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Research Article

**EVALUATION OF ANTIHYPERLIPIDEMIC ACTIVITY OF
METHANOLIC EXTRACT OF CARICA PAPAYA SEEDS ON
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ABSTRACT

The aim of the present study was to elucidate the role of methanolic extract of carica papaya seeds during hyperlipidemia induced by Triton X100 in rats and antherogenic diet rats (AD). Triton X100 and Antherogenic diet was used to induce acute hyperlipidemia. It is well known that triton X100 elevates the total TC and TG levels by altering the hepatic lipid metabolism. Hyperlipidemic rats treated with Atorvastatin, Lovastatin, low dose and high dose of carica papaya seeds (Methanol extract) showed a significant decrease of serum TG's, cholesterol and significant increase of serum HDL-C levels compared to hyperlipidemia control. The potential of protective effect may be due to the rich source of polyphenols present as a chief chemical constituent but the exact mechanism is still not clear. The findings of the present study revealed that carica papaya seeds in both low (100 mg/kg) and high (200 mg/kg) doses show anti-hyperlipidemic activity against Triton X-100 induced hyperlipidemia. Among all treated groups carica papaya seeds-200 mg/kg shown better protection. So, we can conclude that methanolic extract of Carica Papaya seeds treatment produced a marked anti hyperlipidemic activity when rats were acutely treated. In our study no lethality was observed atleast for the dose and duration used.

Keywords: Hyperlipidemia, Antherogenic, Triton X 100, Carica Papaya.

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INTRODUCTION

Papaya [1-4] juice has an in vitro anti proliferative effect on liver cancer cells, possibly due to lycopene or immune system stimulation. Papaya seeds might contain antibacterial properties against *Escherichia coli*, *Staphylococcus aureus* or *Salmonella typhi* and have contraceptive effects in adult male humans. Papaya seed extract may have effects in toxicity-induced kidney failure.

Arteries are normally smooth and unobstructed on the inside, but in case of increased lipid level, a sticky substance called plaque is formed inside the walls of arteries. This leads to reduced blood flow, leading to stiffening and narrowing of the arteries [5]. It has been proved that elevated higher lipids level, especially cholesterol and triglycerides leads to hyperlipidemia and plasma levels of cholesterol and of LDL are responsible for atherosclerosis in man, and epidemiological data suggests that elevated plasma levels of HDL have a protective effect. So they have been developed many methods previously using some plants extract to increase the protective effect [6-15].

MATERIALS AND METHODS

Chemicals: Methanol, TRITON (Finer laboratories limited), Atherogenic diet and Normal Saline. The experimental protocol has been approved by the Institutional Animal Ethics Committee and by the Animal Regulatory Body of the Government (Regd. No. 769/2011/CPCSEA)

Equipment Round bottom flask, Centrifuge, Autoanalyser.

Animals: Albino Wistar rats of both sex (150-250g).

Experimental designs:

Animals were divided into five groups each having six rats and treated accordingly.

Group 1: Administered vehicle and served as normal control.

Group 2: Fed with Atherogenic diet and served as control.

Group 3: Administered Lovastatin 40mg/kg, p.o., and fed with AD

Group 4: Administered lower dose of M.CPS (100mg/kg), p.o., with fed with AD

Group 5: Administered higher dose of M.CPS (200mg/kg), p.o., with fed with AD

Our experiment was carried out based on the following methods.

- Preparation of seed extract
- Selection of dose
- Standardization of Hyperlipidemic dose of Triton X 100
- Evaluation of anti-hyperlipidemic activity

Method Procedure:

Preparation of seed extract:

The plant of *carica papaya* seeds was dried under shade in room temperature for 3 days and powdered by using hammering method and the powder was used for preparation of methanolic extract in the ratio 5:1 (500ml methanol and 100g powder was taken).

The methanol extract of *carica papaya* seeds was prepared by using Methanol, by maceration method for 72hrs at room temperature. The extract was concentrated by simple evaporation at room temperature. A suspension CPS in 5% (w/v) Carboxyl Methyl Cellulose (CMC) was prepared for oral administration.

Selection of dose:

Acute toxicity dose was given in previous literature [16] that is 5000mg/kg. 1/10th of dose was considered as therapeutic dose and to identify the dose dependent action the 50% and 200% of therapeutic dose was considered as minimum and maximum dose for further pharmacological evaluation in animal model.

Standardization of Hyperlipidemic dose of Triton X 100:

To induce the hyperlipidemia rats were kept in fasting for 18 hrs with excess of water and subjected to triton X 100 at the dose of 300, 400, 500, 600 and 700mg/kg p.o. and the different lipoproteins was evaluated at 24, 48 and 72 hrs. It was observed that Triton X 100 in the dose of 400mg/kg p.o. can induce maximum hyperlipidemia after 48 hrs. Hence 400mg/kg p.o. was considered the ideal dose for induction of hyperlipidemia [17].

