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# Evaluation of Antihyperlipidemic Activity of Ethanolic Root Extract of *Carica Papaya* in Poloxamer – 407 Induced Hyperlipidemia in Wistar Rats.

**V. Venkateswaran,[1*] Rafeeka Abdul Rassak R.Shanmuga Sudaram ,[1] R.Sambathkumar[1]**
*1. J.K.K.Nattraja College of Pharmacy, Kumarapalayam, Namakkal,Tamil nadu India - 638183.*

## ABSTRACT

To evaluate the Antihyperlipedimic activity of ethanol root extract of *Carica papaya* in wistar rat .The pulverized plant materials were taken up for extraction using hydro alcohol in the proportion of 5:95. The extraction was carried out by continuous cold percolation method Antihyperlipedimic activity was carried out using poloxamer 407 induced hyperlipidemia in wistar rat at the dose level of 100 mg/kg p.o and 200 mg/kg p.o. Oral administration of ethanol root extract of *carica papaya* (ERCP) significantly reduced the level of TC, TG, LDL and VLDL, while increasing ($p< 0.001$) HDL – C levels compared to control and standard drug Atorvastatin 10mg/kg.. Significant lowering of TC and an increase in HDL are very desirable biochemical state for the prevention of atherosclerosis and ischemic condition. The results of this study suggested that (ERCP) possessed potent anti-hyperlipidemic activity in poloxamer-407 induced hyperlipidemia in Wistar rats, as was evident from the reduced levels of TC, TG, LDL and VLDL.

**Keywords:** *Carica papaya*, Poloxamer 407, Antihyperlipedimic, Atorvastatin.

*Corresponding Author Email: vwaran21@gmail.com
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# INTRODUCTION

Hyperlipidemia or Hyperlipoproteinemia involves abnormally elevated levels of any or all lipids and or lipoproteins in the blood. It is the most common form of dyslipidemia which includes any abnormal lipid levels. Hyperlipidemias are divided into primary and secondary subtypes. Primary hyperlipidemia is usually due to genetic causes (such as a mutation in a receptor protein), while secondary hyperlipidemia arises due to other underlying causes such as diabetes. Lipid and lipoprotein abnormalities are common in the general population, and are regarded as amodifiable risk factor for cardiovascular disease due to their influence on

atherosclerosis. In addition, some forms may predispose to acute pancreatitis [1, 2].

The World Health Organization (WHO) reported that the high blood cholesterol contributes to approximately 56% cases of cardiovascular diseases(CVD) worldwide and causes about 4.4 million deaths each year. In India it is presumed that more than 62.4% of the people's death by cardiovascular disease when compared to the year 1990.[3-6]

Hyperlipidemia is a secondary metabolic dysregulation associated with diabetes, but also represents increased risk factor for development of diabetes[7-9]. Besides the cause effect relationship with diabetes, elevated serum level of triglycerides, cholesterol and LDL are risk factors for the premature development of cardiovascular diseases like atherosclerosis, hypertension, coronary heart diseases etc [10]. Hyperlipidemia is deeply involved in the etiology of atherosclerosis. Moreover, results of various studies have revealed that hyperlipidemia is an important risk factor of coronary artery disease. Thus much attention is being given to primary and secondary prevention of hyperlipidemia.

Currently available drugs have been associated with number of side effects. The consumption of synthetic drugs leads to hyperuricemia, diarrhea, nausea, myositis, gastric irritation, flushing, dry skin and abnormal liver function. Medicinal plants are used for various research purposes [11] .

Medicinal plants are believed to be an important source of new chemical substances with potential therapeutic effects and more than 80% of population of developing countries is dependent on traditional folk medicine therapies for treating their ailments. Carica papaya belongs to family caricaceae. all the parts of carcia papaya used for various medicinal purpose in medicine. this plant have potential anti tumor,hepatoprotective activity ,diuretic activity ,anti malarial activity ,antifungal activity and anti amoebic activity. the present study to evaluate the antihyperlipidimic activity root extract of carcia papaya.[12-14]

# MATERIALS AND METHOD

**Plant Material**

This plant was collected from various areas in bulk such as Namakkal, Tamilnadu, India. This plant was authenticated at paint anatomy research center (PARC), west Tambaram ,Chennai Tamilnadu, India.

