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EVALUATION OF ANTIOBESITY ACTIVITY OF METHANOLIC EXTRACT OF CARALLUMA TUBERCULATA AERIAL PARTS ON HIGH FAT DIET-INDUCED OBESE WISTAR RATS

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ABSTRACT

The present study received a methanolic extract of *Caralluma tuberculata* (MECT) aerial parts on high-fat diet (HFD) induced obese Wistar rats orally. The administration of orlistat at 30 mg/kg of b.w. is a standard treatment. The Wistar rats received MECT, ranging from 150 mg/kg to 300 mg/kg over 49 days. After completion of the experimental period, they tested body weight, food intake, weight of organs (liver, kidney, and heart), body mass index (BMI), and adipose tissue weight. In addition to a histological examination, biochemical markers such as total cholesterol (TC), triglycerides (TG), low-density lipoproteins (LDL), very low-density lipoproteins (VLDL), and high-density lipoproteins (HDL) were measured. The results revealed a significant decrease in body weight, changes in food intake, organ weight, adipose tissue weight, and altered biochemical parameters. The histopathological examination of adipose tissue revealed the alleviating effect of MECT, which is evident by the reduced size of adipocytes.

KEYWORDS: Caralluma tuberculata, Obesity activity, High-fat diet, Orlistat and Histo studies.

1. INTRODUCTION

Obesity is abnormal or excessive fat accumulation that presents a health risk. Excess body weight and elevated body mass index strongly correlate with high bone mineral density.[1] Obesity is a complex condition in which there is an increase in body weight beyond skeletal and physical standards as a result of excessive accumulation of fat in the body.[2] It is associated with increased risk and numerous diseases, including type 2 diabetes, hypertension, osteoarthritis, and cardiovascular and respiratory diseases.[3]

In the present study, *Caralluma tuberculata* (CT) contains pregnane glycosides as a prominent chemical constituent. Pregnane glycosides are responsible for the appetite suppressant activity.[4] So, the objective of the present study is to evaluate the anti-obesity impact of extract of CT in high-fat diet-induced obesity in Wistar rats. The attempt to ascertain the antiobesity activity of this plant will lead to the development of a new herbal formulation for the management of obesity.

2. MATERIALS AND METHODS

2.1. Plant material

Caralluma tuberculata was collected from surrounding areas of Sangareddy, Telangana, India. A taxonomist, Dr. E. Narasimha Murthy, Professor, Department of Botany, Hyderabad, Telangana, verified the plant specimen.

2.2. Drugs and chemicals

Methanol was procured from Hridaan Pharma Chem, Hyderabad, Telangana. Ether provided by Symax Laboratories, Hyderabad. Orlistat was obtained from Rhyme Organics and Chemicals Pvt Ltd, Hyderabad. All other reagents used in the study were analytical grade.

2.3. Preparation of extracts

The 200 gm of air-dried and coarsely ground plant material was defatted with petroleum ether (60-70°c) by Soxhlation for 5 hrs. Then, the solvent-free marc was extracted with the methanol by Soxhlation for three days, and the extract was concentrated in a rotary evaporator. Dried marc was extracted with methanol by maceration in a round bottom flask for 24 hrs. After that, Marc was filtered through muslin cloth, followed by a Buchner funnel. The maceration process was done twice using Marc, and all the filtrates were collected and combined. A rotary evaporator removes the solvent. The % of the extract was calculated. The dried sections were placed in a desiccator and used for further studies.[5]

2.4. Experimental animals

Healthy Wistar rats weighing 180–200 g were used in the study, and the experimental protocol was duly approved by the Institutional Animal Ethical Committee (IAEC). All the animals were kept under standard husbandry

conditions for seven days as per CPCSEA guidelines. Each experimental group has a separate set of animals. All procedures for animal handling were per the guidelines of the CCSEA.

