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The Ameliorative Role of Hibiscetin against High-Fat Diets and Streptozotocin-Induced Diabetes in Rodents via Inhibiting Tumor Necrosis Factor-α, Interleukin-1β, and Malondialdehyde Level

Sadaf Jamal Gilani [1], May Nasser Bin-Jumah [2,3,4], Fahad A. Al-Abbasi [5], Fatima M. Albohairy [6], Muhammad Shahid Nadeem [5], Mohammed Muqtader Ahmed [7], Sami I. Alzarea [8] and Imran Kazmi [5,*]

1 Department of Basic Health Sciences, Preparatory Year, Princess Nourah bint Abdulrahman University, Riyadh 11671, Saudi Arabia; sjglani@pnu.edu.sa
2 Biology Department, College of Science, Princess Nourah bint Abdulrahman University, Riyadh 11671, Saudi Arabia; mnbinjumah@pnu.edu.sa
3 Environment and Biomaterial Unit, Health Sciences Research Center, Princess Nourah bint Abdulrahman University, Riyadh 11671, Saudi Arabia
4 Saudi Society for Applied Science, Princess Nourah bint Abdulrahman University, Riyadh 11671, Saudi Arabia
5 Department of Biochemistry, Faculty of Science, King Abdulaziz University, Jeddah 21589, Saudi Arabia; fabbasi@kau.edu.sa (F.A.A.-A.); mhalim@kau.edu.sa (M.S.N.)
6 Electron Microscope Research Unit, Health Sciences Research Center, Princes Nourah bint Abdulrahman University, Riyadh 11671, Saudi Arabia; fmalbohairy@pnu.edu.sa
7 Department of Pharmaceutics, College of Pharmacy, Prince Sattam Bin Abdulaziz University, Al-Kharj 11942, Saudi Arabia; muqtadernano@gmail.com
8 Department of Pharmacology, College of Pharmacy, Jouf University, Sakaka 72341, Saudi Arabia; samisz@ju.edu.sa
* Correspondence: ikazmi@kau.edu.sa or kazmiimran2005@gmail.com

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Abstract: Hibiscetin, as one of the main bioactive constituents of *Hibiscus sabdariffa*, has many pharmacological activities, but its antihyperglycemic activity has not been fully interpreted yet. The current research was developed from this perspective. The study intended to appraise the antidiabetic capability of hibiscetin in a high-fat diet (HFD) and streptozotocin (STZ; 50 mg/kg, intraperitoneally)-induced diabetes in an experimental animal. The efficiency of hibiscetin at 10 mg/kg in an "HFD/STZ model" remedy in rats with experimentally caused diabetes was explored for 42 days. The efficacy of hibiscetin was observed on several diabetes parameters. The average body weight and an array of biochemical markers were determined, including blood glucose, insulin, total protein (TP), lipid profile, aspartate aminotransferase (AST), alanine aminotransferase (ALT), IL-6, IL-1β, tumor necrosis factor-α (TNF-α), adiponectin, leptin, resistin, malondialdehyde (MDA), catalase (CAT), glutathione (GSH), and superoxide dismutase (SOD). The antidiabetic benefits of hibiscetin were proven by a substantial reduction in blood glucose, lipid profile (TC and TG), total protein, IL-6, IL-1β, MDA, TNF-α, leptin, adiponectin, ALT, and AST in the therapy group compared to the diabetic disease standard. Furthermore, hibiscetin therapy also reversed the lowered levels of insulin, resistin, GSH, SOD, and CAT in diabetic rats. It was determined that hibiscetin may be beneficial in terms of reducing diabetes problems due to its effects on both oxidative stress and inflammation and that more research for this design should be conducted.

Keywords: hibiscetin; antidiabetic activity; HFD/STZ model; tumor necrosis factor-α; malondialdehyde

1. Introduction

Diabetes mellitus (DM) is a significant problem in the modern era due to its vast spectrum of physiological consequences and prevalence [1]. It is understandable that the

expense of treating the condition and its consequences has risen dramatically, putting a financial strain on healthcare systems. The etiology and pathophysiological mechanisms of DM are extremely complicated. However, mounting evidence suggests that oxidative stress and inflammation may be important in the progression of DM.