**Extraction**

The pulverized plant materials were taken up for extraction using hydro alcohol in the proportion of 5:95. The extraction was carried out by continuous cold percolation method. The extracts were then dried in vacuum and they were stored in desiccator and subsequently to a refrigerator.

**Phytochemical screening**

This was done on the different extracts to ascertain the presence of bioactive components present in C. papaya roots. The presence of alkaloids, resins, saponins, glycoside, tannins, flavonoids, cardiac glycoside, steroidal terpenes, anthraquinones and carbohydrates were determined.[15]

**Experimental animals**

Albino wistar rats weight about 180-230gm obtained from J.k.k.Nattraja College of Pharmacy, animal house were used for the study. They were housed, under standard laboratory conditions at room temperature (21ºC±2ºC) and relative humidity of 55-60%. They were fed with standard pellet diet and water *ad libitum*. The study protocol was approved by the Institutional Animal Ethical Committee (IAEC), J.k.k.Nattraja College of pharmacy and experiments were conducted in accordance with guidelines set by the CPCSEA (Committee for the purpose of control and supervision of experiments on animals), 887/PO/Re/S/2005/CPCSEA New Delhi, India.

**Acute Toxicity Studies**

Acute oral toxicity study was performed as per Organization for Economic Cooperation and Development (OECD) guideline 423 method. The Ethanolic root extract of *carica papaya(***ERCP**) 2 g/kg was administered in a single dose by gavage using specially designed mice oral needle. Animals are fasted 3 h prior to dosing (food was withheld for 3 h but not water). Following the period of fasting animals was weighed and test substance was administered. After the test substance administration, food was with held 2 h in mice. Animals are observed individually after dosing at least once during the first 30 minutes, periodically during the first 24 hrs, with special attention given during the first 4 hrs, and daily thereafter, for a total of 14 days.

***In vivo* antihyperlipidemic activity**

Antihyperlipidemic activity of ethanolic root extract of *carica papaya* was examined in Poloxamer-407 induced hyperlipidemic rats.[15] The experimental hyperlipidemia was induced by 300mg/kg of Poloxamer 407 dissolved in cold water (4oC) injected on 14 days, 30 min after the administration of extract and standard ,

**Group 1:** Administered vehicle 1% CMC p.o., served as normal control.

**Group 2:** Administered 300 mg/kg of Poloaxmer 407 in ip ., served as hyperlipidemic control.

**Group 3:** Administered 300 mg/kg of of Poloaxmer 407 in ip. + Atorvastatin 10mg/kg b.w., suspended in 1% CMC p.o.

**Group 4:** Administered 300 mg/kg of of Poloaxmer 407 in ip. + ERCP 100mg/kg b.w., suspended in 1% CMC p.o.

**Group 5:** Administered 300 mg/kg of of Poloaxmer 407 in ip. + ERCP 200mg/kg b.w., suspended in 1% CMC p.o.

At end of the experimental period animal were kept fasted over night blood sample was collected and analysis the TGs, TC, HDL-C, LDL, VLDL, SGOT, SGPT and Atherogenic Index (AI).

Plasma total cholesterol and High Density Lipoprotein–Cholesterol (HDL-C) concentrations were determined using enzymatic kits from Accurex Biomedical Pvt.Ltd., Thane. Triglycerides concentration of Plasma was determined by using Triglyceride kit (Accurex Biomedical Pvt. Ltd., Thane). Low Density Lipoprotein-Cholesterol (LDL-C) concentrations were then determined using the Friedewald equation. SGOT levels were determined by using AST reagent kit (Aspen Laboratories, Baddi, H.P). SGPT levels were determined by using ALT Reagent kit (Aspen Laboratories, Baddi, H.P).

**Statistical Analysis**

Data was expressed as mean ± SEM. Statistical analysis by one-way ANOVA with Tukey's multiple comparison was performed as required using GraphPad Prism version 5.03 for Windows, GraphPad Software, San Diego, CA, USA. $p<0.05$ was considered statistically significant.

## RESULTS AND DISCUSSION

The acute toxicity test was executed as per OECD guidelines adoption 423 in overnight fasted Wistar albino rats at 2000 mg/kg body weight. Oral administration of extracts showed either any sign of clinical abnormality nor any mortality. Hence the sealing doses were considered safe for each extract. One tenth and 1/20$^{th}$of the safe dose was selected for lipid lowering activity.