2.5. Acute oral toxicity studies

The animals were fasted overnight, and a single dose of extract was administered. The amount of extract was not more than 2ml/100 gm of body weight. Methanolic and aqueous extract doses were selected from the sequence of 1.75, 5.5, 17.5, 55, 175, 550, and 2000 mg/kg as recommended in OECD guidelines 425. Body weight, signs of toxicity, and mortality were observed after the administration of the extract for 14 days.[6]

2.6. Induction of obesity

A high-fat diet-induced obesity; the composition of the HFD (g/kg diet) was according to the formula of Ramgopal *et al*., with some changes. The components include a regular powdered diet, lard, milk casein, vitamin and mineral mix, yeast powder, corn oil, L-methionine, cholesterol, and sodium chloride.[7]

2.7. Experimental design

The Wistar rats were randomly divided into five groups containing six rats (n=6). Group I was fed a normal diet and the remaining groups were fed a high-fat diet for 49 days. To test the therapeutic activity of *Caralluma tuberculata*, MECT (150 and 300 mg/kg b.w) was suspended in 0.5% carboxymethyl cellulose (CMC) and orally administered HFD-fed to Wistar rats for 49 days [(7)]. All procedures involving laboratory animals were followed per the IAEC regulations approved by the committee. The schedule of dose and diet administration in experimental groups is as follows.

Group I: Control rats Normal pellet for 49 days
Group II: Positive control group HFD for 49 days
Group III: Standard group HFD with orlistat 30 mg/kg b.w. orally from 16th to 49th day
Group IV: Treated group HFD + MECT 150 mg/kg b.w. orally from 16th to 49th day
Group V: Treated group HFD + MECT 300 mg/kg b.w. orally from 16th to 49th da

At the end of the experimental period, the animals were sacrificed by cervical dislocation. The blood was collected for biochemical analysis. The liver, kidney, and heart were dissected, washed in 0.9% ice-cold saline, bottled dry with a paper towel, weighed quickly, and used for further studies.

2.8. Determination of body weight, food intake, and BMI

Throughout the experimental period, the weight gain of Wistar rats was monitored weekly, and the food intake was monitored weekly. BMI was calculated before and after the treatment as an index of obesity.[7]

2.9. Assessment of serum biochemical parameters

The blood sample was collected under anesthesia by cardiac puncture. Blood samples were centrifuged at 3500 rpm for 15 mins at room temperature to separate serum. The clear, non-haemolysed sera were separated using a clean, dry disposable plastic syringe and stored at -20ºC for TC, TG, LDL, VLDL and HDL measurements using diagnostic kits.[8]

2.10. Histopathological examination of adipose tissue

The adipose tissue (fat pads) from each Wistar rat was removed, weighed, and stored at-80°C. For histological analysis, adipose tissue was fixed in a 10% formalin solution and embedded in paraffin. Standard sections of 5 µm thickness were cut, stained using hematoxylin and eosin, and viewed under an optical microscope (40X).[10]

2.11. Statistical analysis

The study results are expressed as the mean ± SD (n=6). Statistical data analysis was performed with a one-way analysis of variance (ANOVA) followed by a Tukey post hoc multiple comparison test. Significant differences were set at p-values lower than 0.005.[11]

3. RESULTS AND DISCUSSIONS

The presence of phytoconstituents, such as alkaloids, flavonoids, saponins, glycosides, quinines, and phenolic compounds in the methanolic extract, could be responsible for the significant anti-obesity activity.

3.1. Acute toxicity studies

The acute toxicity test was performed on the Wistar rats, and no abnormality or mortality was seen with 100, 500, and 1000 g/kg b.w, a dose of test MECT given orally. Hence, the test dose is 150 and 300 g/kg body weight.[12]

3.2. Effect of MECT on body weight

On the 1st day, there was no significant difference between the body weights of all animals in the five groups. On 9th, 18th, 27th, and 35th day, a considerable increase in body weight was observed in the high-fat diet group compared to the control group. The extract of MECT (150mg/kg and 300mg/kg) treated groups showed significant (*P<0.001, $^{\#}$P<0.001) differences in the reduction of body weights compared to the HFD group. The results are shown in Fig 1.