Hibiscus sabdariffa L. *(roselle)*, a member of the Malvaceae, is extensively planted in many locales. This plant is frequently employed in ethnomedicine due to its high concentration of phytochemicals such as polyphenols, particularly anthocyanins, organic acids, and polysaccharides, which have significant potential in contemporary medicinal applications. Much research has been conducted to examine the phytochemical, pharmacological, and toxicological characteristics of *Hibiscus sabdariffa* [2]. *Hibiscus sabdariffa* is most commonly grown for its calyces, which are widely used in herbal drinks, wine, syrup, pudding, pickles, cakes, ice cream, hot and cold beverages, jams, and jellies [3]. Many studies have found that the bioactives of *Hibiscus sabdariffa*, either combined or alone, have substantial antioxidant and anti-inflammatory, anti-obesity, and antitumor activity and may potentially help in preventing hyperglycemia and cardiovascular disease [4]. According to a in silico docking investigation of the chemical components of *Hibiscus sabdariffa* (hibiscetin, gossypetin, quercetin, and protocatechuic acid), they show a lower docking score and a greater potency as inhibitors of the protein enzyme phosphoenolpyruvate carboxykinase (PEPCK) than the conventional drug metformin [5]. Based on molecular modeling, it appears that hibiscetin, a constituent of *Hibiscus sabdariffa*, binds to the vascular endothelial growth factor receptor's active site. Previous research has shown that anthocyanins are angiogenic regulators that can be used for the treatment of vascular diseases such as age-related macular degeneration. By adopting an in silico screening approach, hibiscetin 3-glucoside, hibiscetin, and delphinidin 3-sambubioside were identified as possible inhibitors of the angiotensin-I converting enzyme [6,7].

Many researchers have reported on the efficiency of *Hibiscus sabdariffa* calyx in terminating and/or scavenging free radicals. The presence of phenolic chemicals in *Hibiscus sabdariffa* calyx might explain its antioxidant action. Furthermore, the extract was discovered to have a significant amount of ascorbic acid, also known as ascorbate, a well-known natural antioxidant and effective reducing agent [3]. Due to poor skin absorption, topical administration of *Hibiscus sabdariffa* is limited, which might be addressed by liposome formulations that improve permeability and antioxidant activity [8]. The polyphenols in *Hibiscus sabdariffa* have been shown to act as anti-inflammatory agents in different experimental models. In hypertrophied 3T3-L1 adipocytes, both polyphenol- and aqueous-enriched *Hibiscus sabdariffa* extracts decreased the production of pro-inflammatory adipokines [9]. Oxidation and inflammation are closely related, so one strategy for *Hibiscus sabdariffa* polyphenols to exert anti-inflammatory effects is to enhance their oxidative state. In this regard, the extract has been shown to inhibit xanthine oxidase activity in vitro and reduce prostaglandin E2 and nitrite secretion in LPS-induced cells.

In addition, *Hibiscus sabdariffa* suppressed inflammation by negatively regulating cyclooxygenase 2 (COX2) and inhibiting p38 kinase and cJun N-terminal kinase (JNK). These results suggest that *Hibiscus sabdariffa* polyphenols are associated with lipopolysaccharide-induced oxidative stress and nuclear factor kB (NFkB) translocation [10]. All of these findings suggest that *Hibiscus sabdariffa's* anti-inflammatory properties are connected to the regulation of oxidative-stress-related mechanisms.

Unfortunately, several oral hypoglycemic medications displayed antidiabetic efficacy via distinct modes of action with adverse side effects. As a result, the use of medicinal plants has emerged as the most important component of all accessible medicines Therefore, we evaluated the preventive potential of hibiscetin against hyperglycemia generated by a high-fat diet and streptozotocin ("HFD/STZ model"). Our research sheds information on the signaling pathways involved in diabetic rats' inflammation and oxidative damage.

2. Methods

2.1. Experimental Animals

Male Wistar rats (n = 6), weighing 150–200 g and aged 10 to 12 weeks, were utilized in this investigation. The five experimental-group rats were retained in an air-conditioned area with a natural light-and-darkness interval in polyacrylic cages, with fewer than three animals per cage, at an institutional animal facility. The experimental animals had unrestricted access to standard food or an HFD, as well as water. For adaptation, all rats were put through a one-week familiarization process. The experimental procedure for employing Wistar rats in the experiments was sanctioned by the institutional animal ethics committee (IAEC-TRS/PT/022/016).