Evaluation of anti-hyperlipidemic activity

A) Triton induced method hyper lipidemia: (Fig 1) Wistar Albino Male rats weighing between 200 ± 20 gm were randomly divided into five groups of 06 animals each. Animals were kept fasting for 18 hrs and injected Triton X100 at a dose of 200 mg/kg p.o. prepared in saline solution. According to treatment protocol, the first dose of the drug treatment was given immediately after triton administration to animals from group 2 to 5. Second and third dose was administered after 24 and 44 hrs respectively. After 4 hrs of third dose the animals are used for the study of various biochemical parameters. Blood was collected by retro orbital plexus of the rat under anesthesia and cold centrifugation at 8000 RPM/15min to get the serum and analyzed for lipoproteins like TG's, TC, HDL-C and glucose.

Group 01: Normal control treated with vehicle p.o

Group 02: Hyper lipidemic control treated with Vehicle p.o

Group 03: Treated with *carica papaya* seeds extract lower dose (100 mg/kg)p.o.

Group 04: Treated with *carica papaya* seeds extract higher dose (200mg/kg) p.o.

Group 05: Treated with standard drug Atorvastatin 10mg/kg body weight p.o.

B) AtherogenicDiet(AD)inducedhyperlipidemia:

Thirty male Wistar Albino rats weighing 190to200gm were randomly divided into five groups of six each and kept in their cages for 5days prior dosing to allow for acclimatization to the laboratory conditions. The chronic experimental hyperlipidemia was produced by feeding cholesterol 1%, Cholicacid0.5% suspended in coconut oil 25% once a day for 26days. The drugs were administer in constant volume of 1ml/100gm body weight .The control group animals received the vehicle in the same volume p.o.

Group 1: Administered vehicle and served as normal control.

Group 2: Fed with Atherogenic diet and served as control.

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RESULTS AND DISCUSSION

All results are expressed as mean \pm standard error. The data was Analyzed using one ways of analysis of variance (ANOVA).

The results are shown in the table 1 and Fig 2, the anti hyperlipidemic drug atorvastatin and *Carica Papaya* seeds methanolic extract (100mg/kg and 200 mg/kg) of Serum HDL were 16.11 \pm 0.58, 47.56 \pm 1.55, 44.13 \pm 1.28, 46.56 \pm 1.57 respectively.

Estimation of Serum TC of the anti hyperlipidemic drug atorvastatin and *Carica Papaya* seeds methanolic extract (CPS) (100 mg/kg and 200 mg/kg) were 123.10 \pm 2.44, 91.24 \pm 1.26, 80.68 \pm 1.86, 90.45 \pm 6.57 respectively.

Estimation of Serum TG levels of the anti hyperlipidemic drug atorvastatin and *Carica Papaya* seeds methanolic extract (CPS) (100 mg/kg and 200 mg/kg) were 89.97 \pm 2.88, 37.33 \pm 1.76, 35.27 \pm 2.11, 36.56 \pm 1.37 respectively.

Estimation of Serum glucose of the anti hyperlipidemic drug atorvastatin and *Carica Papaya* seeds methanolic extract (100 mg/kg and 200 mg/kg) were 236.66 \pm 3.52, 126.33 \pm 1.66, 122.76 \pm 4.16, 125.74 \pm 4.86 respectively.

The methanol extract was found to produce significant decrease in Serum TG, Serum TC, Serum HDL and Serum glucose at higher doses tested (200 mg/kg p.o.). The order of activity, increasing of anti hyperlipidemic output was 200mg>100mg. The anti hyperlipidemic activity demonstrated by the text extract of 200mg/kg was significantly lesser than standard drug atorvastatin.