**Table 1: Preliminary Phytochemical Screening of *Carica Papaya* Root Extract**

| Name of the phytochemical | ERCP Extract |
|---|---|
| Carbohydrates | + |
| Total Phenolic substances | + |
| Glycosides | + |
| Saponins | – |
| Alkaloids | + |
| Proteins and Amino acids | + |
| Tannins | + |
| Terpenoids | – |
| Phytosterols | + |
| Carotenoids | – |

Photochemical screening of *Carica Papaya* root extracts shows the presence of glycosides, flavanoids alkaloids, tannins phenolic and carbohydrates.

Table 2: Effect of *Carica Papaya* Root Extract On Lipid Profile and Liver Marker In Poloxamer 407 Induced Hyperlipidaemia In Rats

| Group | Cholesterol (mg/dl) | TGL (mg/dl) | HDL (mg/dl) | LDL (mg/dl) | VLDL (mg/dl) | AI (mmol/dl) | SGOT (IU/L) | SGPT (IU/L) |
|---|---|---|---|---|---|---|---|---|
| Normal control | 157.10±7.911 | 119.28±8.76 | 47.01±1.522 | 89.9±8.425 | 23.9±3.954 | 0.403.6±0.029 | 23.2±4.464 | 38.5±5.633 |
| Poloxamer 407 | 397.5±44.003$^{###}$ | 298.68±9.215$^{###}$ | 38.016±1.087$^{###}$ | 227.33±27.29$^{###}$ | 66.66±14.82$^{###}$ | 0.895±0.018$^{###}$ | 77.12±6.75$^{###}$ | 65.83±4.42$^{###}$ |
| Atorvas 10mg/kg | 170.85±15.61$^{***}$ | 122.43±4.752$^{***}$ | 44.36±3.934$^{***}$ | 91.10±6.812$^{***}$ | 33.671±4.27$^{***}$ | 0.441±0.043$^{***}$ | 39.51±3.209$^{**}$ | 46.13±3.312$^{**}$ |
| ERCP 100mg/kg | 183.2±26.3$^{***}$ | 165.05±4.742$^{**}$ | 44.26±2.254$^{***}$ | 129.8±20.94$^{**}$ | 36.57±7.83$^{***}$ | 0.571±0.0169$^{**}$ | 50.1±2.00$^{**}$ | 50.91±2.97$^{**}$ |
| ERCP 200mg/kg | 203.2±16.07$^{**}$ | 170.43±5.980$^{**}$ | 45.01±0.88$^{**}$ | 203.22±16.07$^{*}$ | 42.33±11.89$^{*}$ | 0.580±0.0156$^{*}$ | 59.11±2.71$^{##*}$ | 54.03±4.16$^{##*}$ |

The values are expressed as mean ± SEM; ### P<0.001,##P<0.01, #P<0.05 when the similarity with normal control is looked for the same. ***P<0.001, **P<0.01, *P<0.05 when compared to hyperlipidemia control and Atorvastatin 10 mg.

The mechanism of P-407 in hyperlipidemia is enhanced activity of Microsomal 3-Hydroxy-3-methylglutaryl CoA Reductase. So that Poloxamer 407 significantly increased total cholesterol and triglyceride level (P<0.001).[17]

Poloxomer 407 administration caused acute hyperlipidemia in rats where it significantly increased total cholesterol, TG and VLDL, LDL,SGOT,SGPT ,Artherogenic index decreased in HDL in rats treated with Poloxomer 407 group as compared to normal control group (p<0.001).the root extract of carica papaya were taken for the antihyperlipidemic activity in polaxmer 407 induced

hyperlipidemia in rat at different dose level of extract (100,200mg/kg) significantly reduced the lipid profile and liver marker and also increased in HDL level the dose of 100mg/kg and 200 mg/kg when compared to normal control and standard drug Atorvastatin 10mg/kg.

