INVESTIGATION OF ANTI OBESITY ACTIVITY OF ALCOHOLIC EXTRACT OF ROOTS OF CARICA PAPAYA ON OBESITY INDUCED ANIMAL MODEL

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ABSTRACT
The present study is to evaluate the anti-obesity activity of alcoholic extract of roots of Carica Papaya. Phytochemical screening of crude extract reveals the presence of carbohydrates, proteins, flavonoids, saponins, fixed oils, glycosides and steroids. Hence the presence of bioactive constituents was aimed to explore the anti obesity activity of roots extracts in Atherogenic Diet (AD) induced obesity model in experimental animals i.e. mice. Standard reference Orlistat (10 mg/kg) produced a significant (P<0.05) anti obesity activity in AD induced obesity in mice. Plant extracts at both doses i.e., 100 mg/kg and 200 mg/kg exhibited a significant (P<0.05) antiobesity activity by reducing the body weight, food intake, organ and fat pads weight and serum GLU, CHO, TRG, LDL and VLDL cholesterol levels with an increased HDL levels in AD induced obesity models in mice.

Key Words: Carica Papaya, Atherogenic Diet, Obesity, Orlistat.

INTRODUCTION
Obesity is a chronic metabolic disorder caused by an imbalance between energy intake and expenditure. Over weight and obesity are defined as abnormal or excessive fat accumulation.
that presents a risk to health. Obesity is one of the greatest health threats of this century. Chronic obesity is a problem of epidemic proportions, and is rapidly increasing in prevalence such as coronary heart disease, dyslipidemia, glucose intolerance, diabetics, hypertension and some cancers. Several factors, including lack of exercise, sedentary lifestyles and the consumption of energy rich diets are contributory to the etiology of obesity. Despite the urgent need for safe and efficient therapeutics and the potential size of the market for anti-obesity drugs, the current status for the development of such drugs are still unsatisfactory. Some edible medicinal plants have been used as dietary supplements for body-weight management and control in many countries\textsuperscript{[1]}.

The Carica Papaya is a plant of Caricaceae family, which is abundantly found in India. It has not been studied much for significant chemical as well as biological studies; the roots of this plant were reported to contain polyphenolic compounds that showed antioxidant activity. The plant has been used in the indigenous system of medicine for the treatment of various ailments. Decoction of the bark used for diarrhea and fever. An infusion of the young roots and the flowers is drunk to relieve pulmonary complaints and fever\textsuperscript{[2]}. Leaf decoction used for fever, hemorrhage, wounds and ulcers. The crushed seeds have a diuretic action and are claimed to expel bladder and kidney stones and effective in rheumatism. In the present work, the alcoholic extract of roots of Carica Papaya was evaluated for its anti-obesity activity at the dose of 100 and 200 mg/kg, using an Atherogenic Diet induced animal model\textsuperscript{3}.

**MATERIALS AND METHODS**

**Animals**

Albino mice either sex weighing 16-25g were acclimatized to the experimental room having temperature 23±2°C, controlled humidity conditions and 12:12 h light and dark cycle. Animals were caged in polypropylene cages in a group with maximum of three animals per cage. The mice were fed with standard food pellets and water ad libitum. Atherogenic Diet is used to induce the obesity in the experimental animals which consists of 1% cholesterol, 0.5% cholic acid and 5% Lard oil in addition to normal pellet chow diet\textsuperscript{[4]}.

**Preparation of The Plant Extract**

The plant materials which were used for extraction process were primarily collected from locally and it was thoroughly washed with water to remove soil particles. Further these roots were subjected to air dry, powdered and subjected to the extraction procedure by soxholet apparatus. Evaporated extract was preserved in airtight container for the study\textsuperscript{[5]}.
Acute Toxicity Studies

Acute toxicity study of plant extract was performed as per the Organization for Economic Co-operation and Development (OECD) guideline No. 425 followed by up and down dose method. Based on these agreements, a limit test was performed to categorize the toxicity class of the compound and then main test was performed to estimate the exact 50% of lethal dose (LD50). The dose range of 100 and 200 mg/kg was selected for plant extract. No sign of toxicity observed even at the dose of 2000mg/kg\(^6\).