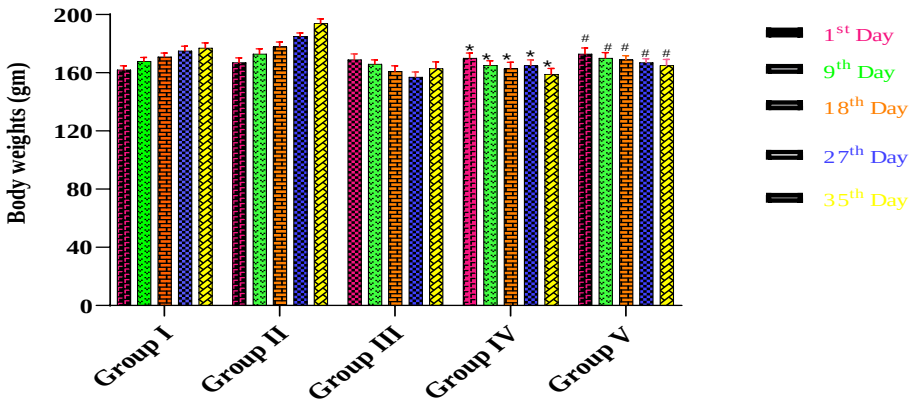

Fig 1: Effect of MECT on body weight.

3.3. Effect of MECT on food intake

The rats fed a high-fat diet (HFD) exhibited a significant increase in food consumption compared to control. As per the results of the studies, treatment with MECT showed a significant (*P<0.001, #P<0.0001) decrease in food consumption compared to HFD Wistar rats.[13] The results are displayed in Fig 2.

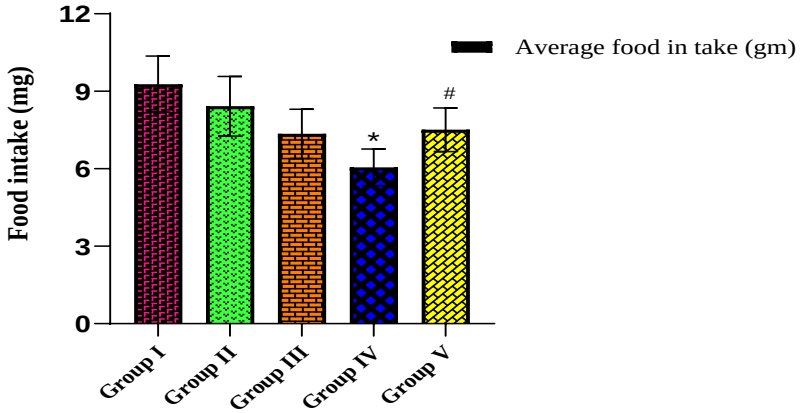

Fig 2: Effect of MECT on food intake in obesity-induced Wistar rats.

3.4. Effect of MECT on the weight of organs

The mean kidney, liver, and heart weights of rats from all groups were obtained. The HFD group had significantly higher liver, heart, and kidney weights than the control group. In our investigations, the MECT extract 300 mg/kg group substantially decreased organ weights (#P<0.0001) compared to the high-fat control group.[14] The results are shown in Fig 3.

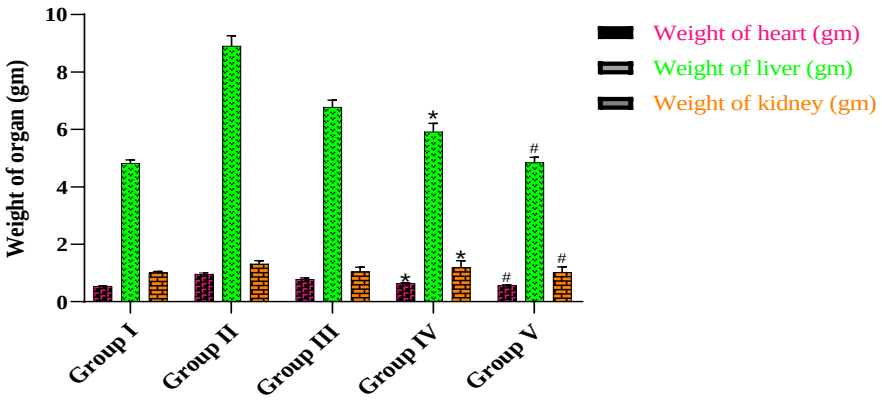

Fig 3: Effect of MECT on organ weights of obesity-induced Wistar rats.

3.5. Effect of MECT on lipid profiles

The HFD group had higher TC, TG, LDL, and VLDL levels than the control group. The HFD group had significantly lower serum HDL levels than the control group. In the present study, MECT treatment led to substantial ($^{\#}P<0.0001$) decreases in serum lipid profiles of TC, TG, LDL, VLDL, and elevated HDL levels compared to HFD. The parameters such as TC, TG, LDL, and VLDL values did not drop significantly in the MECT group compared to the control group.[15] The results are shown in Fig 4.