## DISCUSSION

Preliminary phytochemical screening of ethanolic root extracts of *carica papaya* were done. Result showed the presence of the following phytochemical constituents such as total phenolic substances, glycosides, alkaloids, flavanoids, tannins(table : 1). The acute toxicity study does not show any deviation from the normal behaviour. It is found that the extract is non-toxic and well tolerated. Fromthis,$LD_{50}$isdetermine from that the effective oral dose for the anti hyperlipidemic study was selected. So, the present study was aimed to evaluate the anti-hyperlipidemic activity of the *carica papaya* root extract on Poloxamer 407 induced hyperlipidemia in wistar rats. The Atorvastatin at a dose level of 10mg/kg was used as the standard drug.[18]

The *in vivo* antihyperlipidemic activity was evaluated on Poloxamer 407 induced hyperlipidemic rats. Poloxamer 407 is a nonionic surfactant and is nontoxic to cellular membranes, was used successfully to induce hyperlipidemia in previous studies. It causes these effects by activating HMG- CoA and inhibiting lipoprotein lipase activity). Poloxamer 407 has been utilized in the hyperlipidemic model due to its convenience, reproducibility, and lack of undesirable underlying pathological conditions .[19-20].

The significant reduction in serum cholesterol, TG, LDL,VLDL, AI, SGOT ,SGPT and also increased in total HDL level in the different dose level(100,200 mg/kg) in poloxamer 407 induced hyperlipidemia in rats(table 2). Extract of carica papay showed( $P<0.001$) significant reduction in poloxamer 407 induced hyperlipidemia was compared with normal control and standard drug atorvastatin 10mg/kg.

ERCP also decreased atherogenic index which are Atherogenic coefficient, Cardiac risk ratio and Atherosclerosis index. Atherogenic index are powerful indicators of the risk of heart disease: In this study, we observed that the ERCP significantly reduced atherogenic index. According to (Ikewuch *et al)* lower atherogenic index is protective against coronary heart disease.[21]

Liver damage is always associated with cellular necrosis, increase in lipid peroxidation and depletion in the tissue GSH levels. In addition serum levels of many biochemical markers like SGOT, SGPT, ALP and bilirubin levels are elevated .[22-23]

Serum levels of SGOT and SGPT, the level, are significantly increased ($p<0.01$) in hyperlipidemia control group compared to normal group. Atorvastatin (10mg/kg); ERCP(100, and 200 mg/kg)

pointed out a significant decrease (P<0.001) SGOT, SGPT, level when compared to hyperlipidemia control group. The SGOT and SGPT levels of ERCP showed significant decrease (P<0.001) when compared to Atorvastatin (10mg/kg) treated group. SGOT and SGPT levels significantly reduced.

## CONCLUSION

The carica papaya root extract are found to be of a potential anti-hyperlipidemic activity in poloxamer -407 induced hyperlipidemia in *Wistar* rats and it is observed to reflect a significantly reduction of cholesterol, triglycerides, LDL-C, VLDL-C, and increases HDL-C. The also reduces SGOT and SGPT levels particularly in liver and also reduced the atherogenic index. The result reviewed ERCP have a potent antihyerlipidemic activity may be the presence of phytochemicals. compared to current lipid lowering drug ERCP does not produced any side effect.

## REFERENCES

1. 1.Abbasi PA, Dahmani J, Sahin F, Hoitink HAJ, Miller SA. Effect of compost amendments on disease severity and yield of tomato in organic and conventional production systems. Plant Disease. 2002; 86: 156-161.
2. Grundy SM. Cholesterol and coronary heart disease a new era. Journal of American Medicine. 1986; 256: 2849-58.
3. Gupta R, Gupta VP, Sarna M, Bhatnagar S, Thanvi J, Sharma V, Singh AK, Gupta JB, Kaul V. Prevalence of coronary heart disease and risk factors in an urban Indian population: Jaipur Heart Watch-2. Indian Heart J. 2002; 54: 59-66.
4. Harnafi H, Aziz M, Amrani S. Sweet Basil (*Ocimum basilicum* L.) improves lipid metabolism in hypercholesterolemic rats. Eur J Clin Nutr Metab. 2009; 4: 181-6.
5. Jayashree V, Solimabi W, Kamat SY. Distribution of tocopherol (Vitamin E) in marine algae from Goa, West coast of India. Indian J, Mar. Scie. 1985; 14: 228-229.
6. Abouzari A, Rouhi S, Eslami A, Kaviani B. Comparison of the effect ofdifferent soilless growing media on some growth characteristics of benjamintree (Ficus benjamina). International Journal of Agriculture and Biology.2012; 14: 985-988.
7. Abreu P, Relva A, Matthew S, Gomes Z, Morais Z. High performance liquid chromatographic determination of glycoalkaloids in potatoes from conventional, integrated and organic crop systems. Food Control. 2007; 18:40-44.

