RESEARCH PAPER

Anti-obesity and hypolipidemic potential of *Desmidorchis indica* stem extract against high fructose diet induced rats

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ABSTRACT

Objectives: The purpose of this study was to assess the *in vivo* antiobesity, and hypoglycemic properties of *Desmidorchis indica* stem extract in in Wistar rendered obese by a high-fructose diet.

Methods: Body weight of the animals was recorded and they were divided into 4 groups of 6 animals. Group I: Normal rats fed with the control diet. Group II: High fructose diet-fed animals received a fructose enriched diet for a period of 8 weeks. Group III: High fructose diet fed animals co-administered with hydro-ethanolic extract of *Desmidorchis indica* by oral gavage daily at a dose of 200 mg/kg body weight (Based on effective dosage fixation studies) for 8 weeks. Group IV: High fructose diet fed animals treated with standard drug Orlistat at a dose of 10 mg/kg body weight for 8 weeks. On completion of the experimental period, animals were anaesthetized with thiopentone sodium (50mg/kg). The blood was collected with and without EDTA as anticoagulant. Plasma and serum were separated for the estimation of various biochemical parameters. Adipose tissue used for histological analysis.

Results: Over the course of the trial, the animals' body weight gradually increased. However, compared to rats fed a high-fat diet, administration of *Desmidorchis indica* stem extract resulted in only a slight increase in body weight. Photomicrographs of the control and treated rats, along with morphometric analysis of adipose tissue, were examined. Supplementation with *Desmidorchis indica* reduced both the size and yellowish discoloration of the abdominal region in rats fed a high-fat diet. Comparable effects were observed in rats treated with orlistat. Furthermore, the hydro-ethanolic extract of *Desmidorchis indica* improved serum liver and kidney function markers, reduced plasma malondialdehyde (MDA) levels, enhanced antioxidant enzyme activity, and improved plasma lipid profiles. Histological analysis of adipose tissue revealed better structural preservation in groups treated with *Desmidorchis indica* extract.

Conclusion: These findings demonstrate the anti-obesity, hypolipidemic, and antioxidant properties of *Desmidorchis indica* extract. Further clinical studies are warranted to validate its beneficial potential and support its pharmacological applications.

Keywords: *Desmidorchis indica;* Anti-adipogenic activity; Oxidative stress reduction; Blood glucose-lowering effect; Tissue histology study

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INTRODUCTION

Over the past few decades, obesity, a metabolic disorder, has become a major global public health problem. Globally, the obesity percentage among individuals of all ages is still rising in spite of continuous awareness programs. When the body's adipocytes cause hypertrophy or hyperplasia, obesity results (Prim et al., 2005). Increased morbidity and a shorter life expectancy are clearly positively correlated with obesity (Garruti et al., 2008; Saad et al., 2023). Obesity develops as a result of sedentary lifestyles, environmental and socioeconomic changes (de Freitas Junior and de Almeida Jr, 2017), a decline in physical activity, mental health problems, and the intake of meals high in calories (Rippe et al., 1998). Research indicates that around 10% of children and 1.1 billion people globally suffer from obesity (Nguyen and El-Serag, 2010). More than 1 billion people are overweight, and over 300 million are obese, according to a World Health Organization (WHO) research (Flegal et al., 2012). Triglycerides, cholesterol, and lipid levels are all negatively impacted by obesity. It causes coronary heart disease (Csige et al., 2018), fatty liver (Ng et al., 2014), type 2 diabetes (Puoane et al., 2002), dyslipidemia (Mopuri et al., 2018), musculoskeletal disorders, especially osteoarthritis (Nedunchezhiyan et al., 2022), and an increased risk of cancer (Avgerinos et al., 2019). The pathologic accumulation of lipid droplets within hepatocytes is the basis for the development and progression of non-alcoholic fatty liver disease (Karmakar et al., 2016; Marović, 2008). Over time, this can lead to cirrhosis, steatohepatitis, and end-stage liver disease (Pagotto et al., 2008; Fried et al., 2007). Body weight homeostasis, cholesterol levels, fibrinolysis, and inflammation are all impacted by the dysregulation of hepatic bioactive mediators and cytokines, including adiponectin, leptin, tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6) (Surendran et al., 2020). Obesity remains the leading avoidable cause of mortality in spite of these issues (Cho et al., 2020). The traditional approach to treating obesity mostly consists of following a rigid diet, engaging in regular exercise, and receiving medicinal or surgical therapy (bariatric surgery). However, using such chemical medications may result in unpleasant side effects such as headache, nausea, constipation, sleeplessness, elevated blood pressure and pulse rate, tachyarrhythmias, and angina pectoris (de Freitas Junior and de Almeida, 2017; Youn et al., 2024). In light of these factors, research has been directed toward the creation of safe, tolerant, and user-friendly alternatives to traditional anti-obesity medications, especially in cases when patients treated with these traditional approaches do not react to the therapy. The usage of different medicinal herbs is the foundation of one of these novel strategies. (Ryan *et al.,* 1999; Slovacek *et al.,* 2008; Laouani *et al*., 2024). Natural materials and plants have recently been seen as attractive sources for the development of novel pharmaceutical medicines to treat obesity and its associated consequences. It is generally acknowledged that polyphenols, namely flavonoids and phenolic acids, are the substances implicated in the management of obesity and the disorders that are linked to it. The polyphenols found in plant extracts have been considered a natural remedy for a variety of illnesses, including obesity, for all of these reasons (Van Gaal et al., 2006; Kalai et al., 2021). In order to investigate the anti-obesity, and hypolipidemic effects of the hydro-ethanolic extract of the stem of *Desmidorchis indica*, this study used Wistar rats that were fed high fructose. Morphological, biochemical, and histological data were examined.