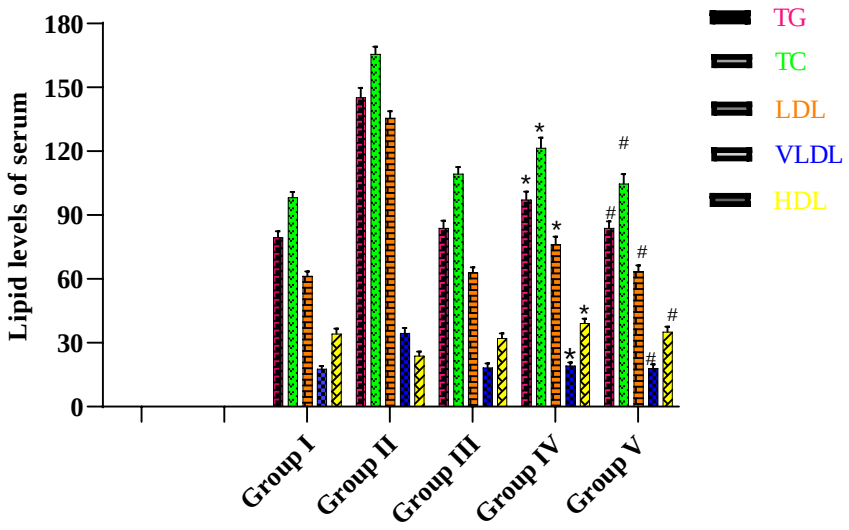

Fig 4: Effect of MECT on lipid levels.

3.6. Effect of MECT on weight of adipose tissue

The size of the fatty cells in the fed group was significantly increased compared to the control group. Whereas Treatment with MECT 300 mg/kg showed a significant ($^{\#}P<0.0001$) decrease in adipose cell size when compared with HFD fed wistar rats.[16] The results are displayed in Fig 5.

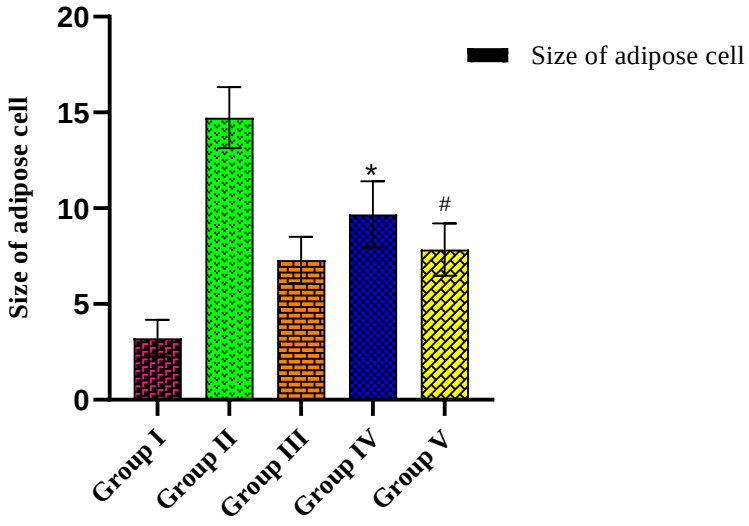

Fig 5: Effect of MECT on adipose cell size.

3.7. Effect of MECT on Body Mass Index (BMI)

The rats fed with HFD exhibit a significant increase in BMI compared to normal control animals. Whereas the groups treated with MECT 300 mg/kg had shown a considerable decrease ($^{\#}P<0.0001$) in BMI when compared with HFD.[17] The results are displayed in Fig 6.