8. Abu ZTR, Al Ismail K, Shatat F. Effect of organic and conventional systems on fruit quality of strawberry (fragaria x ananassa duch) grown under plastic house conditions in the Jordan Valley. Acta Horticulture (ISHS). 2007; 741:159-171.
9. Agbenin ON, Marley PS. In-vitro assay of some plant extracts against Fusarium oxysporumsp. Lycopersici causal agent of tomato wilt. Journal of Plant Protection Research. 2006; 46 (3): 215-220.
10. Ahmad AK, Ghulam J, Mohammad SA, Syed MSN, Mohammad R. Phosphorus Solubilizing Bacteria: occurrence, mechanisms and their role in crop production. Journal of Agricultural and Biological sciences. 2009; 1 (1):48-58.
11. Brown SL. Lowered serum cholesterol and low mood: British Journal of medicine.1996; 313: 637-638.
12. Y.Adam . Diuretic Activity of Roots from Carica papayaL. and Ananas comosus L. Int. J. Pharm. Sci. Rev. Res., 23(1), Nov :2013:32;163-167.
13. Sheikhfauziya and R Krishnamurthy. Papaya(Carica Papaya): Source Material For Anticancer. Cibtech Journal of Pharmaceutical Sciences. 2013; 2 (1):25-34.
14. Senthilkumaran Jagadeesh and Shalini N. An Overview of Carica papaya and its Medicinal Uses.RJPBCS;5(2): 641-648.
15. Jigna P, Sumitra C (2006). In-vitro antimicrobial activities of extracts of Launaea procumbns Roxb. (Labiateae), Vitis vinifera L. (Vitaceae) and Cyperus rotundus L. (Cyperaceae). Afr. J. Biomed. Res. 9(2): 89-93.
16. Nash VJ, Johnston TP, Palmer WK . Effects of nicotinic acid on poloxamer 407-induced hyperlipidemia. Pharmacotherapy. 1996 Jan-Feb;16(1):10-5.
17. Johnston TP, Palmer WK. Effect of Poloxamer 407 on the activity of microsomal 3-hydroxy-3-methylglutaryl CoA reductase in rats. J Cardiovasc Pharmacol. 1997; 29: 580-5.
18. Kalpana Patil, Swati Dhande, Vilasrao Kadam. Antihyperlipidemic And Antioxidant Activity Of Aerial Parts Of *Swertia Chirata* (Buch-Ham) In Poloxamer 407 Induced Hyperlipidemic Rats. IJP. 5(3), 2014, 221-226.
19. Kim HY, Jeong DM, Jung HJ, Jung YJ, Yokozawa T, Choi JS. Hypolipidemic Effects of Sophora flavescens and its Constituents in Poloxamer 407-Induced Hyperlipidemic and Cholesterol-Fed Rats. *Biological and Pharmaceutical Bulletin*, 31, 2008, 73–78.
20. Subramaniam S, Ramachandran S, Uthrapati S, Ganamanickam VR, Dubey GP, Anti-hyperlipidemic and antioxidant potential of different fractions of Terminalia arjuna Roxb.

bark against PX- 407 induced hyperlipidemia. *Indian Journal of Experimental Biology*, 49, 2011, 282–288.

21. Ikewuch CJ, Ikewuchi CC. Alteration of Plasma Lipid Profiles and Atherogenic Indices by Stachytarpheta jamaicensis L. (Vahl). *Biokemistri*, 21, 2010, 71-77.
22. Felig P, Marils E, Ohman JL , Cahil Cf. plasma aminoacid level in diabetic ketoacidosis. Diabets 1970; 19: 727-28.
23. Mascolo N, Sharma R, Jain SC, Capasso F. Ethnopharmacology of Calotropis procera flowers. J Ethnopharmacol. 1988 ;22: 211-21.

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