MATERIALS AND METHODS

Animals

In this investigation, male Wistar strain albino rats weighing between 170 and 190 grams were employed. They came from Sri Venkateswara Enterprises in Bangalore, India, and were healthy animals. The animals were kept in roomy polypropylene cages with rice husk bedding. Throughout the experiment, the animal room was kept in regular circumstances with a 12-hour light/dark cycle and a temperature of 27±2ºC. It was also adequately ventilated. Every animal was given a regular pellet meal and unlimited access to water. Before being used in the experiment, they were given a week to become used to the surroundings. The experiment was carried out according to the guidelines of the Committee for the Purpose of Control **(SU/CLATR/IAEC/XXIII/37/2024)** and Supervision of Experiments on Animals (CPCSEA), New Delhi, India.

Chemicals

Casein, sucrose, 1-chloro-2,4-dintirobenzene (CDNB), 5,5'-dithio-bis (2-nitrobenzoic acid), ethylenediaminetetra acetic acid (EDTA), nitroblue tetrazolium (NBT), trichloro acetic acid (TCA), thiobarbituric acid (TBA), reduced and oxidized glutathione, nicotinamide adenine dinucleotide phosphate (NADP+/NADPH), and L-ascorbic acid were all acquired from Sigma Chemical Company. The remaining substances utilized in the study were all analytical grade and came from Sisco Research Laboratories and Glaxo Laboratories in Mumbai, India.

Preparation of control and high fructose diet

The control and high-fructose diets were prepared according to the method described by Nandhini *et al.,* (2002).

Standard Orlistat preparation

Orlistat was purchased from a local medical store and freshly prepared by dissolving it in animal ghee to achieve the required concentration (10 mg/kg body weight) (Mohammed & Mutlag, 2023).

Experimental design

Body weight of the animals was recorded and they were divided into 4 groups of 6 animals each as follows.

Group I: Normal rats fed with the control diet

Group II: High fructose diet-fed animals received a fructose enriched diet for a period of 8 weeks (Yuan *et al*., 2020).

Group III: High fructose diet-fed animals co-administered with hydro-ethanolic extract of *Desmidorchis indica* by oral gavage daily at a dose of 200 mg/kg body weight (Based on effective dosage fixation studies) for 8 weeks.

Group IV: High fructose diet fed animals treated with standard drug Orlistat at a dose of 10 mg/kg body weight for 8 weeks.

Collection of samples

On completion of the experimental period, animals were anaesthetized with thiopentone sodium (50mg/kg). The blood was collected with and without EDTA as anticoagulant. Plasma and serum were separated for the estimation of various biochemical parameters. Adipose tissue dissected out and used for histological study.

Determination of marker enzymes

The protein content was estimated by the method of Lowry *et al.,* (1951). The activity of aspartate and alanine aminotransferase was estimated by the method of King (1965a). Serum alkaline phosphatase activity was estimated by the method of Kind and King's (1954). Acid phosphatase activity was measured by the method of Annon (1963). γ- Glutamyl transpeptidase was assayed by the method of Orlowski and Meister (1965). Lactate dehydrogenase was assayed by the method of King (1965a). Urea was estimated by the method of Natelson (1957). Serum creatinine was carried out by alkaline picrate method Boneses and Taussk (1945). Serum uric acid was measured by the method of Fossati *et al.,* (1980).

Estimation of lipid profile

Werner *et al* (1981) developed a method to determine triglycerides. Cholesterol was estimated by Allain *et al.,* (1974). Fatty acids were estimated by using the method developed by Falholt *et al.,* (1973). Zilversmit *et al.,* (1950) developed a method to estimate phospholipid content was estimated by using Fiske and Subbarrow method (1925). Allain *et al.,* (1974) proposed a method to estimate the amount of HDL cholesterol. This LDL and VLDL cholesterol was calculated as per Friedewald's (1972). Atherogenic Index (AI) (Abbott *et al.,* 1988) and Coronary Risk Index (CRI) (Adeneyea and Olagunjub, 2009).