Preparation of For Induction of Obesity

Albino mice (16-25g) were randomly divided into five groups of six animals in each\(^7\). Group 1 acted as Normal control, received normal pellet chow diet and water for a period of 40 days. Group 2, which received AD + normal pellet Chow diet for a period of 40 days acted as AD control. Group 3 received AD+ orlistat 10 mg/kg, p.o for a period of 40 days. Group 4 received AD+ Lower dose of plant extract (100 mg/kg) p.o for a period of 40 days. Group 5 received AD+ Higher dose of plant extract (200 mg/kg) p.o for 40 days.

Statistical Analysis

The values Mean±SEM are calculated for each parameter. For determining the significant inter group difference each parameter was analysed separately and one-way analysis of variance was carried out\(^12,13\).

RESULTS & DISCUSSION

Excessive energy rich food intake and lack of physical exercise leads to accumulation of body fat, the adipose tissue stores excess energy in the form of lipids, free fatty acid is liberated from lipoproteins by lipoprotein lipase and enters the adipocyte where it is reassembled into triglycerides\(^8\). Cholesterol is a chemical compound that is naturally produced by the body and is a combination of lipid and steroid. About 80% of the body cholesterol is produced by the liver, while the rest comes from our diet. The liver is able to regulate cholesterol levels in the blood stream and can secrete cholesterol if it is needed by the body.

Feeding animals with Atherogenic Diet (AD) has often been used to elevate serum or tissue cholesterol levels to study the etiology of hypercholesterolemia-related metabolic disturbances. Exogenous hypercholesterolemia causes fat deposition in the liver and depletion of the hepatocyte population; it can also cause malfunctioning of the liver, which
apparently follows micro vesicular steatosis due to the intracellular accumulation of lipids. In addition, feeding cholesterol rich diets induces free radical production followed by oxidative stress and hypercholesterolemia. Oxidative stress, which results from impairment of the equilibrium between production of free radicals and antioxidant defense systems, is one of the factors that link hypercholesterolemia with atherogenesis.  

Preliminary Phytochemical Investigations  
The plant extract is subjected for preliminary phytochemical screening and extract found to contain carbohydrates, proteins, flavonoids, saponins, fixed oils, glycosides and steroids.  

Anti Obesity Activity  
Effect of Plant Extract on Body Weight  
In normal control animals the body weight is noted as 22 g on 1st initial day and 45 g on 40th final day model. A significant (P<0.05) increase in final body weight with 79 g is noted in AD induced obese rats. Orlistat (10 mg/kg) significantly (P<0.05) reduced the final body weight to 40 g in this AD induced obese rats. All two doses of plant extract has reduced the final body weight as low dose by 62 g (P >0.05), And high dose body by 68 g (P<0.05) respectively.  

Effect Of Plant Extract on Food Intake  
In normal control animals the daily food intake is noted as 12.5 g/day. A significant increase (P < 0.05) in daily food intake is noted in AD induced obese rats as 23 g/day. Orlistat (10 mg/kg) significantly (P < 0.05) reduced the daily food intake in AD induced obese rats i.e. 14 g/day. Plant Extract significantly reduced. The daily food intake with low and high doses i.e. 20 and 18 g/day (P < 0.05) respectively.  