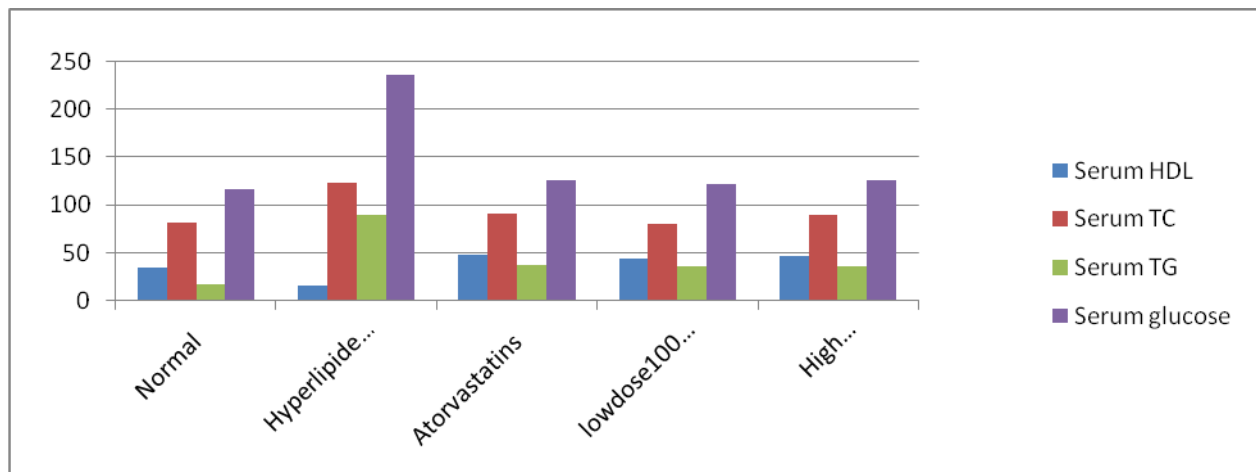


Fig 1: Effect of *carica papaya* seed extract on triton induced rats

Table No.1; Effect of MCPS (100/200mg/kg,p.o, daily for 26 days)/lovastatin (40mg/kg p.o once daily) on serum lipid and glucose parameter levels in rats feed with AD for 26 days.

S. No	Groups	Serum lipid and glucose parameter					
		TG	TC	HDL-C	LDL-C	VLDL-C	Glucose
I	Normal control	59.0±3.67	63.0±3.86	53.4±4.56	23.2±3.83	16.8±3.1	87±6.92
II	AD control	175.8±4.8 ^A	136.8±5.2	14.0±2.00 ^A	81.0±7.89 ^A	36.4±4.97 ^B	116.0±4.78 ^B
III	AD+lovastatin(40mg/kg) treated	128.2±6.3 ^D	95.4±2.01 ^E	38.4±2.13 ^E	60.6±17.2 ^E	22.2±4.39	39.8±2.74
IV	AD+MCPS (100mg/kg)	131.2±6.6 ^D	92.4±5.32	38.8±4.91 ^E	52.4±2.97 ^D	37.2±4.0	95±1.87 ^E
V	AD+MCPS (200mg/kg)	103.4±5.1 ^C	84.8±3.20 ^D	42.8±3.89 ^D	47±3.57 ^C	19.2±2.65 ^E	91.4±3.57 ^D

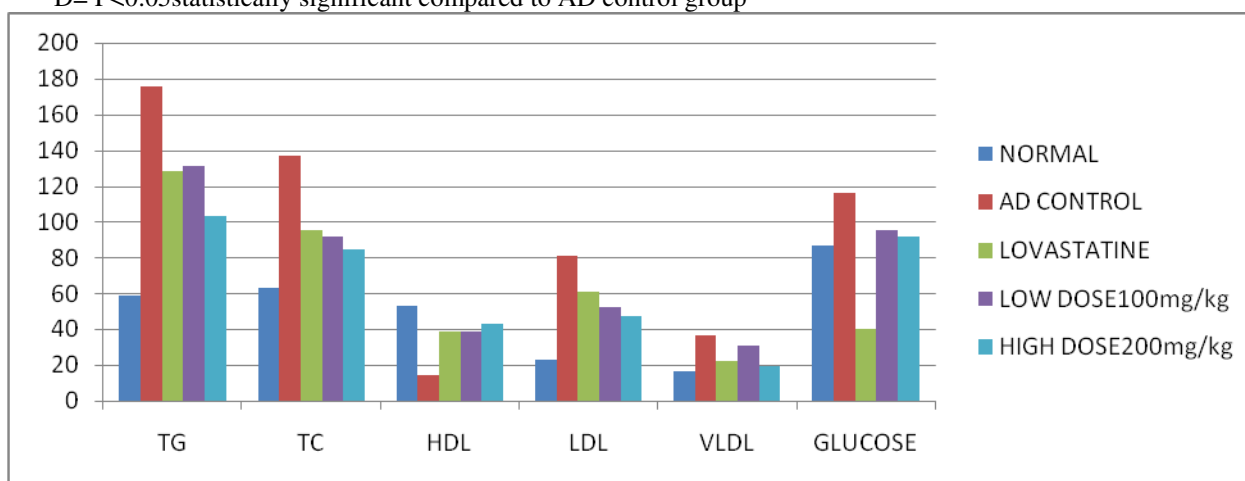
Values are expressed as mean ±SEM for five animal groups

A=P<0.001 statistically significant compared to normal control group

B=P<0.01statistically significant compared to normal control group

C=P<0.001 statistically significant compared to AD control group

D= P<0.05statistically significant compared to AD control group

**Fig 2: Effect of methanolic extract of carica papaya seeds on AD treated rats.**

Values are expressed as mean± S.E.M; n=6, *P<0.05, **P<0.01, ***P<0.001 considered for significance, (ANOVA followed by Dunnett's test).

CONCLUSION

On basis of the investigation and interpretation results, we can conclude that methanolic extract of *Carica Papaya* seeds treatment produced a marked anti hyperlipidemic activity when rats were acutely treated. In our study no lethality was observed atleast for the dose and duration used. From the results, we confirm that there is a significant decrease in Serum TG, Serum TC, Serum HDL and Serum glucose. The results suggested that the effectiveness of extract

depends on effect of active constituents of *Carica Papaya* seed and they showed anti hyperlipidemic activity against in vivo Triton X 100 and antherogenic diet induced hyperlipidemia rats.

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