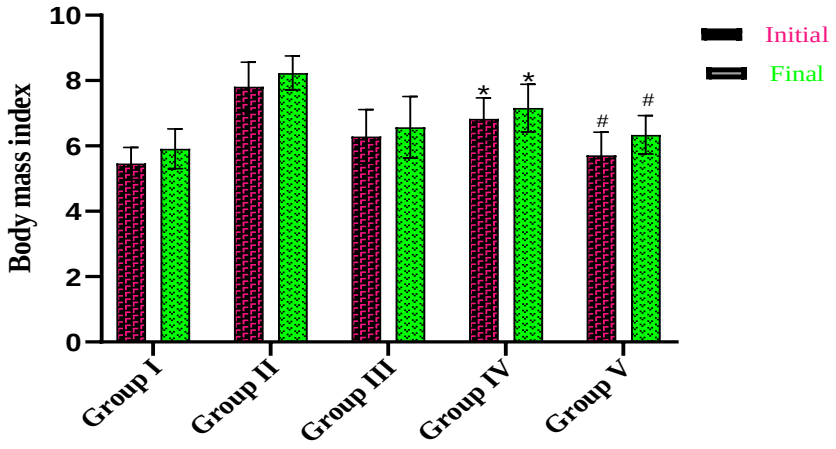

Fig 6: Effect of MECT on body mass index.

3.8. Histopathological studies

The fat deposition and degenerated necrotic cells were observed in the HFD-induced obese group (II) compared to a control group (I). The treatment groups (IV & V) with MECT 150 mg/kg and MCT 300 mg/kg to HFD-induced rats restored the structure of adipocytes and reduced fat deposition. The higher dose of MECT showed almost preserved the standard adipocyte structure [18], and the results are shown in Fig 7.

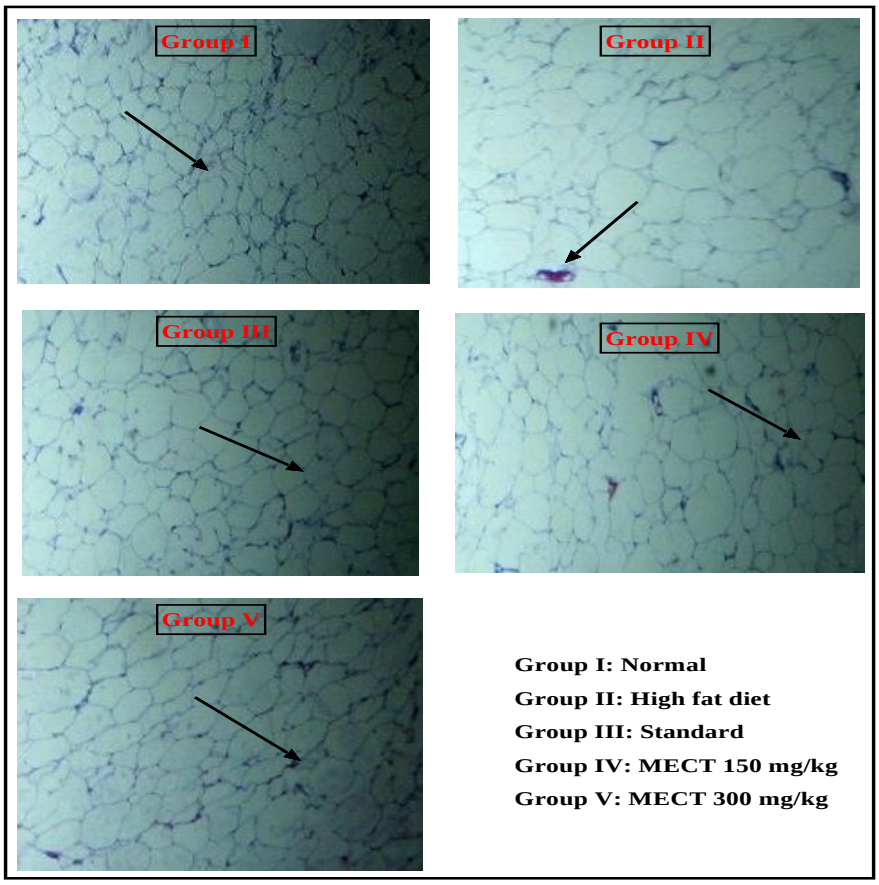

Fig 7: Effect of MECT on histopathology of adipose tissue.

4. CONCLUSION

In conclusion, this study provides evidence of the solid antiobesity properties of the methanolic extract of caralluma tuberculata, as supported by morphological, biochemical, and histological analyses. The potential mechanism behind the anti-obesity properties of MECT

appears to involve a decrease in adipocyte hypertrophy. In conclusion, it strongly suggests that a larger dosage of MECT at 300 mg/kg be considered a viable therapeutic option for addressing obesity.

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