Statistical Analysis

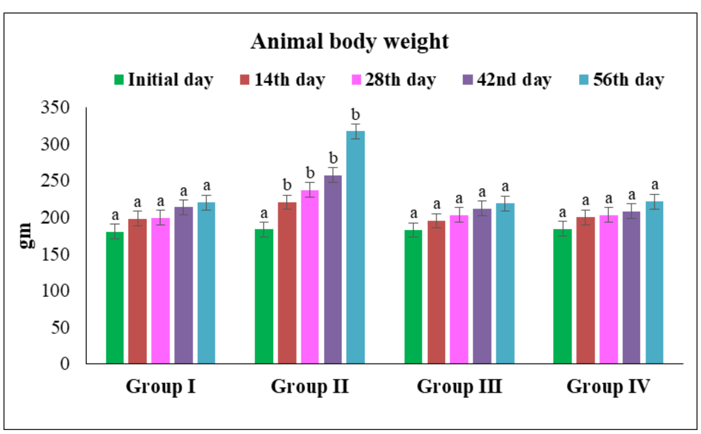
The results were analyzed by SPSS Software ver. 20. Values are expressed as Mean ± SD for six rats. Mean values within the row followed by different letters (Superscript) are statistically significant (P<0.05) from each other, and the same letter is non-significant (P>0.05). The analysis was an ANOVA followed by post-hoc Duncan's multiple range test (DMRT).

RESULTS

This study assesses the anti-obesity activity of the hydro-ethanol extract of *Desmidorchis indica* in high fructose diet induced obese Wistar rats. Orlistat has been approved by the FDA as an anti-obesity agent used to compare the results.

Effect on *Desmidorchis indica* stem extract on body weight in high fructose diet fed Wistar albino rats

Obesity has been associated with decreased antioxidant capacity and increased systemic oxidative stress. Obesity-related chronic illnesses may arise as a result of enhanced systemic oxidative stress caused by the increased formation of reactive oxygen species (ROS) from stored fat, according to recent studies. The initial and final body weights of the rats during the experimental period of 8 weeks are given in figure 1. The body weight of the animals increased progressively during the experimental period. There was a trend for the HFD (High fructose diet) animals to gain more weight than other groups, which was significant as compared with those of the control group. It was observed that the administration of *Desmidorchis indica* stem extract shows only a gradual rise in the body weight of animals when compared to HFD fed rats.



Mean ± SD for six rats is used to express values. SPSS version 20 was used to analyze the data using a one-way

ANOVA and a post-hoc DMRT test. The row's mean values are separated by several letters. The homogeneous subgroups indicated by superscripts are statistically significant ($P<0.05$), whereas the same letter indicates that the other groups were statistically non-significant ($P>0.05$), with a significant threshold of alpha 0.05. Group II was significant when compared to Group I, Group III, and Group IV, however Group I, Group III, and Group IV were not significant when compared to each other.

Figure 1: Effect of *Desmidorchis indica* stem extract on body weight (gm) in control and experimental rats

Effect of *Desmidorchis indica* stem hydro-ethanolic extract in high fructose fed male albino rats (morphological studies)

Photomicrographs of the Morphometric study of white adipose tissue (WAT) and appearance of skin colour of control and treated rats were observed at the end of the study are presented in Plate 1. High fructose diet fed rats appear obese and yellow coloration on abdominal front and back view. Supplementation of *Desmidorchis indica* to HFD fed rats reduced the size and yellow coloration of abdominal area and orlistat treated rats were also observed similarly.

High fructose feeding causes adipocyte hypertrophy and massive lipid accumulation (Plate 2) in white adipose tissue when compared with control rats. The fat accumulated in retroperitoneal, epididymal, and perirenal areas in rats treated with high fructose diet. In *Desmidorchis indica* and orlistat treated rats reduced lipid accumulations in white adipose tissue were observed.