2.2. Chemicals and Drugs

STZ was obtained from Sigma-Aldrich, St. Louis, USA. Hibiscetin (TRS, Maharashtra, India), glibenclamide, dimethyl sulfoxide (DMSO), and other expendables used were all of the analytical standard quality and came from an authenticated vendor.

2.3. HFD/STZ-Induced Type II Diabetes Study Design

OECD ANNEX-423 standards were used to assess the acute oral toxicity of hibiscetin (LD50). Hibiscetin was administered orally to rats for 28 days. Until the end of the six-week paradigm, all of the experimental test animals were fed a high-fat diet with 60% calories. After two weeks of food modification, the rats fasted for 12 h and received 50 mg/kg, intraperitoneally (i.p.), of STZ prepared in a 0.1 M cold citrate buffer on the 14th day of the research regimen. The therapy began on the 14th day after the STZ injection, which was defined as the start day of the treatment plan, and lasted four weeks, with conventional medicine glibenclamide 5 mg/kg and hibiscetin 10 mg/kg/day test therapy orally administered. Animals with hyperglycemia, defined as 250 mg/dL blood glucose after 1 week of STZ injection, were designated as type 2 diabetics and included in the experimental research design. For biochemical parameter evaluation, blood samples from all test animals were collected through the retroorbital plexus under moderate anesthesia. The current experimental research design was based on a previously published study with minor changes [10].

2.4. Evaluation Criterion

2.4.1. Body Weight

A calibrated weighing balance was used to measure the body weight on a weekly basis.

2.4.2. Blood Glucose

To establish DM induction, we applied a blood-glucose-strip-operated monitor to ascertain the blood glucose levels through a tail prick. The tail vein (6 h) of the fasted rat was torn, and a drop of blood was placed on the glucose meter strip for analysis. Throughout the experiment, blood glucose was checked at regular intervals.

2.4.3. Determination of Serum Adiponectin, Resistin, Leptin and Insulin

Serum insulin, leptin, adiponectin, and resistin were determined by using ELISA kits, using formerly reported methodologies and procedures modified slightly by the construct. Serum was extracted from the experimental rats and centrifuged at 14,000 rpm for 10 min, according to the procedure. A holder was used to retain the requisite number of coated strips, and standard (e.g., insulin, leptin, adiponectin, and resistin) control and samples were pipetted into the appropriate wells. The samples were incubated for 60 min at 20–25 °C after adding functional enzyme conjugates. The samples were washed with 300 L of wash buffer after each incubation. Following the addition of tetramethylbenzidine substrate at 100 L, the samples were incubated for 15 min at room temperature. Following the final incubation, the desired amount of stopping solution was applied to all wells, and the absorbance was calculated at 450 nM, using a monochromatic microplate reader [11].

2.4.4. Biochemical Markers

The total cholesterol (TC), triglyceride (TG), and high-density lipoprotein cholesterol (HDL) in the serum, as well as the liver enzyme, were measured in accordance with the producers. The parameters were performed by using a microplate reader and enzymatic assay kits, as directed by the manufacturer [12]. An ELISA method was used to assess the serum concentrations of TNF-α, IL-1β, and IL-6 [13]. Throughout the appraisal, a liver sample was taken from experimental rats and homogenized separately, using a homogenizer. The tissues were homogenized in 7.4 pH phosphate buffer saline (PBS) at concentrations of 10 and 50 mM for detection of malondialdehyde (MDA) by thiobarbituric acid reactive compounds, as well as a reduction in catalase (CAT), glutathione (GSH), and superoxide dismutase (SOD) activity. The resultant tissue homogenate was centrifuged at 10,000 rpm, following the protein measurement protocol reported by Lowry et al. [14]. The formation of pink chromogen implies the eventual formation of MDA. TBARS, a pink chromogen measurable spectrophotometrically at 532 nm, is formed when MDA, a lipid peroxidation biomarker, interacts with TBA. The absorption of the samples was evaluated against a standard curve that was created by using an MDA standard [15]. Likewise, when spectrophotometrically examined by using commercially available assays and their manufacturers' estimation instructions, GSH produced a yellow molecule at 405 nM [16]. Sinha [17] assessed the CAT enzyme activity, using previously established methodologies, including a colorimetric estimate at 570 nM, in the presence of glacial acetic acid and hydrogen peroxide. The superoxide dismutase enzyme action was evaluated by using a calibrated 96-well microplate reader to 490 nM, commercial kits, and the manufacturer's guide to calculating the quantity of protein necessary to prevent auto-oxidation of 6-hydroxydopamine [18].

