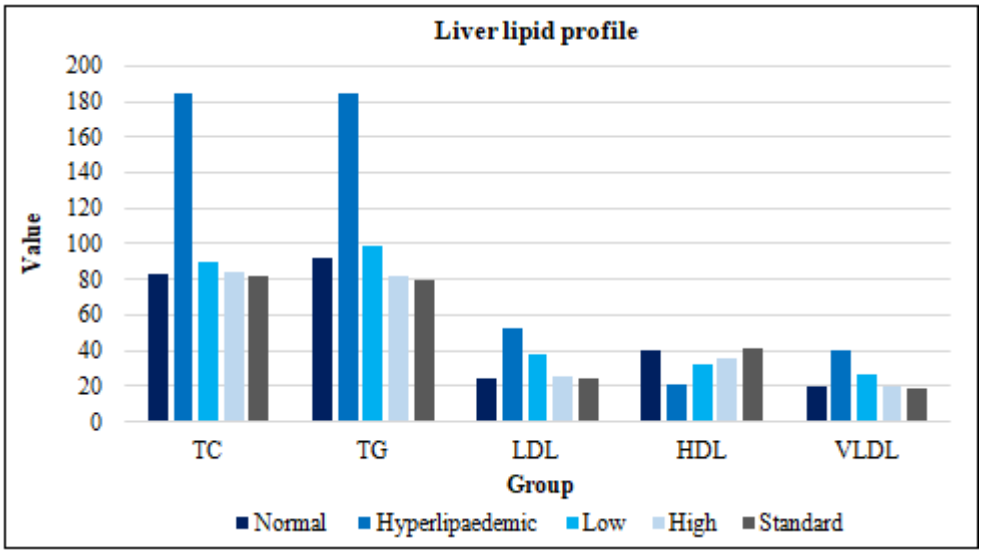

Figure 2: Effect of *CC* on liver lipid profile

As per table no: 03 and figure no: 02, total cholesterol levels in the hyperlipidemia induced group have significantly increased compared to normal rats. The values have risen to 184.10±1.12mg/dl compared to Group I (normal rat group), in which values lie in the range 83.70±0.12mg/dl. This indicates hypercholesterolemia. In the treatment group treated with *CC* (200 mg/kg) and *CC*(400 mg/kg), the values are reduced 90.15±0.06 ($P < 0.001$) and 84.3±0.68mg/dl ($P < 0.01$), respectively. There is a significant reduction in total cholesterol values in *CC* treatment group. On the other hand, atorvastatin also has significantly reduced serum total cholesterol levels to 82.05±1.60 mg/dl ($P < 0.001$).

The TG levels have reached as 184.02±1.10mg/dl in hyperlipaedemia induced group compared to normal rats where the values are 91.70±1.27mg/dl. This indicates

triglyceridaemia. In the group treated with CC (200 mg/kg) and (400 mg/kg), the values are significantly reduced to 99.15±1.21mg/dl ($P < 0.01$) and 82.12±1.12/dl ($P < 0.01$), respectively. In the atorvastatin treated group, the values are reduced to 79.25±1.01mg/dl ($P < 0.001$) [Table no: 03 and figure no: 02].

LDL-cholesterol in atherogenic induced group has significantly increased to 53.25±2.16mg/dl compared to normal rat group, 24.17±1.24mg/dl. In the group treated with *CC*(200 mg/kg) and (400 mg/kg), the values were reduced to 38.12±1.05and 26.3±1.02mg/dl ($P < 0.001$), respectively. There is a significant reduction in LDL-cholesterol values in *CC* treatment group. Atorvastatin has significantly reduced LDL-cholesterol level to 24.90±1.15mg/dl ($P < 0.001$) [Table no: 03 and figure no: 02].

HDL-cholesterol in atherogenic induced group has significantly decreased compared to normal rats. The values have reduced to 21.10±1.2mg/dl compared to normal rat group, 40.07±0.10mg/dl. In the group treated with *CC* (200 mg/kg) and (400 mg/kg), the values were 32.9±0.90 ($P < 0.01$) and 36.05±1.4/dl ($P<0.01$), respectively. In atorvastatin treated group, the values were 41.1±1.23mg/dl ($P < 0.001$) [Table no: 03 and figure no: 02].