Group I

Group II

Group III

Group IV

Plate 1: Effect of *Desmidorchis indica* extract on morphometric studies of control and experimental rats (Fat accumulation indicates the Circle mark – Yellow coloration)

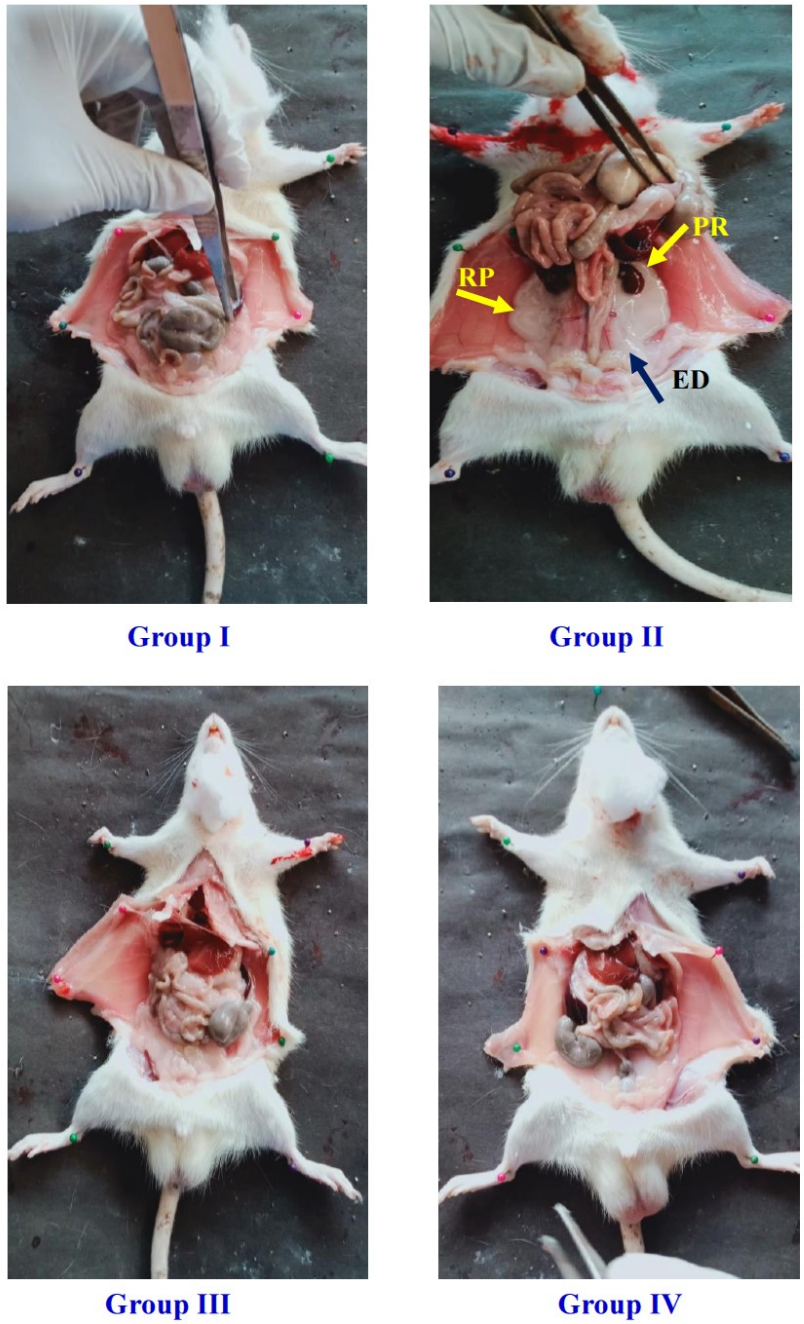
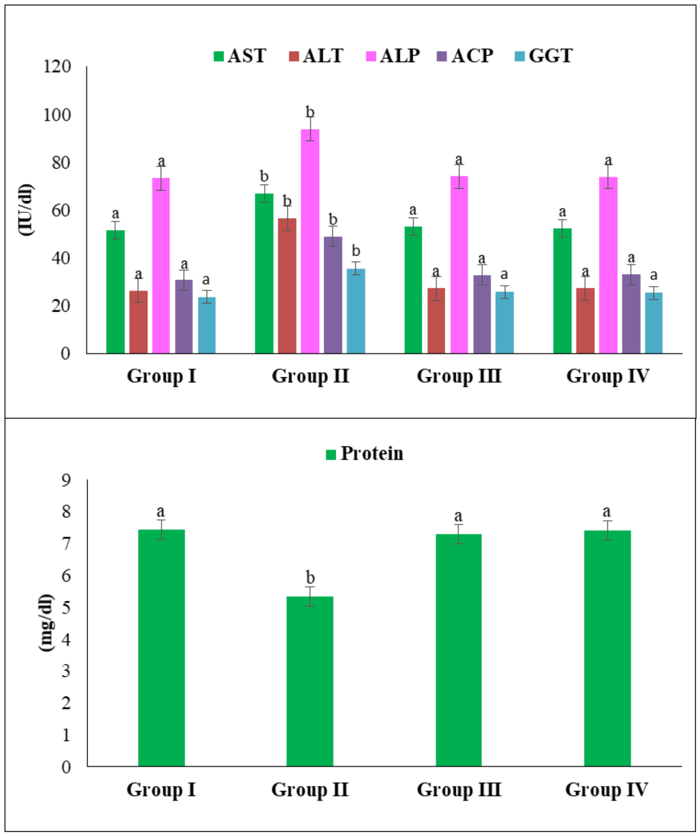


