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Original Article

Mitigation of Insulin Resistance, Inflammation, Oxidative Stress, and Metabolic Abnormalities by Bavachalcone in High-Fat/High-Fructose Diet-Fed Rats

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ABSTRACT

Background: Obesity is defined by an excess of body fat, together with insulin resistance and dyslipidemia. These factors significantly elevate the risk of acquiring chronic disorders such as Diabetes Mellitus (DM), cardiovascular diseases, neurological disorders, etc. **Objectives:** The goal of the current study was to evaluate bavachalcone's beneficial effects on insulin resistance and obesity in experimental rats fed a High-Fat and High-Fructose (HFa-HFr) diet. **Materials and Methods:** The metabolic complications were induced in rats by HFa-HFr diet feeding for a period of 10 weeks and treated with bavachalcone from the 5th to the 10th weeks. The effects of bavachalcone on various parameters such as food and water consumption, body weight, insulin, blood glucose level, serum biochemical markers, liver oxidative stress markers, and proinflammatory cytokine levels were assessed after treatment. Additionally, a histopathological examination was conducted on the liver tissues. **Results:** The findings showed that the rats fed with the HFa-HFr diet exhibited a notable elevation in blood glucose, insulin level, body weight, fat deposits, and liver marker enzyme activities. These changes were effectively mitigated by the bavachalcone treatment. Furthermore, the HFa-HFr diet resulted in elevated fat accumulation, oxidative stress, and inflammatory biomarker levels. In contrast, bavachalcone treatment successfully reduced insulin resistance, fat deposition, inflammatory, and oxidative stress conditions in the HFa-HFr diet-fed rats. **Conclusion:** The results clearly showed that bavachalcone treatment successfully mitigated the HFa-HFr diet-caused metabolic abnormalities by reducing fat deposition and inflammatory and oxidative stress markers.

Keywords: Metabolic syndrome, Fatty liver, Bavachalcone, Insulin resistance, Inflammation.

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INTRODUCTION

A sedentary lifestyle coupled with the intake of energy-dense foods high in fats and sweets (often referred to as the "Western style" or "junk food" diet) may cause a positive energy balance that leads to obesity. Since obesity accelerates the onset of metabolic abnormalities, Diabetic Mellitus (DM), and Cardiovascular Disease (CVD), it is currently a major global public health concern.[1] Additionally, a chronic inflammatory condition in peripheral tissues and an excess of free radical generation are also associated with obesity.[2,3] Obesity has experienced periodic growth over the last two decades and is steadily evolving into a global crisis that requires immediate attention. Obesity is a persistent metabolic disorder characterized by the over-deposition of body fat. The increasing incidence of obesity can be attributed to increased accessibility and intake of high-calorie foods, coupled with inadequate physical exercise.[4] Consuming an excessive amount of calories, which exceeds the amount of energy expended, leads to adverse alterations in the body's metabolism. Specifically, the production and buildup of store lipids are elevated in adipose tissue, leading to an increase in body mass. In addition, the accumulation of fat is associated by the occurrence of inflammation and oxidative stress in adipose tissue and other tissues.[5]

Diets that contain large amounts of lipids and sugar are commonly considered to be major factors linked to obesity, insulin resistance, and other metabolic complications. Reports have extensively documented the effects of certain foods on insulin sensitivity and fat accumulation.[6] Among other nutrients, fructose is important; in fact, over the last few years, consumption of fructose has significantly increased due to dietary changes, including a rise in the intake of sugar-sweetened beverages and processed foods high in sugar.[7] According to the experimental research, a high-fructose diet is a significant contributing factor to

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metabolic disorders linked to oxidative stress and an exaggerated inflammatory response.[8]

DM, a chronic metabolic disease characterized by hyperglycemia due to deficiencies in insulin production and/or activity, affects approximately 25% of adults worldwide. DM is a most common condition, affecting the elderly population as well as youngsters worldwide.[9] Studies have demonstrated that oxidative stress plays a pivotal role in the etiology of DM. During diabetic conditions, glucose oxidation produces excessive free radicals. Elevated free radical levels and a simultaneous drop in both endogenous and exogenous antioxidants may damage cellular organelles, make insulin resistance worse, and weaken the antioxidant defenses.[10] Insulin resistance, a prominent contributing factor in obesity, is strongly associated with lipid accumulation, oxidative stress, and inflammation. Furthermore, obesity is characterized by an abnormality in lipid metabolism, which results in hyperlipidemia.[11,12] Although the medical sciences have made significant progress, most of the therapies presently employed for obesity have not attained complete effectiveness. Hence, there is a growing interest in alternative medicines, particularly those derived from natural sources, that have the ability to effectively combat obesity.[13,14]

Bavachalcone is a major bioactive compound, mostly present in medicinal plants such as *Psoralea corylifolia* and *Cullen corylifolium*. Several previous studies have already reported the pharmacological properties of bavachalcone, such as inhibition of osteoclast differentiation,[15] anticancer,[16] antimicrobial,[17] and anti-neuroinflammatory and antidepressant[18] properties. A previous study[19] also highlighted the various biological properties of bavachalcone. Despite the numerous pharmacological effects attributed to bavachalcone, there is currently no documented evidence regarding its impact on insulin resistance and obesity. This work examined the impact of bavachalcone on reducing obesity in rats fed a High-Fat and Fructose Rich (HFa-HFr) diet.

MATERIALS AND METHODS

Chemicals and reagents

Bavachalcone and other chemicals were procured from Sigma Aldrich, USA. To determine the biochemical marker levels, the assay kits were purchased from Abcam, USA; Thermofisher, USA; and Elabscience, USA, respectively.

Experimental animals and treatment protocols

The present study utilized adult male Wistar rats weighing 160-190 g body weight. The rats were kept in a controlled atmosphere with a temperature of 22±2°C, a humidity of 55±10%, and a light-dark cycle of 12 hr. Following a 7-day period of acclimation, the animals were provided with either a standard rat food or a high-fat food supplemented with 15% fructose. With the exception of the normal control group, each group of rats was given a high-fat and fructose diet (HFa-HFr diet) for 5 weeks. At the start of the 6th week, rats were also given bavachalcone (25 and 50 mg/kg, respectively) along with the HFa-HFr diet for another 5 weeks. The nutritional ingredients of the prepared HFa-HFr diet include a normal pelletized diet (520 g/kg), casein (65.7 g/kg), coconut oil (13.4 g/kg), butter (275 g/kg), methionine (1.35 g/kg), and mineral mix (22.8 g/kg), respectively.