2.5. Statistical Analysis

The information is displayed as a standard error of the mean (SEM). Statistical analysis was exploited by one-way ANOVA, using Graphpad Prism. The $p < 0.05$ was considered significant when comparing the control and experimental groups.

3. Results

During acute oral toxicity testing, hibiscetin was found to be safe in rodents with no mortality or adverse effects. The dose of hibiscetin selected was 10 mg/kg based on safety data.

3.1. Body Weight

Figure 1 represents the body weight of experimental animals. When compared to the healthy rats, HFD/STZ caused the diabetic group rats to considerably increase the animal's body weight. In treatment-group rats, the conventional medicine (glibenclamide 5 mg/kg) and hibiscetin 10 mg/kg in HFD/STD model led to a significant reduction in their body weight ($p < 0.05$).

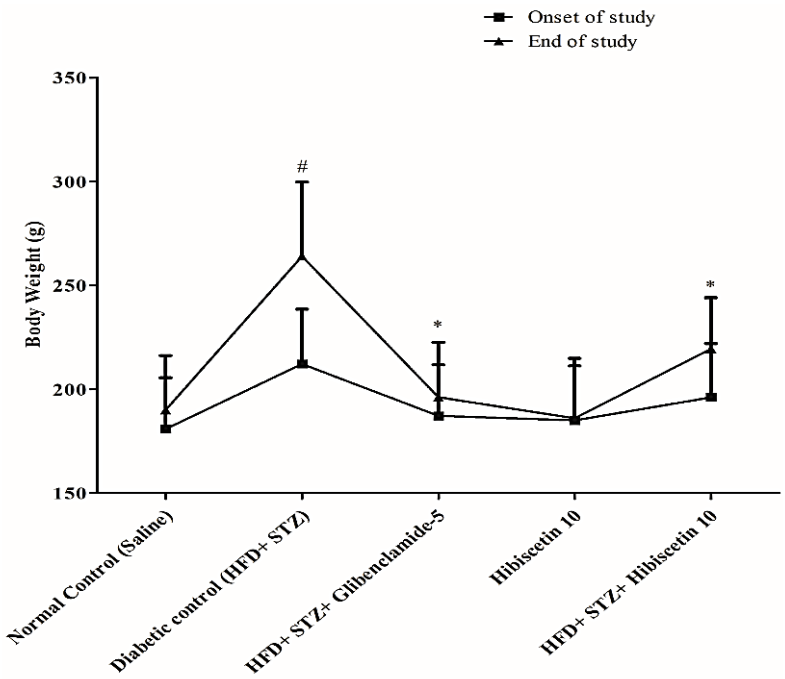
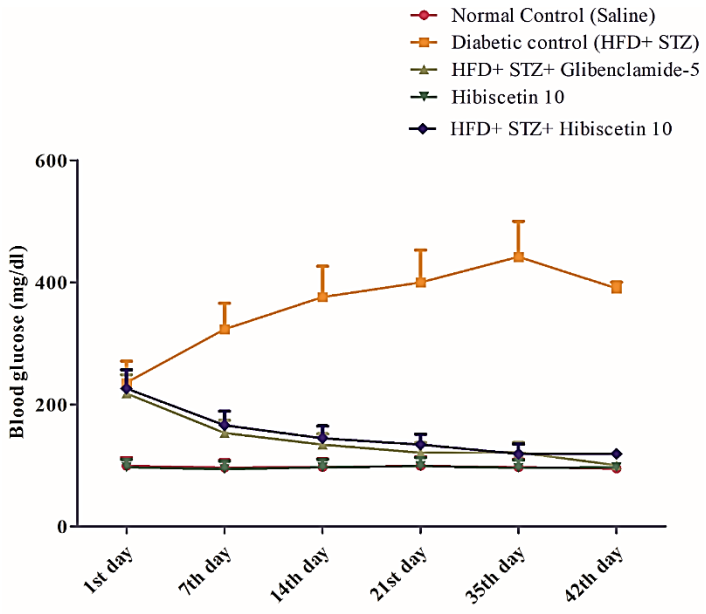


Figure 1. Hibiscetin affects body weight monitoring (n = 6). The mean SEM is used to express the data. The mean SEM is used to express the data; (# $p < 0.05$) saline vs. HFD+STZ; (* $p < 0.05$) HFD+STZ vs. treatment group.