Plate 2: Effect of *Desmidorchis indica* extract on morphometric studies (Dissection view) on fat accumulation (Arrow marks; RP: Retroperitoneal, PR: Perirenal, ED: Epididymal) of control and experimental rats

Effect of *Desmidorchis indica* hydro-ethanolic extract on liver and kidney markers in experimental rats

The effects of hydro-ethanolic extract of *Desmidorchis indica* on serum liver and kidney markers in HFD fed rats are shown in Table 2 and Figure 2a and 2b**.** Hepatic enzymes altered by HFD caused significant rise in marker enzymes AST, ALT, ALP, ACP, LDH and GGT and decreased the protein content. Administration of *Desmidorchis indica* ameliorated the altered levels of the serum enzymes and proteins in HFD fed rats and caused a subsequent recovery towards normalization. HFD caused significant rise in the content of urea, creatinine and uric acid. Supplementation of *Desmidorchis indica* at a 500 mg/kg dose level to HFD fed rats attenuated the altered levels of the urea, creatinine and uric acid.



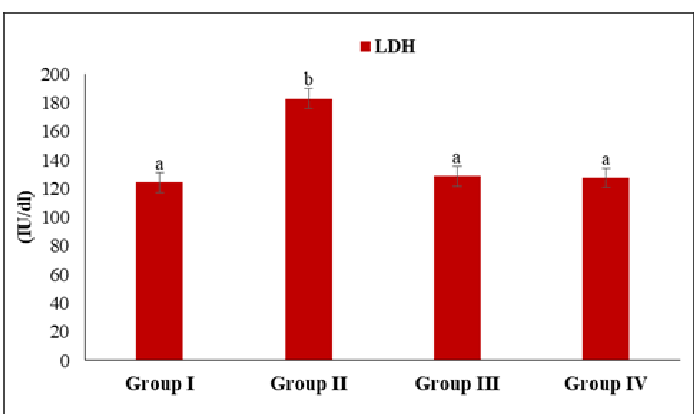
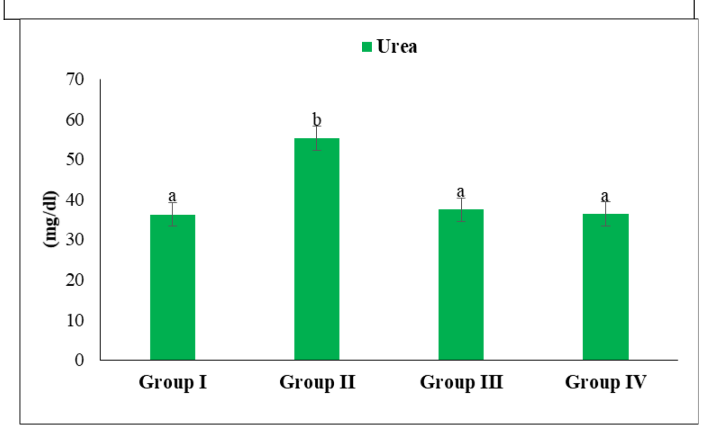
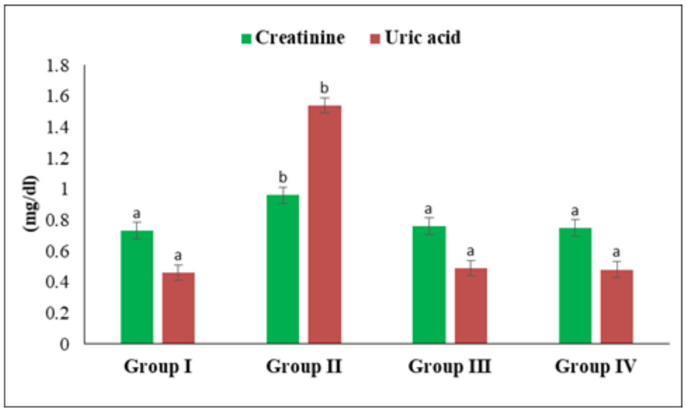


Figure 2a: **Effect of *Desmidorchis indica* on liver markers in experimental rats**