The experimental groups consisted of a normal control group (Group I), an HFa-HFr diet-only-fed group (Group II), and HFa-HFr diet + bavachalcone (25 and 50 mg/kg)-treated groups (Groups III and IV). Following a 10-week treatment period, the rats underwent an overnight fast, and their blood glucose levels were assessed using a glucometer (AccuCheck, Roche, Germany).

Analysis of Insulin Tolerance Test (ITT) and Intra-Peritoneal Glucose Tolerance Test (IPGTT)

Following the completion of 10 weeks, the rats underwent a 12-hr fast and were then administered a glucose solution intraperitoneally at a concentration of 2 g/kg. This was done in order to conduct the IPGTT. Blood glucose status was determined at 0, 30, 60, 90, and 120 min time period. During the ITT, animals underwent a 6-hr period of fasting and were then administered 0.75 U of insulin per kg into their peritoneal cavity. Blood samples were obtained at time periods of 0, 30, 60, 90, and 120 min to measure the glucose concentration. The glucose status in a plot at a specific time period was utilized to compute the Area Under the Curves (AUC) of ITT and IPGTT.

Collection of samples

Following the treatments, the animals underwent a 12-hr period of fasting and were then sacrificed under anesthesia through cervical dislocation. The blood was obtained through a heart puncture and then centrifuged at 3000 rpm for 15 min in order to separate the plasma. The epididymal, retroperitoneal fat pads, and liver was meticulously removed, rinsed with PBS, and their weight measured. One portion of the liver was stored in a solution of formalin (10%) for histological assessment, while the other portion was homogenized in a phosphate buffer to prepare the tissue homogenate. The homogenate was then centrifuged at 3000 rpm for 15 min. The liquid portion obtained after centrifugation was utilized for subsequent biochemical analyses.

Analysis of the biochemical parameters

The Total Cholesterol (TC), Triglycerides (TG), Low-Density Lipoprotein (LDL), and High-Density Lipoprotein (HDL) was determined using an assay kit (Abcam, USA). The serum activities of the ALT and AST was investigated with the aid of commercial assay kits (Thermofisher, USA). The serum insulin and Free Fatty Acid (FFA) was examined using a kit (Elabscience, USA) following the protocols given by the manufacturer. The HOMA-IR index was determined using the equation shown below: HOMA-IR = insulin level (expressed in μU/mL) X blood glucose level (expressed in mg/dL) / 22.5.

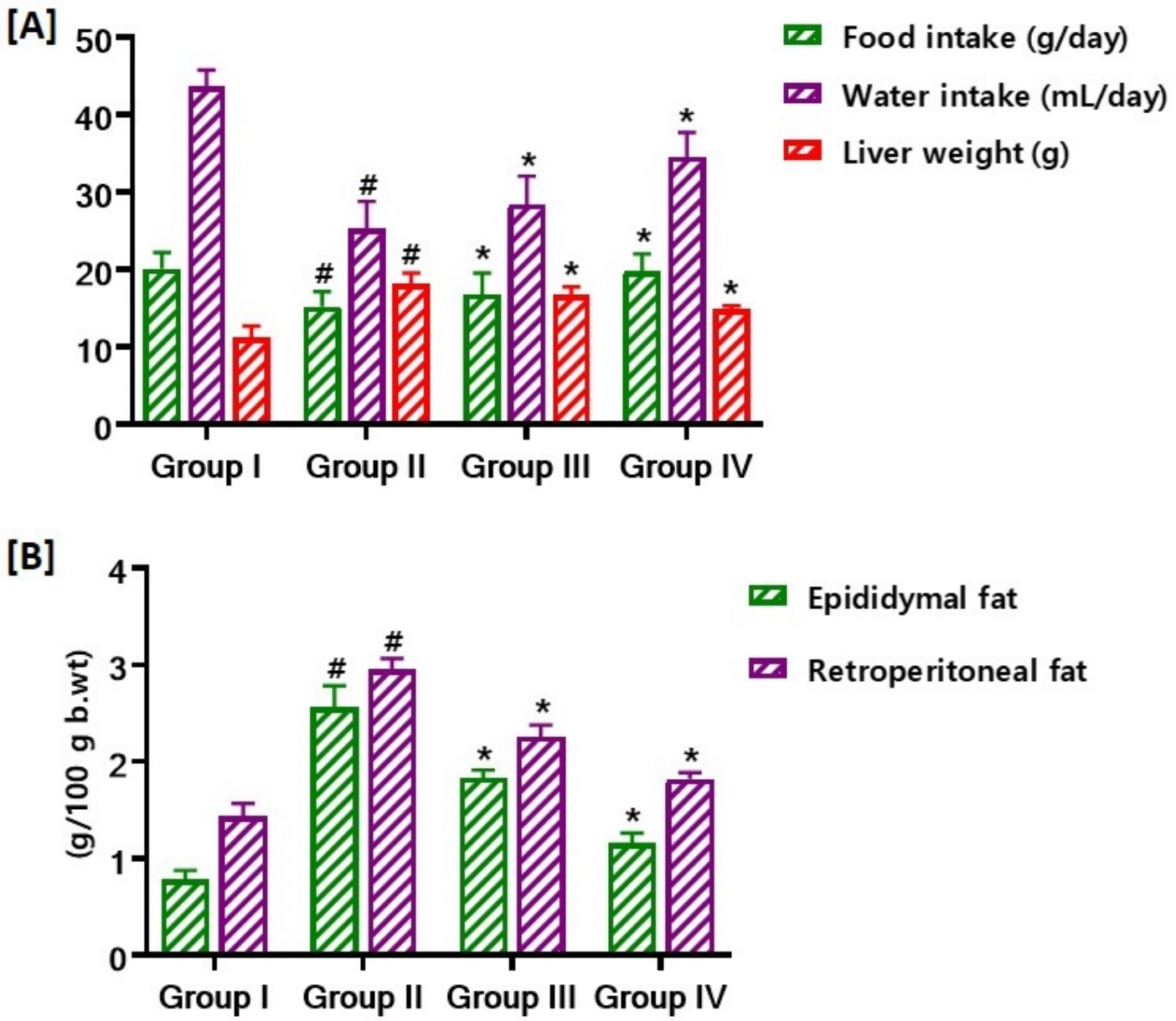

Figure 1: Effect of bavachalcone on the food and water consumption and organ weights in the experimental rats.