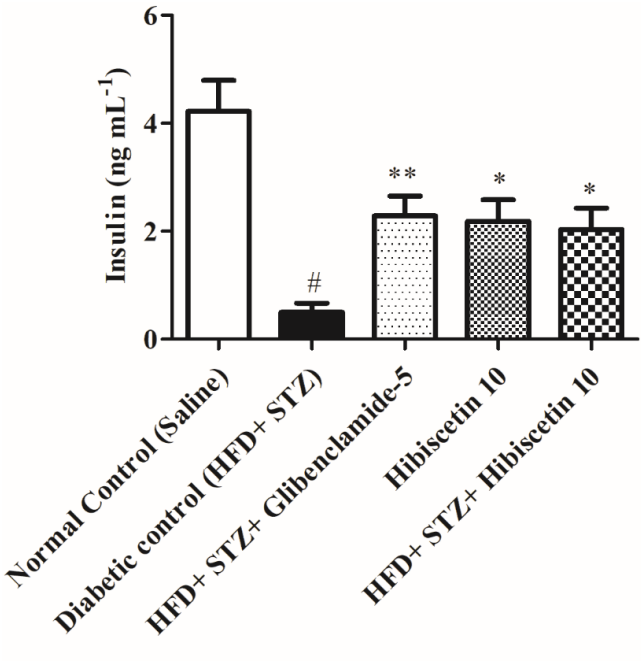
3.2. Effect of Hibiscetin on Diabetes Parameters

As displayed in Figure 2A, substantial rises were ascertained in blood glucose levels in the disease control as compared to the normal healthy rats. The co-treatment of HFD/STZ-treated animals with glibenclamide 5 mg/dL or the test medicine hibiscetin 10 mg/dL decreased significant blood glucose in rats. Furthermore, antidiabetic benefits are confirmed by serum insulin measurement. Diabetic rats subjected to the standard drug, glibenclamide, and the test drug, hibiscetin, displayed increased levels of insulin in comparison with those in the disease model group (Figure 2B).



(**A**)

Figure 2. *Cont.*

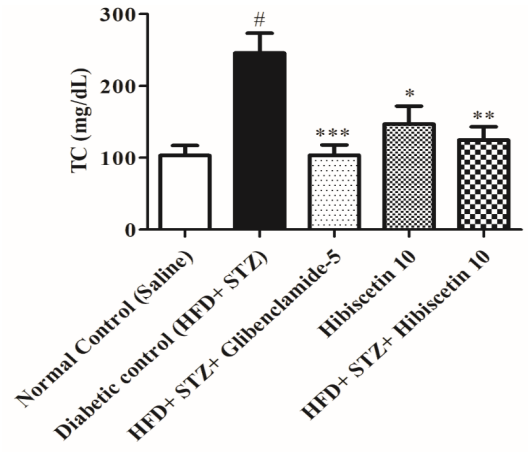


(**B**)

Figure 2. (**A**,**B**) Effect of hibiscetin on blood glucose (**A**) and insulin (**B**) (n = 6). The mean SEM is used to express the data; ($^{\#}$ $p < 0.05$) saline vs. HFD+STZ; (** $p < 0.01$, and * $p < 0.05$) HFD+STZ vs. treatment group.

3.3. Effect of Hibiscetin on Lipid Profile

In contrast to the disease control group, hyperlipidemia was revealed during HFD/STZ induction by a substantial drop in HDL and an increase in blood TC and TG. In comparison to the untreated group, the administration of hibiscetin 10 mg/dL or the conventional medicine glibenclamide 5 mg/kg to HFD/STZ rats resulted in an evidentiary drop-off in TC and TG levels, as well as a rise in HDL levels. Furthermore, in normal experimental animals, therapy with 10 mg/kg hibiscetin resulted in a more significant decline in the lipid profile. Reduced plasma protein levels have been associated with HFD/STZ-induced diabetes. The protein levels in diabetic control rats decreased, but they were recovered after treatment with standard and test medicines due to glucose management (Figure 3A–D).