Effect Of Plant Extract on Serum Biochemical Parameters  
When compared to normal control group the serum biochemical parameters like GLU, CHO, TRG, LDL and VLDL except HDL levels were significantly higher in AD induced obese rats. Orlistat treated group exhibited a significant anti obesity activity by reducing all the biochemical parameters except HDL. Plant extract significantly reduced the serum biochemical parameters like GLU, CHO, TRG, LDL and VLDL levels. Where in HDL levels are increased in a dose dependent manner in AD induced obese groups (Table No.1).
Table No:-1 Anti Obesity Effect of Carica Papaya Roots Extract on Serum Biochemical Parameters In Atherogenic Diet Induced Obesity In Rats.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Glucose (mg/dl)</th>
<th>Cholesterol (mg/dl)</th>
<th>Triglycerides (mg/dl)</th>
<th>H.D.L. (mg/dl)</th>
<th>L.D.L. (mg/dl)</th>
<th>V.L.D.L. (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal control</td>
<td>86±1</td>
<td>58.2±0.5</td>
<td>66.7± 1.7</td>
<td>18.8± 1.0</td>
<td>35.2±1.9</td>
<td>36.1± 1.1</td>
</tr>
<tr>
<td>Disease control</td>
<td>160±3</td>
<td>74.2± 0.1</td>
<td>98.2± 1.2</td>
<td>11.2± 0.8</td>
<td>87.6±2.1</td>
<td>89.5± 1.5</td>
</tr>
<tr>
<td>Orlistat10 mg/kg</td>
<td>105±1</td>
<td>60.3± 0.1</td>
<td>75.5± 1.6</td>
<td>17.1±1.2</td>
<td>39.0±0.5</td>
<td>41.3± 1.4</td>
</tr>
<tr>
<td>Test Extract 20 mg/kg</td>
<td>146±2</td>
<td>69.9± 0.5</td>
<td>86.5± 2.1</td>
<td>13.3± 0.7</td>
<td>65.8± 1.8</td>
<td>68.5± 2.2</td>
</tr>
<tr>
<td>Test Extract 40 mg/kg</td>
<td>139±2</td>
<td>66.2± 0.4</td>
<td>81.4± 1.4</td>
<td>15.9± 0.2</td>
<td>49.2± 2.1</td>
<td>54.5± 1.2</td>
</tr>
</tbody>
</table>

All values are mean ±SEM (n=6); *p< 0.05 when compared to control.

Effect of Plant Extract on Organ And Fat Pads Weights

When compared to normal control group the organ (Liver, Heart, Spleen, Kidneys) and fat pads weights (Peri renal) were significantly higher in AD induced obese groups. Orlistat treated group exhibited a significant reduction in these organ and fat pads weights and exhibited an anti obesity activity. Plant Extract significantly reduced the organ and fat pads weights in a dose dependent manner in AD induced obese groups (Table No.2).

Table:-2 Anti Obesity Effect Of Carica Papaya Roots Extract on Organs And Fat Pad Weights In Atherogenic Diet Induced Obesity In Rats.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Liver(g)</th>
<th>Heart(g)</th>
<th>Spleen(g)</th>
<th>Left Kidney(g)</th>
<th>Right Kidney(g)</th>
<th>Peri Renal Fat Pad.(g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal control</td>
<td>3.98±0.20</td>
<td>0.65±0.05</td>
<td>0.92±0.01</td>
<td>0.74±0.05</td>
<td>0.72±0.05</td>
<td>0.25±0.05</td>
</tr>
<tr>
<td>Disease control</td>
<td>6.90±0.10</td>
<td>1.20±0.05</td>
<td>1.28±0.01</td>
<td>0.84±0.05</td>
<td>0.83±0.05</td>
<td>0.51±0.05</td>
</tr>
<tr>
<td>Orlistat10 mg/kg</td>
<td>4.20±0.10</td>
<td>0.75±0.01</td>
<td>0.98±0.05</td>
<td>0.78±0.02</td>
<td>0.78±0.05</td>
<td>0.29±0.05</td>
</tr>
<tr>
<td>Test Extract 20 mg/kg</td>
<td>5.35±0.10</td>
<td>0.95±0.02</td>
<td>1.15±0.01</td>
<td>0.82±0.05</td>
<td>0.82±0.01</td>
<td>0.49±0.01</td>
</tr>
<tr>
<td>Test Extract 40 mg/kg</td>
<td>4.90±0.20</td>
<td>0.70±0.05</td>
<td>1.10±0.05</td>
<td>0.81±0.02</td>
<td>0.81±0.05</td>
<td>0.35±0.02</td>
</tr>
</tbody>
</table>

All values are mean ±SEM (n=6); *p< 0.05 when compared to control.

CONCLUSION

Preliminary phytochemical investigations on plant extract was noted with carbohydrates, flavonoids, saponins, fixed oils, steroids, alkaloids and glycosides. Standard reference Orlistat produced a significant anti obesity activity in the selected models from this
studies it can be concluded that plant extract with low and high doses exhibited a significant anti obesity activity by reducing body weight, food intake, organ and fat pads weight and serum GLU, CHO, TRG, LDL and VLDL cholesterol levels with an increase in HDL levels in AD induced obesity models in rats.

REFERENCES