The values are given as an average value (mean) ± SD of three repeated assays. The statistical studies of the results are performed using one-way ANOVA and Tukey's multiple comparison tests. An asterisk '#' reveals the statistical significance at $p<0.01$ when compared with the control group. An asterisk '*' reveals the statistical significance at $p<0.05$ when compared with the HFa-HFr diet fed group. [A]: Food and water consumption and liver weight; [B]: Epididymal and retroperitoneal fat weights.

To estimate the lipid profiles in the liver tissue, the hepatic fats were separated by blending the hepatic tissues in a methanol/chloroform solution. Subsequently, the hepatic tissue homogenate underwent centrifugation at 3000 rpm for 15 min, and the resulting supernatant was subjected to lipid extraction by dissolving in a 2-propanol solution containing 1% Triton X100. These dissolved lipids were then utilized to determine the amounts of TC and TG using the assay kits (Abcam, USA).

Analysis of oxidative stress markers

The hepatic tissues were blended together in 10% PBS and then centrifuged at 3000 rpm for 15 min. The resultant liquid portion was utilized to measure the oxidative stress parameters, i.e., MDA, CAT, SOD, and GSH-Px, using commercially available assay kits (Abcam, USA) using the given protocols of the manufacturer.

Pro-inflammatory cytokines

The serum concentrations of pro-inflammatory biomarkers such as NF-kB, IL-1β, TNF-α, and IL-6 were assessed using assay kits

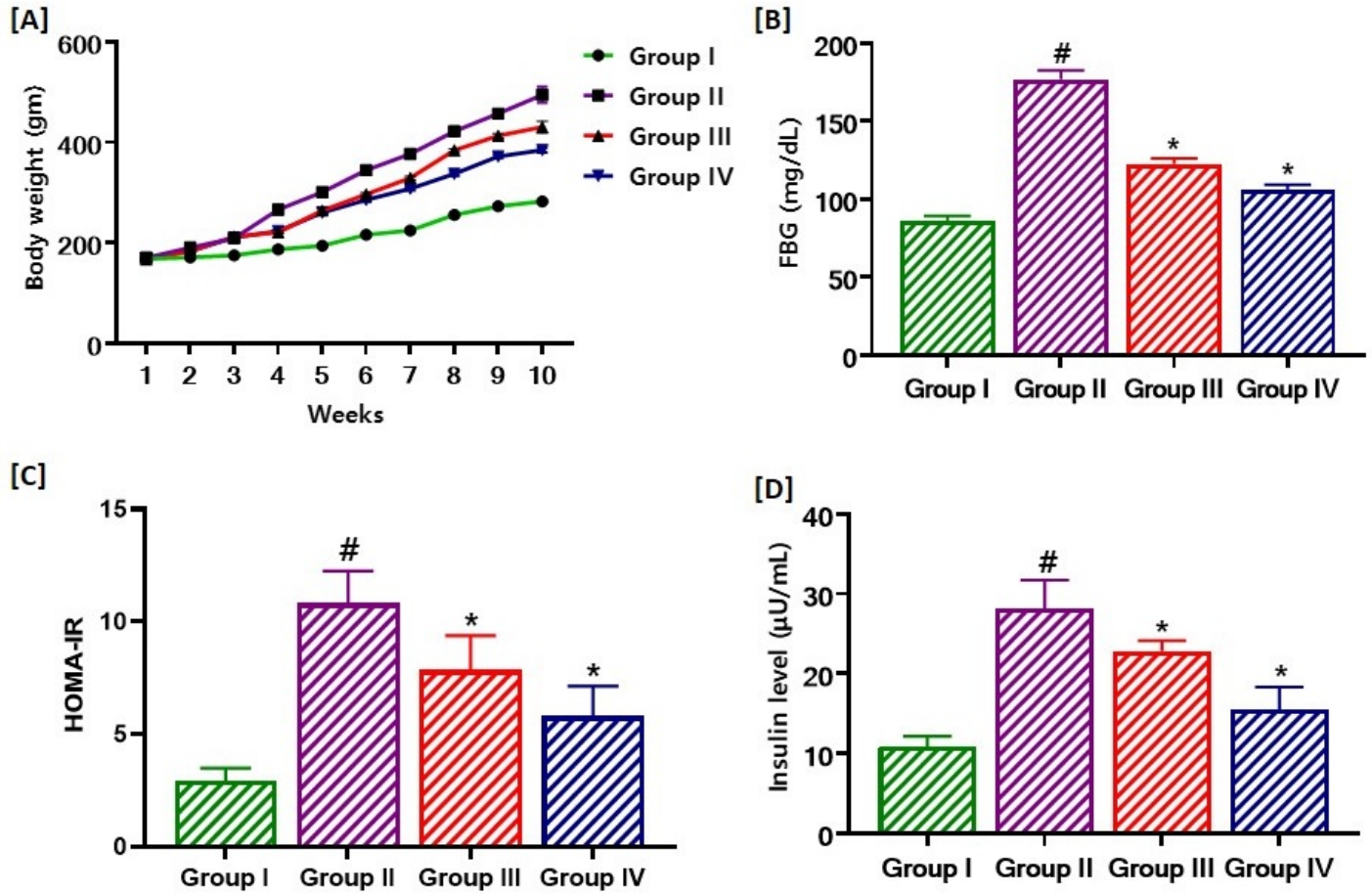

Figure 2: Effect of bavachalcone on the body weight, FBG, insulin, and HOMA-IR levels in the experimental rats.

The values are given as an average value (mean) ± SD of three repeated assays. The statistical studies of the results are performed using one-way ANOVA and Tukey's multiple comparison tests. An asterisk '#' reveals the statistical significance at $p<0.01$ when compared with the control group. An asterisk '*' reveals the statistical significance at $p<0.05$ when compared with the HFa-HFr diet fed group. [A]: Body weight; [B]: Fasting blood glucose; [C]: HOMA-IR level; [D]: Insulin level.

(Elabscience, USA). The tests were conducted in triplicate using the instructions of the kit's manufacturer.

Histopathological analysis

The collected hepatic tissues were treated with the 10% buffered formalin solution, dried out using a series of alcohol solutions of increasing concentration, paraffinized, and then cut into pieces at 5 µm in diameter. The slides were stained using eosin and hematoxylin, and histopathological alterations of the hepatic tissues were examined using an optical microscope.

