SUMMARY AND CONCLUSIONS
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Carica Papaya commonly known as 'Papita' (Hindi), PAPAYA (ENGLISH) belongs to the family Caricaceae. Its unripe fruit is used as vegetable and ripe form is taken as a fruit after meals and considered to be good for health. In old literature of traditional medicine, it has been mentioned to possess curative and ameliorative effects in the human body in many diseases specially related to liver, spleen and heart. It reduces obesity and urinary concretions and helps in the digestion. There is almost no report regarding the biochemical effects which this fruit exerts in body when taken in unripe or ripe form. Perusal of existing literature reveals that some works on the seeds and ripe fruit has been done from the point of view of its chemical analysis, physiological and pharmacological effects. Recently effects of feeding ripe and unripe fruits in the normal male albino rabbits have been investigated on certain biochemical parameters of blood lipid profile and organ function tests and reported that both fruit possessed strong protein anabolic, hypolipidemic and hypocholesterolemic effects. Hepatoprotective and tissue protective role of ripe fruit have also been shown in the CCl₄ induced hepatotoxic rabbits which not only normalized serum bilirubin levels but also prevented RBC hemolysis and decreased the cholesterol and triglyceride levels.
In view of the above facts an attempt has been made to investigate hypolipidemic and cardio protective role of ripe *Carica papaya* fruit pulp by taking various parameters of blood lipid profile in hyperlipidemic and normolipidemic rabbits and then cardioprotective role of fruit was investigated in these animals. A preliminary attempt had also been made to evaluate the presence of hypolipidemic active principle in aqueous, alcoholic and ketonic fractions of ripe fruit pulp.

1. Hyperlipidemia was produced in animals by giving them hyperlipidemic diet which consisted of 120 gm Gold Mohar rabbit feed + 200 mg of cholesterol + 20 gm of saturated fat daily to each rabbits continuously for 42 days. There after at 0, 21st and 42nd day of hyperlipidemia production trial, blood collected from median ear vein of the rabbits, were investigated for the various parameters of blood lipid profile, SOD (Superoxide dismutase) and LPO (Lipid peroxide) of the different groups. Sufficient hyperlipidemia was produced in the hyperlipidemic groups A and B. The IHD risk factors STL (Serum total lipid), TC (Total Cholesterol), LDL-C (Low density lipoprotein cholesterol), VLDL-C (Very low density lipoprotein cholesterol) and TG (Triglyceride) were increased many folds while cholesterol scavangers HDL-C (High density lipoprotein cholesterol) and PL (Phospholipid) increased with insignificant difference between group A and B animals.
2. Daily schedule of feeding to animals in different groups during trial period had been as follows: **Hyperlipidemic control** fed on hyperlipidemic diet only, **Hyperlipidemic experimentals** received hyperlipidemic diet + 30gm of deseeded unskinned ripe fruit pulp, **Normal control** were given 120 gm rabbit feed only and **Normal experimentals** were given 120 gm of rabbit feed + 30 gm of ripe fruit pulp. During the trial period the animals of different groups had been on isocaloric diet as control group animals ate about 80% and experimentals between 80-85% of Gold Mohar rabbit feed. Papaya fruit consuming group animals ate the rabbit feed slightly more.

Above schedule of feedings in different groups was continued for a total of 42 days of trial period and blood was collected from the median ear vein at 0, 21st and 42nd day and analysed for various parameters under study. Results obtained are summarised as below:

(a) Regular administration of the ripe fruit pulp resulted in significant increase of body weights in the experimental groups of normals and hyperlipidemics probably may be due to the protein anabolic effect of fruit as reported earlier.

(b) Serum total lipid (STL), Serum total cholesterol (STC),
VLDL-C (very low density lipoprotein cholesterol), LDL-C (Low density lipoprotein cholesterol), TG (Triglyceride) levels decreased manifolds by the regular administration of ripe fruit pulp to rabbits of both normal and hyperlipidemic experimental groups. Slight increase in the high density lipoprotein cholesterol (HDL) and phospholipid (PL) were also noticed in the experimentals.

Such a change in lipid profile brought about by papaya fruit administration is highly significant from clinical point of view as it will prevent the onset of atherosclerosis and reduces the IHD risk factors.

(c) Regular intake of Papaya pulp had shown no influence on SOD (Superoxide dismutase) and LPO (Lipid peroxide) levels.

(d) Lowering of total cholesterol, LDL-C (Cholesterol), VLDL-C and triglyceride (risk factors) level and increase of HDL-C (Scavanger) and phospholipid level is an ideal condition for prevention of any atherogenic developments, fatty liver, ischaemic changes and consequential myocardial infarction. These results suggest that similar studies be done on hyperlipidemic, normal and atherosed human beings. These observations clearly support the traditional medicinal claim that C. papaya
fruit is beneficial for heart, it is cardiotonic and reduces obesity. A compound, carpain, which is also considered to be cardiotonic by pharmacologists is also present in C. papaya fruit.