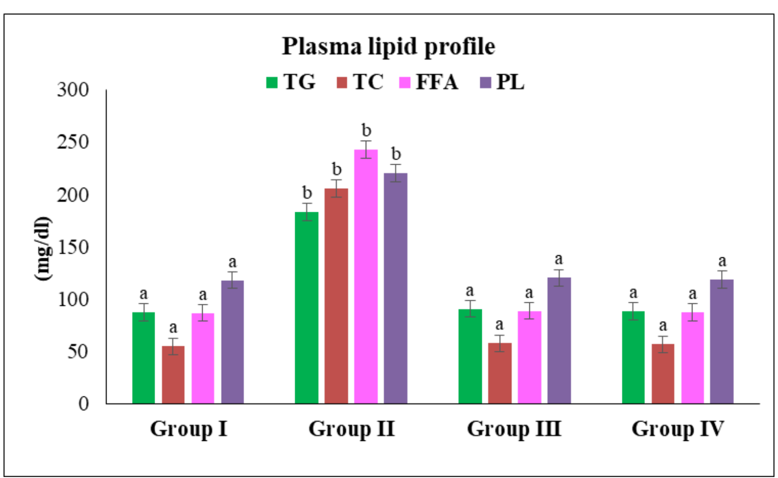
The values are given as Mean ± SD for six rats. Using SPSS version 20, the data were analyzed using a one-way ANOVA and a post-hoc DMRT test. Within the row, mean values are followed by various letters. At the significant level alpha 0.05, homogeneous subgroups denoted by superscripts are statistically significant (P<0.05), whereas the same letter indicates statistical non-significant (P>0.05) differences between the groups. Group II was significant in comparison to Group I, Group III, and Group IV, but Group I, Group III, and Group IV were not significant.

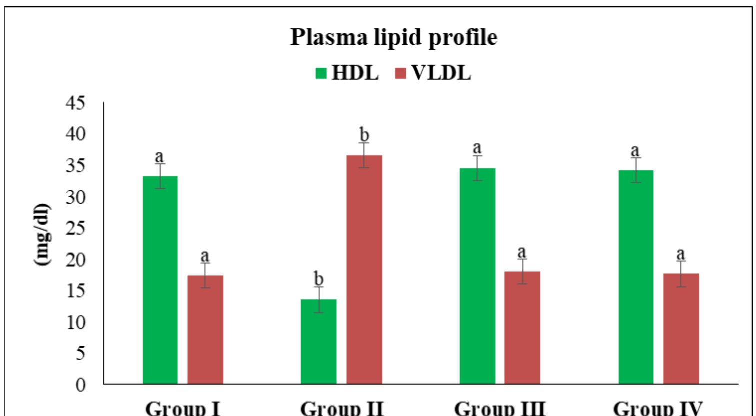
Figure 2b: Effect of *Desmidorchis indica* on kidney markers in experimental rats

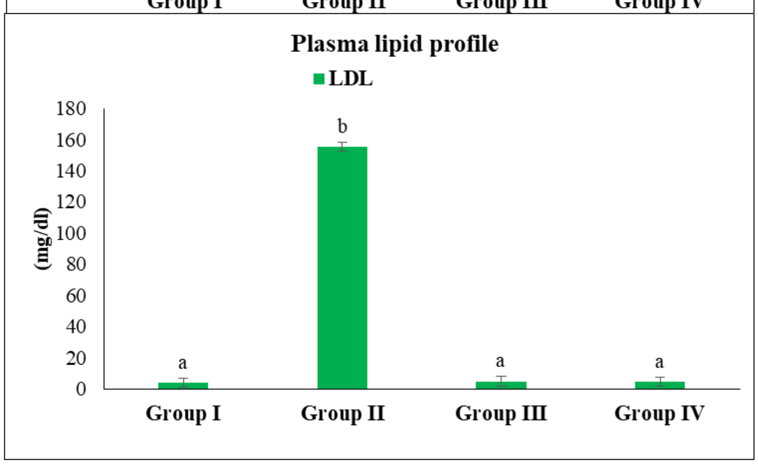
Effect of *Desmidorchis indica* hydro-ethanolic extract on plasma lipids in experimental rats

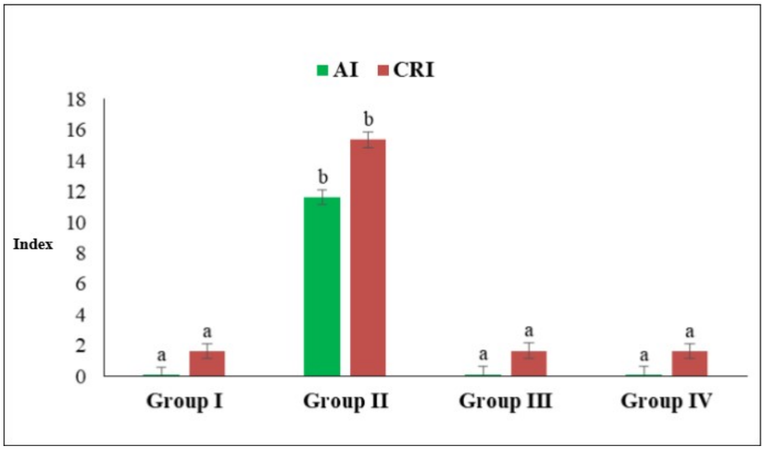
The plasma lipid concentrations in control and experimental animals are given in Table 3 and Figure 3. There was a significant increase in cholesterol, triglyceride, LDL-C and VLDL-C concentrations whereas a decrease in HDL-C was observed in high fructose fed rats. These alterations were reversed and the values were near normal in *Desmidorchis indica* treated rats.