Statistical analysis

The values are given as the average value (mean) ± SD of triplicate assays. The variations between groups were assessed using a one-way ANOVA and Tukey's multiple comparison tests, conducted with SPSS software. A significance at $p<0.05$ was utilized for all tests.

RESULTS

Effect of bavachalcone on the food and water uptake and organ weights in the experimental rats

The changes in the levels of organ weights and food and water intake of the control and experimental rats are illustrated in Figure 1. The rats fed with the HFa-HFr diet displayed significantly decreased food and water consumptions when compared to the control. However, the treatment with 25 and 50 mg/kg of bavachalcone slightly increased the food and water uptake in the experimental rats. Furthermore, the liver weight, epididymal fat, and retroperitoneal fat weights were drastically elevated in the HFa-HFr diet-fed rats when compared to the control. Captivatingly, the bavachalcone (25 and 50 mg/kg) treatment remarkably reduced the liver weight, epididymal, and retroperitoneal fat weights in the HFa-HFr diet-fed rats. These data suggest that bavachalcone treatment had a significant impact on the physiological alterations in the HFa-HFr diet-fed rats.

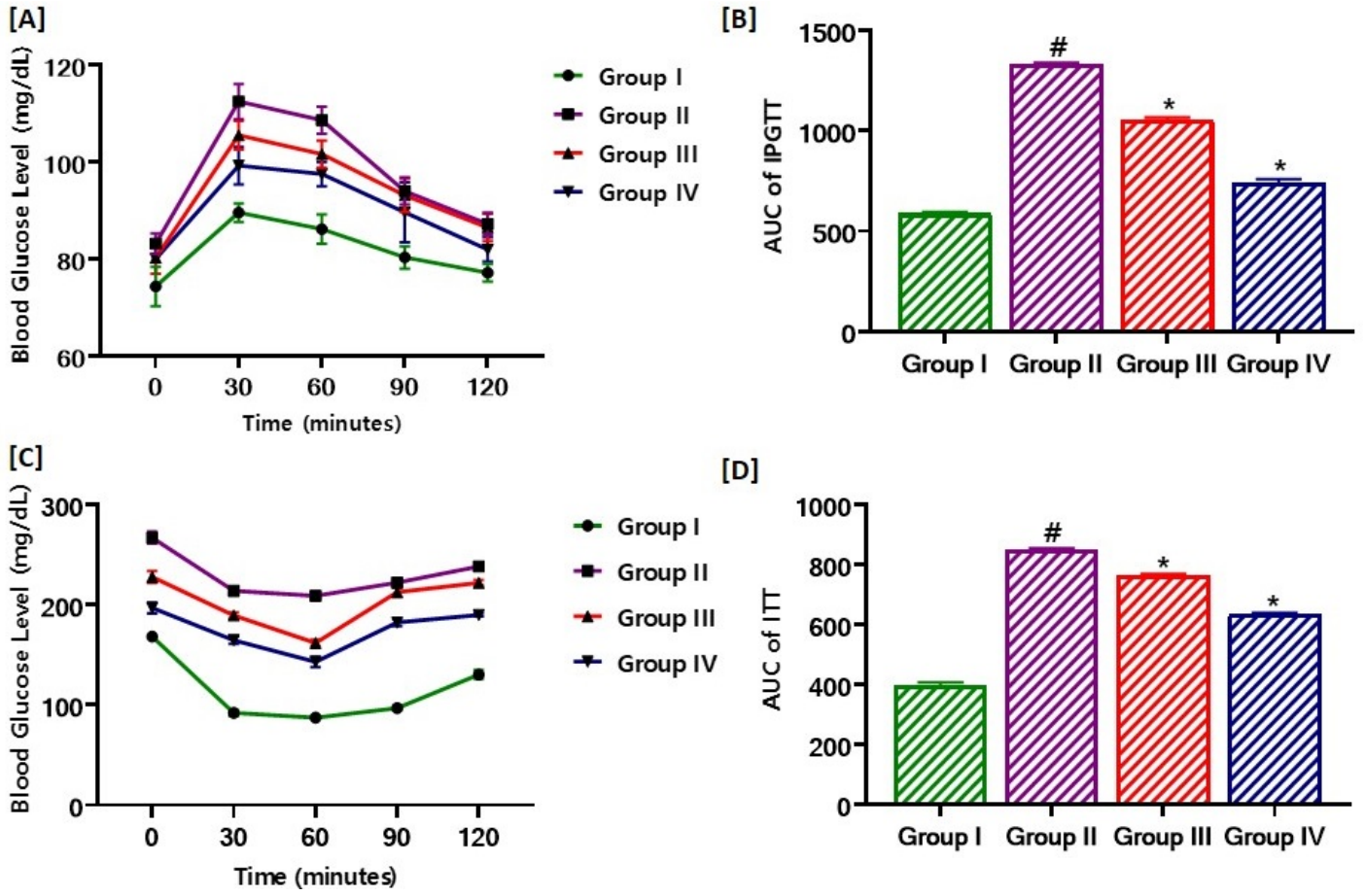

Figure 3: Effect of bavachalcone on the glucose and insulin tolerance in the experimental rats.

The values are given as an average value (mean) ± SD of three repeated assays. The statistical studies of the results are performed using one-way ANOVA and Tukey's multiple comparison tests. An asterisk '#' reveals the statistical significance at $p<0.01$ when compared with the control group. An asterisk '*' reveals the statistical significance at $p<0.05$ when compared with the HFa-HFr diet fed group. [A]: IPGTT level; [B]: AUC from the IPGTT; [C]: ITT level; [D]: AUC from the ITT.

Effect of bavachalcone on the body weight, FBG, insulin, and HOMA-IR levels

Figure 2 shows the body weight, insulin level, FBG, and HOMA-IR levels in the control and treated rats. The body weight, insulin level, FBG, and HOMA-IR of the HFa-HFr diet-fed rats were remarkably augmented when compared with control. Interestingly, the treatment of HFa-HFr-fed rats with 25 and 50 mg/kg of bavachalcone effectively decreased these elevations.