Chemical composition of C. papaya fruit shows that it contains substantial quantities of alkaloids, sterols and rich amounts of pectins. Pectin has been reported to lower blood cholesterol by reducing its absorption and increases its faecal loss. By binding bile salts, pectins impair not only cholesterol absorption but also impairs digestion and absorption of all fats and suppresses hepatic lipogenesis. Further more, plant sterols also suppress the absorption of dietary cholesterol by competing with cholesterol esterase. Since, these substances are present in plenty in C. papaya this could well explain the Hypocholesterolemic and hypotriglyceridemic effect of this fruit. The possibility of increased hepatoenteric excretion of cholesterol can also not be ruled out.

3. Ischaemia protective role of ripe Carica papaya fruit pulp was investigated by giving subcutaneous injection of isoproterenol (IPT a drug known to cause temporary Myocardial Ischaemia) 5 mg/kg of body weight to each animals of different groups belonging to normals and hyperlipidemics control and experimentals. Blood
samples were collected before IPT administration i.e. 0 hours and 6, 24, 48 hours after IPT injection to analyse the serum enzymes LDH, ALT, CK-MB and AST to assess the extent of ischaemia production. Simultaneously EKG were also recorded at 0, 6, 24 and 48 hours of IPT injections in these animals of different groups. Following results came into light which is summarised as follows:

(a) Highly significant and marked increase in enzyme levels of LDH, AST, CK-MB and ALT the indicator of myocardial insult, were observed in the animals of all the groups after IPT administration. CK-MB levels increased manifold and more as compared to LDH and AST levels in both controls and experimentals of hyperlipidemic and normolipidemic animals. The increase in ALT levels were slight.

(b) As compared to control groups of normal and hyperlipidemic animals the experimental group animals fed on papaya fruit pulp have significantly low AST, LDH and CK-MB levels at 0, 6, 24 and 48 hours after IPT injection which might be due to the cardioprotective role of the fruit pulp.

(c) EKG analysis revealed significant increase in heart rate of all the group animals irregular cardiac rhythm.
83.33% was found in animals not consuming papaya as compared to 50% irregular rhythm in group of animals which consumed papaya. Q wave changes were found as in 67.34% and 100% in control and experimentals (which received papaya) respectively. Similarly ST segment and T wave confirmed the protection of heart by intake of papaya pulp.

(d) All the hyperlipidemic and normolipidemic animals not recieving papaya suffered cardiac failure but all the animals which received papaya were able to sustain the impact of myocardial insult.

4. Presence of active/hypolipidemic principle, their evaluation have been investigated by partially fractionating the ripe papaya fruit pulp as aqueous, alcoholic and ketonic fraction in the tissue (liver) and serum of temporarily produced hyperlipidemia in rats by feeding them intragastrically 30% alcohol and these fractions separately. Control group also run simultaneously. After 16 hours of alcohol ingestion, the blood was drawn directly by puncturing the heart and liver was collected by sacrificing the albino rats. Serum total cholesterol (TC), TG and liver T-C, TG and MDA levels were estimated. Results obtained are summarised and conclusion drawn as:
(a) Alcohol ingestion caused the increase in T-C and TG levels in serum and liver in the control group, animals received alcohol alone as compared to animals fed on normal saline alone in the fasting conditions. The liver MDA levels were found to be high in normal saline fed group animals.

(b) Animals of the groups III, IV and V received 30% alcohol + aqueous, alcoholic and ketone fractions of ripe fruit pulp respectively showed little or no increase in these parameters and had significantly low levels as compared to control group - II animals fed on 30% alcohol alone. Thus, observations suggested the presence of hypolipidemic principle in all the three fractions, the nature of principle seems to be water soluble and lipid soluble.

Maximum hypolipidemic action exhibited by aqueous fraction as compared to the alcoholic and ketonic fractions. Therefore, the active/hypolipidemic principle in the ripe fruit pulp are present in more than one numbers. And fruits when consumed as such showed a cumulative hypolipidemic effects by these principles.

(c) Alcohol feeding increase the biosynthesis and decrease the catabolism of fatty and acids cholesterol. Their accumulation in liver consequently cause hyperlipidemia.
Acetaldehyde the possible metabolite of ethanol forms stable adducts with the hepatic protein and cause fatty liver and hepatic protein drainage.

(d) Low MDA levels in the investigated fractions rule out their lipid lowering effects through increasing TAG and T-C catabolism. Probably active principles may interfere in alcohol induced/increased biosynthesis of TAG and T-C. However, it needs further investigation.

(e) The earlier reported strong protein anabolic effects, increased secretion/excretion of bile salts by the ripe fruit pulp may be possible mode of its action as by providing more amino acids to increase protein biosynthesis substantiating drainage of liver proteins by acetaldehyde as well as increasing cholesterol excretion (bile salts) through enterohepatic circulation. It needs investigation and confirmation.

Present study have shown the hypolipidemic, cardioprotective and hepatoprotective effects of ripe C.papaya fruit pulp and claims regarding its fruit in the old literature of traditional medicine is in conformity to the findings of present study.