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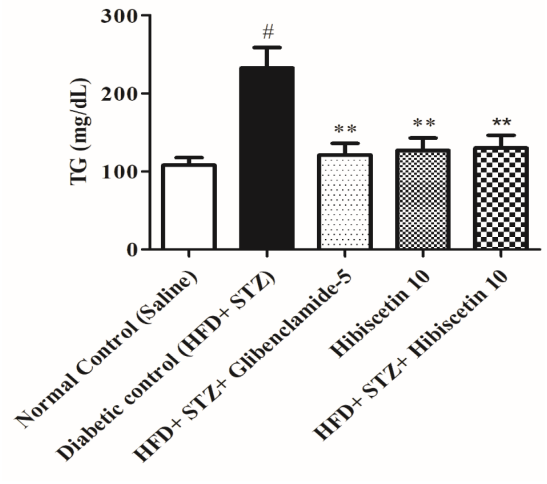

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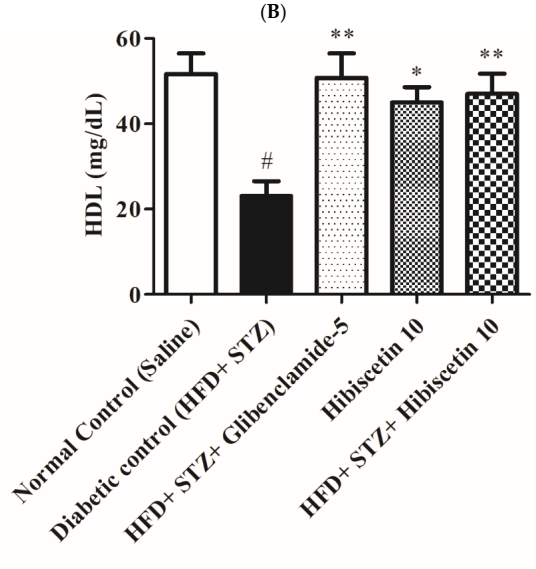

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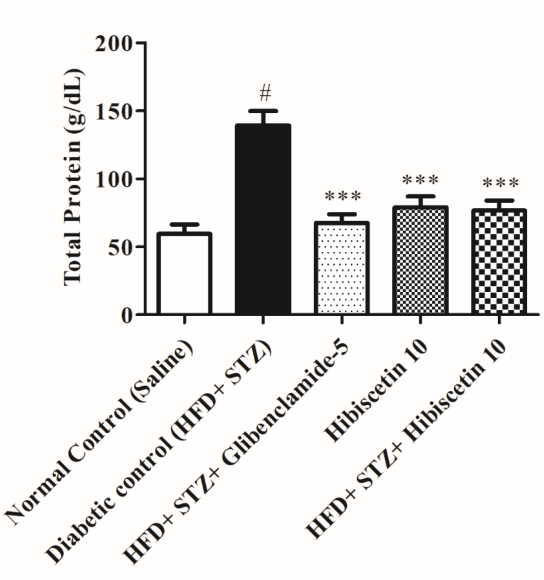
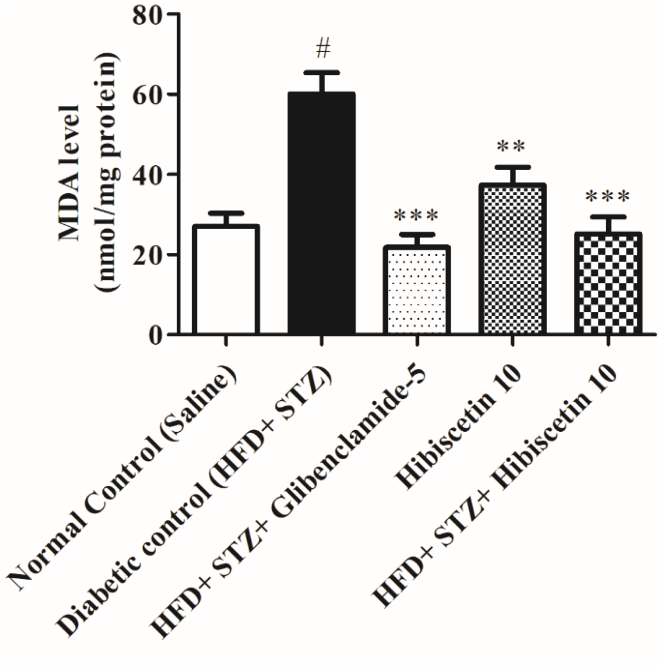


(**D**)

Figure 3. (**A**–**D**) Effect of hibiscetin on lipid profile (**A**–**C**) and total protein (**D**) (n = 6). The mean SEM is used to express the data; ($^{\#}$ $p < 0.05$) saline vs. HFD+STZ; (*** $p < 0.001$, ** $p < 0.01$, and * $p < 0.05$) HFD+STZ vs. treatment group.