Effect of bavachalcone on the glucose and insulin tolerance in the experimental rats

Figure 3 demonstrates that the HFa-HFr diet-fed rats exhibited significantly elevated FBG status at all the time periods examined (0, 30, 60, 90, and 120 min) compared with the control in the IPGTT. In contrast, the glucose levels of the bavachalcone-treated rats showed a significant decrease at each time point following the glucose injection. In addition, the AUC in the bavachalcone-treated rats was significantly reduced than the HFa-HFr diet-fed rats (Figure 3). In an ITT, the glucose status of the control and bavachalcone-treated rats was considerably lower than the blood glucose of the HFa-HFr diet-fed rats. This indicates that insulin sensitivity was impaired in the HFa-HFr diet-fed rats. The rats treated with bavachalcone at a dosage of 25 and 50 mg/kg exhibited a reduction in glucose levels when compared with HFa-HFr diet-fed rats. Figure 3 provides an analysis of the AUC, which shows that the AUC for the ITT in the HFa-HFr diet-fed rats was considerably higher than that of the normal control. Nevertheless, bavachalcone treatment substantially decreased blood glucose levels.

Effect of bavachalcone on the lipid profiles and liver marker enzyme activities

Figure 4 illustrates the impact of bavachalcone on the levels of lipid contents and liver marker enzymes in the experimental rats. A remarkable elevation in the concentrations of TC, TG, LDL, and FFA was noted in HFa-HFr diet-fed rats as compared to the normal control. However, following a 5-week treatment with bavachalcone, the lipid profiles showed a considerable reduction in comparison to the HFa-HFr diet-fed rats. The HFa-HFr diet-fed rats also revealed a substantial decrease in HDL levels than the control. In contrast, bavachalcone showed an elevation in HDL

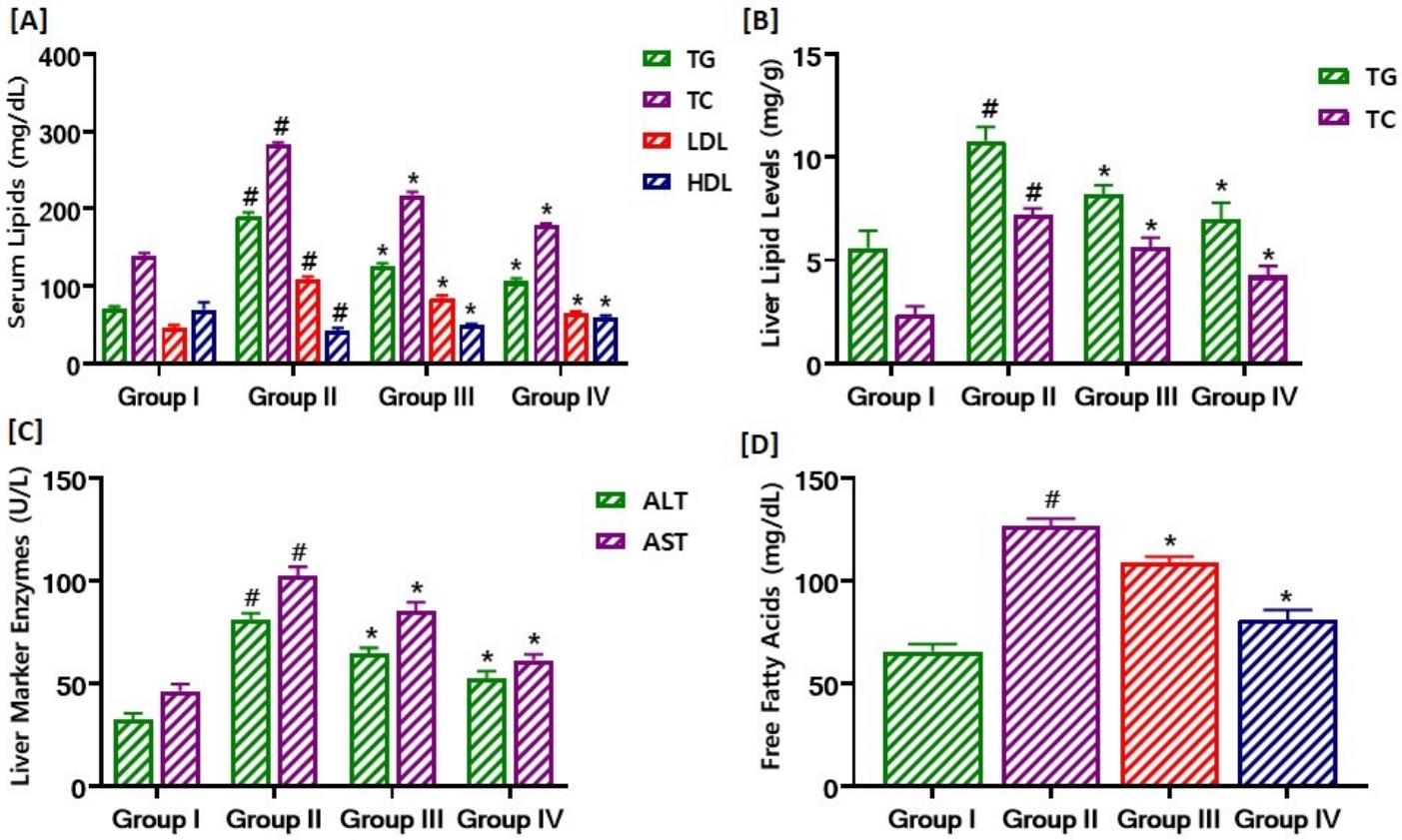

Figure 4: Effect of bavachalcone on the lipid profiles and liver marker enzymes in the experimental rats.

The values are given as an average value (mean) ± SD of three repeated assays. The statistical studies of the results are performed using one-way ANOVA and Tukey's multiple comparison tests. An asterisk '#' reveals the statistical significance at $p<0.01$ when compared with the control group. An asterisk '*' reveals the statistical significance at $p<0.05$ when compared with the HFa-HFr diet fed group. [A]: Serum lipid (TG, TC, LDL, and HDL) levels; [B]: Liver lipid (TG and TC) levels; [C]: Liver marker enzyme (ALT and AST) activities; [D]: Free fatty acid levels.

levels compared to the HFa-HFr diet-fed rats. Furthermore, the HFa-HFr diet-fed rats exhibited elevated liver levels of TG and TC than the control. Notably, bavachalcone treatment significantly reduced TG and TC status in the hepatic tissues of the HFa-HFr diet-fed rats. The liver marker enzymes ALT and AST activities were considerably elevated in the serum of HFa-HFr diet-fed rats than the control. However, the treatment with bavachalcone resulted in a substantial decrease in the serum activities of ALT and AST compared with HFa-HFr diet-fed rats. These findings demonstrated that bavachalcone mitigated abnormalities in liver function and lipid metabolism induced by the HFa-HFr diet in rats.