The AI and CRI were significantly (P < 0.05) higher in obese rats than in the normal control one. Oral administration of *Desmidorchis indica* or Orlistat significantly (P < 0.05) lowered both values versus those recorded in the untreated obese counterparts. High fructose supplemented rats had elevated concentrations of free fatty acid and phospholipids in plasma as compared to control rats. *Desmidorchis indica* supplementation normalizes the levels of free fatty acid and phospholipids in plasma of the high fructose fed rats. Lipid profile content is near normal in Orlistat treated animals.




Plasma lipid profile
HDL
VLDL
(mg/dl)
45
40
35
30
25
20
15
10
5
0
a
a
b
b
a
a
a
a
Group I
Group II
Group III
Group IV


Plasma lipid profile
LDL
(mg/dl)
180
160
140
120
100
80
60
40
20
0
a
b
a
a
Group I
Group II
Group III
Group IV



The values are given as Mean ± SD for six rats. Using SPSS version 20, the data were analyzed using a one-way ANOVA and a post-hoc DMRT test. Within the row, mean values are followed by various letters. At the significant level alpha 0.05, homogeneous subgroups denoted by superscripts are statistically significant ($P<0.05$), whereas the same letter indicates statistical non-significant ($P>0.05$) differences between the groups. Group II was significant in comparison to Group I, Group III, and Group IV, but Group I, Group III, and Group IV were not significant. Atherogenic Index (AI) and Coronary Risk Index (CRI)

Figure 3: Effect of *Desmidorchis indica* on plasma lipid profile in experimental rats

Histological observation of adipose tissues

Photomicrographs of the histology of epididymal white adipose tissue (WAT) of the control and treated rats at the end of the study are shown in plate 3. The histology of WAT showed numerous adipocytes tightly packed, clumped together in the obese rats and an increase in cell size of adipocytes, compared to the control which showed normal adipocytes distribution and cells of regular sizes. However, *Desmidorchis indica* supplemented diet indicated histology similar to the control, suggesting inhibition of the hyperplasic growth of the adipocytes. The effects of orlistat treatment exhibited mild change on the histological architecture of the adipose tissue.

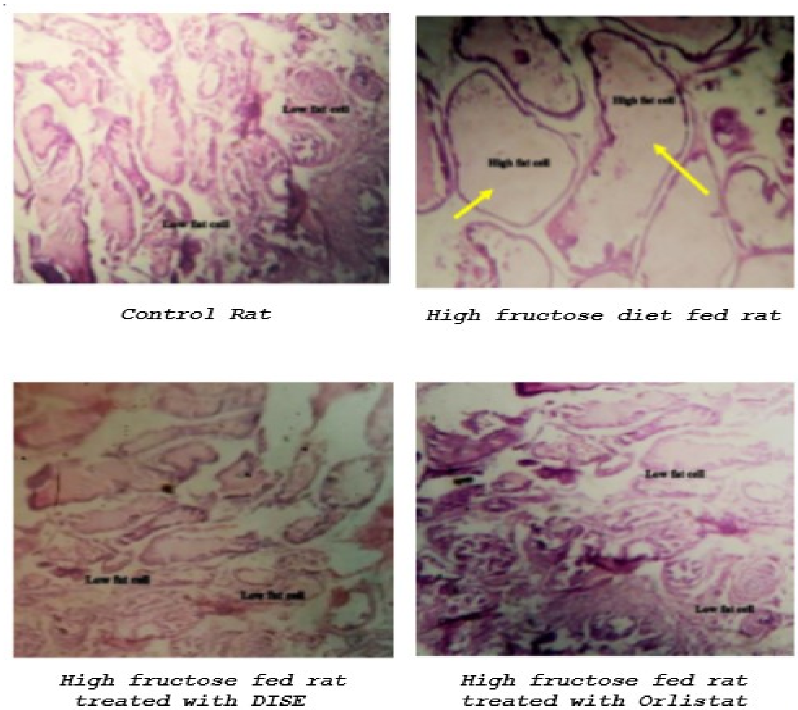


Plate 3: Effect of *Desmidorchis indica* extract in high fructose fed male albino rats adipose tissue (Arrow indicates that increase in cell size of adipocytes due to high fats accumulation)

DISCUSSION

In the current investigation, albino rats were made obese using a recipe. Rats fed HFD acquired a notably greater amount of weight than rats fed the control diet. Using various high fructose diet formulae, several researchers were able to make rats obese (Kim et al., 2005; Milagro et al., 2006), and body weights fell when *Desmidorchis indica* was added. These findings indicated that rats given a high-fat diet were obese, as shown by the morphometric analysis of the rats. Our findings concur with the previous study (Hemmat et al., 2011).