VLDL-cholesterol in atherogenic induced group has significantly increased to 41.01±0.17mg/dl compared to normal rat group, 19.99±1.18 mg/dl. In the group treated with *CC* (200 mg/kg) and (400 mg/kg), the values are reduced to 27.02±0.10 ($P < 0.01$) and 19.88±1.00mg/dl ($P < 0.01$), respectively. There is a significant reduction in *CC* treatment group. Atorvastatin has significantly reduced VLDL-cholesterol level to 18.78±0.05 mg/dl ($P < 0.001$) [Table no: 03 and figure no: 02].

5. Discussion

The reduction in cholesterol may show the increased oxidation of mobilized fatty acids by inhibition or lipolysis.[1, 6, 7]The present investigation exhibited that all atherogenic induced rats displayed hyperlipidemia as shown by their elevated levels of serum and liver cholesterol, triglyceride, VLDL and LDL level. The strong association among the risk of coronary artery diseases (CAD), high levels of LDL-C and low levels of HDL-C has been well established.[7, 12] Atherogenic has been widely used to block the clearance of triglyceride-rich lipoproteins to induce acute hyperlipidemia mostly in rats and it has been used for screening natural or chemical hypolipidaemic drugs. [8, 9]

The results showed that, the *CC* produced a significant reduction in cholesterol level and also it reversed atherogenic induced hypolipidaemic in rats. [Table no:02, figure no:01] Similarly, *CC* at a dose of 200 and 400mg/kg significantly reduced both plasma triglycerides and cholesterol levels.[Table no: 02, figure no: 01] The reduction of total cholesterol by the *CC* at the dose level of 200 and 400 mg kg may be associated with a reduction of LDL level.

This study recommends that cholesterol-lowering activity of the *CC* may increase the fecal excretion of bile acids and neutral sterols with the consequent reduction of hepatic cholesterol because of its use in the biosynthesis of these bile acids. These fractions also slow down the rate of diffusion through the intestinal mucosa thereby decreasing the absorption of cholesterol and triglycerides.

6. Conclusion

The results obtained from the pharmacological screening have led to the conclusions that, *CC* has significant anti-hyperlipidaemic activity. Hence it can be exploited as anti-hyperlipidaemic therapeutic agent or adjuvant in existing therapy for the treatment of hyperlipidemia and hypertension.

References

[1] Castelli WP. Cholesterol and lipids in the risk of coronary artery disease-the Framingham Heart study. Canadian Journal Cardiology. 1988; 4:5–10.
[2] Dhandapani S, Subramanian VR, Rajagopal S, Namasivayam N. Hypolipidemic effect of *Cuminum cyminum* L. on alloxan-induced diabetic rats. Pharmacology Research. 2002 Sep; 46(3):251–5.
[3] High cholesterol - symptoms and causes - Mayoclinic, www.mayoclinic.org.
[4] Igweh JC, Nwagha IU, Okaro JM. The Effects of Menopause on the Serum lipid profile of Normal Females of South East Nigeria. Nigerian Journal of Physiological Sciences. 2005; 20(1–2):48–53.
[5] Keihan Ghatre, Effet Farohi, Effects of cumin extract on oxLDL, paraoxanase 1 activity, FBS, total cholesterol, TGL, HDL-C, LDL-C, in the patients of hypercholesterolemia, International journal of health science, 8(1), 2014; 39-43.
[6] Kellner A, Correll JW, Ladd AT. Sustained hyperlipidemia induced in rabbits by means of intravenously injected surface Active agents. Journal of Experimental Medicine. 93:373-384(1951).
[7] Masaru Sakurai, Jeremiah Stamler, Relationship of Dietary cholesterol to blood pressure: The intermap study, Journal of hypertension.
[8] Pourush Badal, Rajendra Mani Badal. Hypolipidemic activity of Perosolinum cripsum plant in Triton WR-1339 induced rats. Herbal Tech Industry; 89
[9] Schurr PE, Schultz JR Parkinson TM. Triton induced hyperlipidemia in rats as an animal model for screening hypolipidemic drugs. Lipids. 7:69-74(1972).
[10] Shirke SS, Jagtap AG. Effects of methanolic extract of *Cuminum cyminum* on total serum cholesterol in ovariectomized rats. Indian Journal of Pharmacology, 2009 Apr; 41(2):92–3.
[11] Thippeswamy N, Naidu KA. Antioxidant potency of cumin varieties - cumin, black cumin and bitter cumin - on antioxidant systems. European Food Research andTechnology, 2005 May; 220(5–6):472–6.
[12] Yiyi Zhang, Andrew E. Moran, Associations of blood pressure and cholesterol levels during young adulthood with later cardiovascular events, Journal of the American College of Cardiology, 74(3); 2019 July: 330-41.