Effect of bavachalcone on the pro-inflammatory cytokine levels in the experimental rats

The changes in the inflammatory cytokine levels in the serum of experimental rats are presented in Figure 5. The HFa-HFr diet fed rats exhibited a drastic elevation in the NF-kB, IL-1β, TNF-α, and IL-6 levels when compared with control rats. Remarkably, the bavachalcone treatment at 25 and 50 mg/kg concentrations, respectively, exhibited a considerable decrease in the NF-kB, IL-1β, TNF-α, and IL-6 levels in the serum of HFa-HFr diet-fed rats. These findings highlighted the inflammation-lowering effect of bavachalcone in rats with metabolic abnormalities.

Effect of bavachalcone on the oxidative stress marker levels

The oxidative stress markers, such as MDA, CAT, SOD, and GSH-Px levels, in the hepatic tissues of the experimental rats are presented in Figure 6. The HFa-HFr diet-fed rats demonstrated a considerable reduction in the CAT, SOD, and GSH-Px levels in their hepatic tissues while increasing their MDA levels. Whereas, the treatment of 25 and 50 mg/kg of bavachalcone in the HFa-HFr diet-fed rats led to a considerable increase in the antioxidant marker levels in their hepatic tissues. Furthermore, the MDA level also reduced the hepatic tissues of the HFa-HFr diet-fed rats by the bavachalcone treatment. These findings proved the antioxidant activity of bavachalcone.

Effect of bavachalcone on the liver histopathology

The therapeutic effect of bavachalcone on the histopathological changes in the liver tissues of the HFa-HFr diet-fed rats is exhibited in Figure 7. As presented in Figure 7, the normal control rats did not exhibit any histological abnormalities. However, the

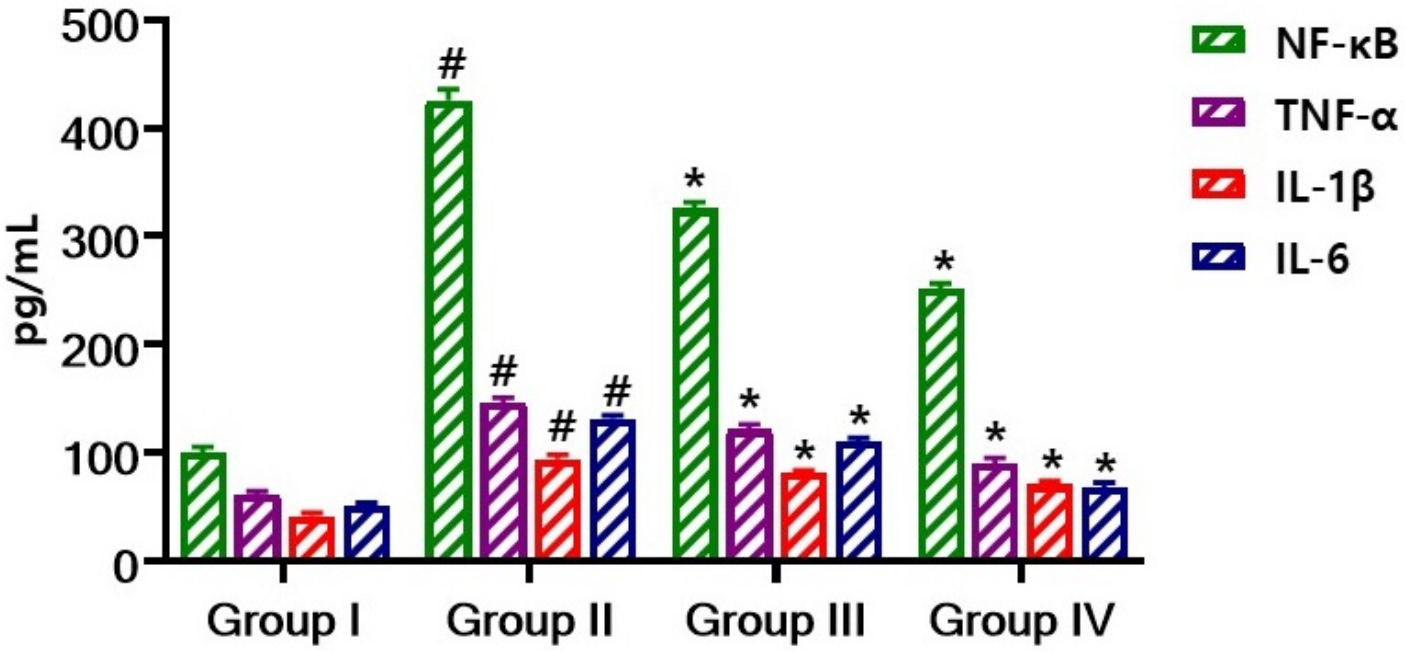

Figure 5: Effect of bavachalcone on the pro-inflammatory cytokine levels in the experimental rats.

The values are given as an average value (mean) ± SD of three repeated assays. The statistical studies of the results are performed using one-way ANOVA and Tukey's multiple comparison tests. An asterisk '#' reveals the statistical significance at $p<0.01$ when compared with the control group. An asterisk '*' reveals the statistical significance at $p<0.05$ when compared with the HFa-HFr diet fed group.