Increased adipose tissue mass, which comes from both an increase in the number and size of fat cells, is a characteristic of obesity. According to Lafontan and Langin (2009), adipose tissue is a dynamic organ that is crucial for energy balance and mass variations in response to the body's metabolic needs. Obesity may occur as a result of abnormally high white adipose tissue (WAT) expansion brought on by excessive calorie intake and decreased energy expenditure (Jo et al., 2009). Rat epididymal adipose tissue is typically regarded as WAT, with a distinct structure and function (Lonçar et al., 1988). According to these findings, *Desmidorchis indica* may stop WAT from building up in rats given a high-fat diet. This outcome was consistent with research by Lim et al. (2012) and Bhandari et al. (2013).

The current data showed a significant increase in the activity of enzymes SGPT, ALP, ACP, and SGOT in the HFD fed rats compared with control rats. According to Basaranoglu et al. (2013), there is a correlation between fructose consumption and the higher incidence of fatty liver. The free fatty acids (FFA) that flow from the adipose tissue into the portal circulation overwhelm the liver. According to Fielding and Frayn (2000), this may directly result in inflammation inside the liver cells, which may then promote the production of more pro-inflammatory cytokines, causing further hepatocyte damage that compromises the integrity of the liver cells. Administration of *Desmidorchis indica* exhibits a significant lowering effect in the activity of SGPT, ALP, ACP, and SGOT in HFD fed rats, a result in agreement with Amin and Nagy (2009) studies.

Few studies have been conducted on the metabolism of lipids in the heart. According to research by Bieger et al. (1984), a rise in triglyceride levels might lead to a reduction in insulin receptors and, consequently, insulin sensitivity. Thorburn et al (1989) found a causal relationship between decreased insulin action and higher circulation triglycerides in HF-fed rats. An action of insulin is to regulate the metabolism of FFA. FFA levels may rise as a result of an insulin malfunction that affects the regulation of FFA metabolism. Impaired insulin activity may be the cause of the metabolic alterations seen. Through substrate competition in the glucose-FFA cycle, elevated plasma FFA concentrations might hinder the effect of insulin on glucose elimination (Boden et al., 1991; Jaradat et al., 2024). Rats given a high fructose supplement showed higher plasma levels of phospholipids and free fatty acids than control rats. *Desmidorchis indica* supplementation normalizes the levels of free fatty acid and phospholipids in plasma of the high fructose fed rats. Lipid profile content is near normal in Orlistat treated animals. These results support the findings of other researchers (Thorburn et al., 1989; Iheagwam et al., 2024) and are in line with previous research (Dharmarajan et al., 2012; Thirunavukkarasu et al., 2004; Nandhini et al., 2002).

In comparison to the control group, which displayed normal adipocyte distribution and cells of regular sizes, histopathological analyses of group II epididymal white adipose tissue (WAT) at the end of the study revealed a large number of adipocytes tightly packed, clumped together, and an increase in adipocyte cell size (high fat accumulation) in the obese rats. However, *Desmidorchis indica* supplemented diet indicated histology similar to the control, suggesting inhibition of the hyperplasic growth of the adipocytes. In rats, adipose tissue develops in two stages: the first is stem cell differentiation, and the second is the increasing filling of the differentiated tiny cells with triacylglycerol (MacKellar et al., 2010). Animals fed with *Desmidorchis indica* showed reduced fat accumulation. Likewise, the standard-treated group was also noted. Adipose tissue histology supported the shifts in total body weight. This suggested that *Desmidorchis indica* supplemented food inhibited adipocyte formation in a manner similar to that described by Atangwho et al. (2012), who found that obese rats given Vernonia amygdalina showed a reduction in adipose size and fat storage.

CONCLUSION

Desmidorchis indica has demonstrated significant potential as an antioxidant, hypoglycemic, and anti-obesity agent when it comes to regulating enzymes in rats on a high-fructose diet. Overall, the current study suggests that *Desmidorchis indica* extract may have anti-obesity, and hypoglycemic, properties. *Desmidorchis indica* may therefore be a useful dietary supplement for the treatment and prevention of obesity. The ingestion of *Desmidorchis indica* has scientific legitimacy because this study has provided supporting evidence for its relevance and anti-obesity capabilities. To have a better understanding, more research is necessary to elucidate the molecular mechanism of the many intracellular signaling pathways. For the best outcome, clinical research and study on *Desmidorchis indica* will result in pharmacological treatments for obesity that are safer and more efficient.

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