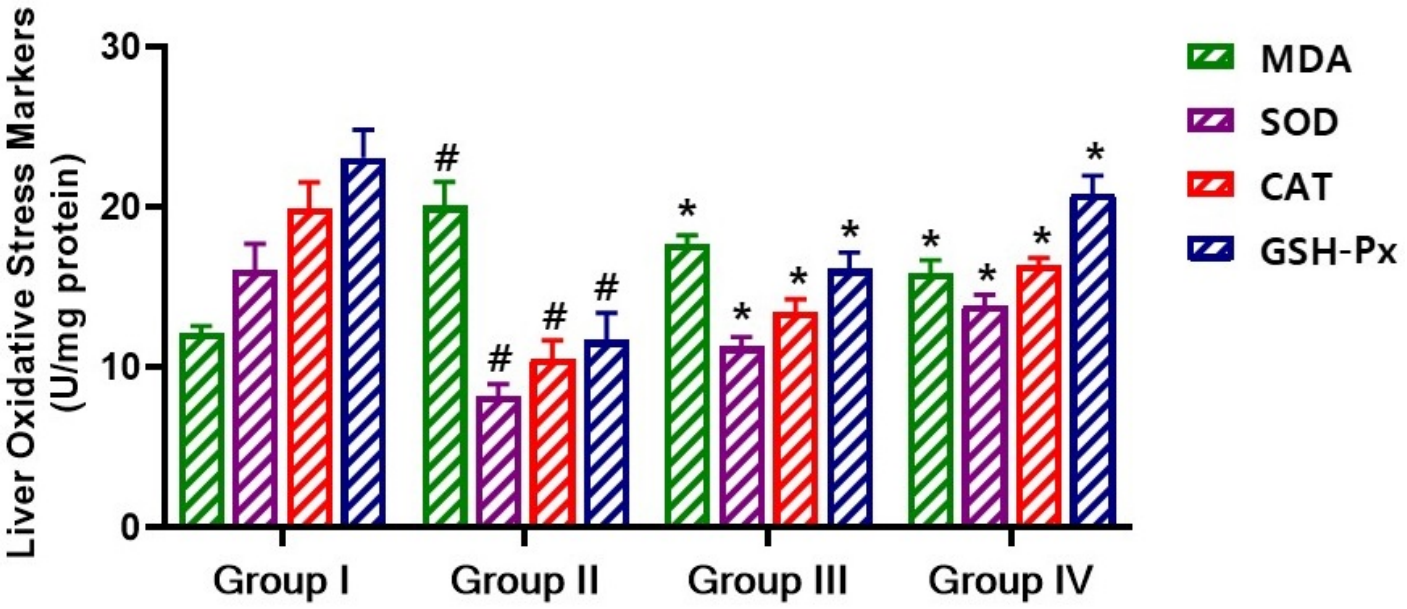

Figure 6: Effect of bavachalcone on the oxidative stress markers in the experimental rats.

The values are given as an average value (mean) ± SD of three repeated assays. The statistical studies of the results are performed using one-way ANOVA and Tukey's multiple comparison tests. An asterisk '#' reveals the statistical significance at $p<0.01$ when compared with the control group. An asterisk '*' reveals the statistical significance at $p<0.05$ when compared with the HFa-HFr diet fed group.

liver histology of the HFa-HFr diet-fed rats revealed the presence of hepatocyte lipid droplet accumulation and inflammatory cell infiltrations. Interestingly, the bavachalcone treatment of the HFa-HFr diet-fed rats resulted in amelioration of these degenerative and pathological changes in their hepatic tissues.

DISCUSSION

Dietary fructose, a type of simple sugar, has the ability to trigger metabolic syndrome, a condition that plays a pivotal role in the onset of DM and atherosclerosis. Research has documented that consuming a fructose-rich diet in humans and animal models

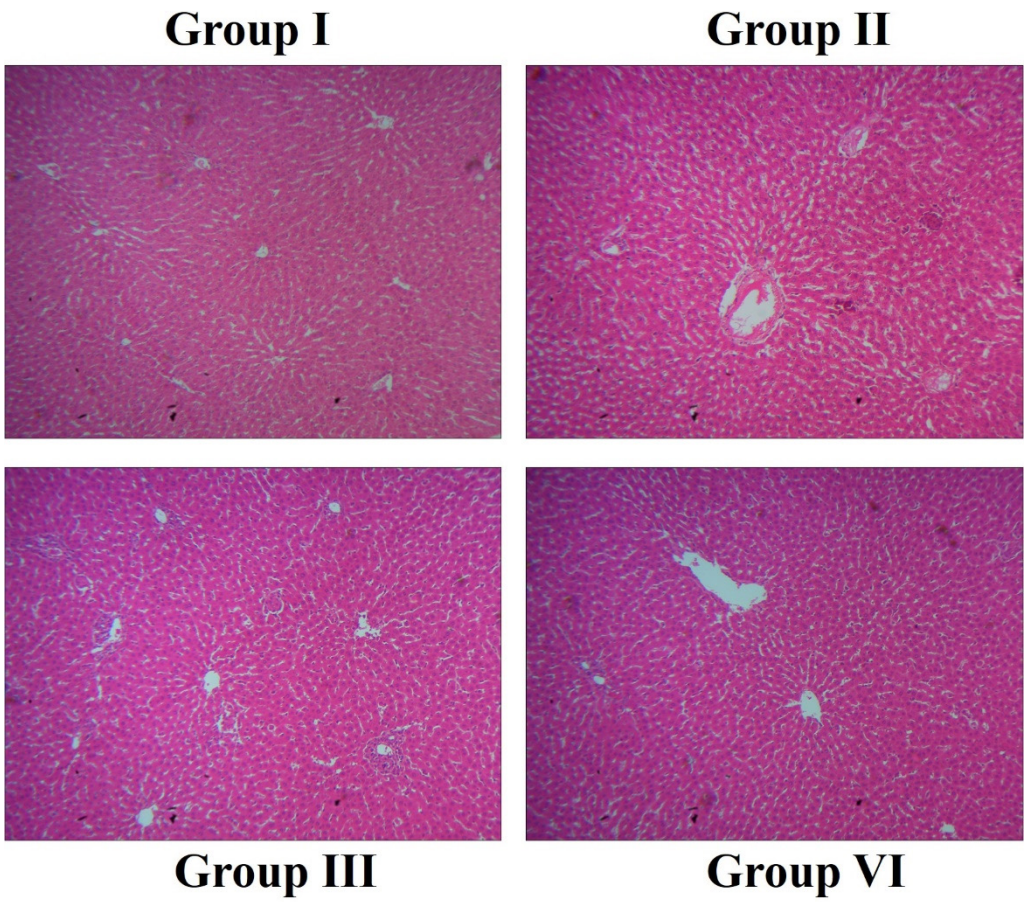

Figure 7: Effect of bavachalcone on the liver histopathology of the experimental rats.

The normal control rats did not exhibit any histological abnormalities (Group I). The liver histology of rats fed the HFa-HFr diet revealed hepatocyte lipid droplets and increased inflammatory cell infiltration (Group II). The 25 and 50 mg/kg of bavachalcone treatment, respectively, in the HFa-HFr diet-fed rats resulted in amelioration of these degenerative and pathological changes in their liver tissues (Groups III and IV).

leads to significant consequences such as increased body weight, elevated blood sugar levels, and increased insulin levels.[20] The HFa-HFr diet, due to its twofold increase in calorie consumption compared to standard diet regimens, resulted in a substantial, gradual, and statistically significant rise in body weight, thus confirming its ability to promote obesity. Our findings align with previous research that discovered a strong correlation between the intake of high fructose diets and the development of high blood sugar levels, accompanied by excessive insulin production.[21] The present findings revealed that the bavachalcone treatment effectively reduced bodyweight, FBG, and liver weight in the HFa-HFr diet fed to rats.

Insulin resistance is a medical disorder characterized by a decrease in the capacity of the body's tissues to respond to insulin, resulting in reduced insulin sensitivity, impaired use of insulin by peripheral tissues, and decreased uptake of glucose. This leads to the excessive production and circulation of insulin in the bloodstream, a condition known as hyperinsulinemia. Hyperinsulinemia can lead to many metabolic complications, including DM, heart disease, dislipidemia, and obesity.[22,23] In addition, the HFa-HFr diet resulted in significant insulin resistance, as demonstrated by the ITT findings. These findings align with previous studies that have reported HFa-HFr as the most efficient diet for inducing insulin resistance.[24] A simple plasma measurement to assess insulin sensitivity will not give a reliable indication of β-cell malfunction in diabetes. OGTT is used to evaluate β-cell dysfunction in DM and obesity, as well as to test glucose tolerance in experimental models.[25] The current research clearly demonstrated that bavachalcone significantly enhanced the insulin resistance that the HFa-HFr diet induced. The bavachalcone treatment effectively reduced blood glucose levels, insulin levels, serum lipids, hepatic lipids, and liver function enzymes. These findings indicate that bavachalcone improves the body's response to insulin, prevents the onset of insulin resistance, and mitigates other metabolic abnormalities associated with insulin resistance in the HFa-HFr diet-fed rats.

The over-deposition of fats in adipose tissue can lead to the production of lipid products. These lipid products disrupt

various bodily processes, particularly in the liver tissues, causing metabolic abnormalities.[26,27] Multiple investigations have unequivocally demonstrated that lipid profiles undergo considerable changes in cases of diet-caused obesity and metabolic disorders. Consumption of the HFa-HFr diet promotes fat buildup and, consequently, leads to an elevated release of lipids into the bloodstream.[28] Elevated TC, TG, and LDL levels, along with decreased HDL levels, are important markers that have been linked with the onset of DM and coronary heart diseases.[29] The present work revealed that the bavachalcone treatment decreased TC and TG levels in both the plasma and liver, as well as levels of FFA and LDL in the plasma. Furthermore, the treatment of bavachalcone also demonstrated an enhancement in HDL levels in the HFa-HFr diet fed rats.

The pathophysiology of insulin resistance is complex and not fully understood. However, research has strongly linked factors like inflammation and oxidative stress to the development of obesity and insulin resistance. Multiple studies have demonstrated the current agreeable correlation between obesity, insulin resistance, and inflammation. An insulin-resistant condition reduces the antioxidant enzyme activity and increases the production of free radicals in the body tissues.[30] Excessive fat buildup, as seen in obesity or eating a high-fat, high-fructose diet, leads to an increase in FFA oxidation, which in turn causes an excessive production of ROS. Furthermore, earlier studies have linked oxidative stress with the accumulation of excessive levels of fat.[31]

Moreover, oxidative stress extensively recognizes its ability to initiate inflammation and the secretion of inflammatory markers. Oxidative stress can trigger an inflammatory response, which in turn causes insulin resistance. Chronic inflammation triggers the release of many inflammatory markers, including TNF-α, IL-6, and IL-1β. These mediators can worsen insulin resistance and decrease tissue sensitivity to insulin, thereby restricting the absorption of glucose.[32,33] The inflammation associated with insulin resistance heavily relies on NF-B. Activation of NF-B leads to an elevation in the generation of inflammatory cytokines.[34] It has been demonstrated that TNF-α enhances adipocyte lipolysis, which raises FFA levels and has direct detrimental effects on the insulin signaling pathway.[35] Immune cells and adipocytes secrete elevated levels of cytokines in obesity cases. These cytokines participate in the onset of insulin resistance.[36] Previous findings have unambiguously revealed that the HFa-HFr diet triggers the stimulation of inflammatory and oxidative stress parameters.[37] Our research showed that rats that were fed a HFa-HFr diet had higher amounts of inflammatory and oxidative stress markers, such as IL-6, TNF-α, IL-1β, NF-kB, and MDA. Additionally, the rats showed reduced levels of antioxidants such as CAT, GSH-Px, and SOD. Interestingly, the bavachalcone treatment effectively mitigated inflammatory and oxidative stress conditions by increasing antioxidant levels and reducing the secretion of pro-inflammatory cytokines associated with inflammation.

CONCLUSION

In conclusion, the present findings found that bavachalcone treatment mitigated the insulin resistance and metabolic abnormalities in the HFa-HFr diet-fed rats by regulating dyslipidemia, oxidative stress, and inflammation. Therefore, it became evident that bavachalcone could potentially serve as a salutary candidate to mitigate metabolic diseases. As a result, these findings demonstrate that bavachalcone has the capacity to be a talented therapy option for the treatment of diet-induced metabolic disorders. Furthermore, additional works are still required to assess the molecular mechanism by which bavachalcone regulates insulin resistance and its associated metabolic disorders.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

DM: Diabetes mellitus; **HFa-HFr:** High-fat and high-fructose; **CVD:** Cardiovascular disease; **ITT:** Insulin tolerance test; **IPGTT:** Intra-peritoneal glucose tolerance test; **TC:** Total cholesterol, **TG:** Triglycerides, **LDL:** Low-density lipoprotein; **HDL:** High-density lipoprotein; **FFA:** Free fatty acid.

SUMMARY

Obesity is a persistent metabolic disorder characterized by the over-deposition of body fat. Diets that contain large amounts of lipids and sugar are commonly considered to be major factors linked to obesity, insulin resistance, and other metabolic complications. Bavachalcone is a major bioactive compound, mostly present in medicinal plants such as Psoralea corylifolia and Cullen corylifolium. Bavachalcone treatment mitigated the insulin resistance and metabolic abnormalities in the HFa-HFr diet-fed rats by regulating dyslipidemia, oxidative stress, and inflammation.

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