3.4. Effect of Hibiscetin on the Oxidative Stress Biomarkers

The disease control animals demonstrated a considerable free fall in intracellular levels of CAT, GSH, and SOD activity, but an evidentiary rise in MDA compared to the saline-treated rats at the conclusion of the experimental phase. The treatment regimen that includes the conventional medicine glibenclamide 5 mg/kg and the therapy hibiscetin 10 mg/kg considerably reduced the increased intracellular indices of MDA. Furthermore, as compared to the disease group, it recovers the inhibited antioxidant enzymes CAT, GSH, and SOD. However, as compared to the diabetes disease group, the test medicine hibiscetin 10 mg/kg recovers the raised intracellular levels of MDA less considerably and slightly raises the SOD, GSH, and CAT levels (Figure 4A–D).



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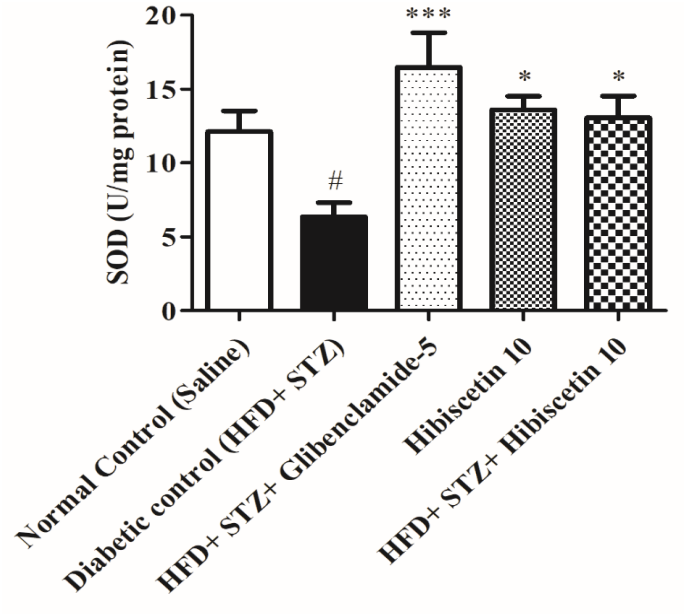

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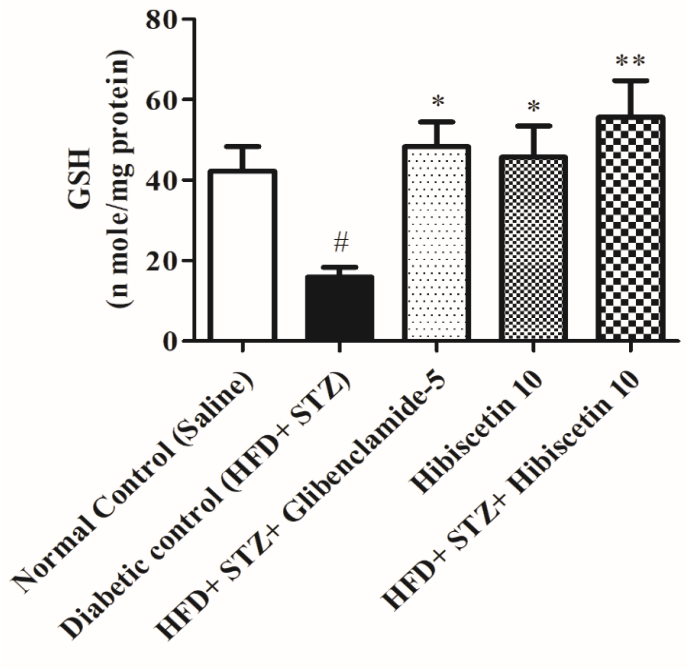

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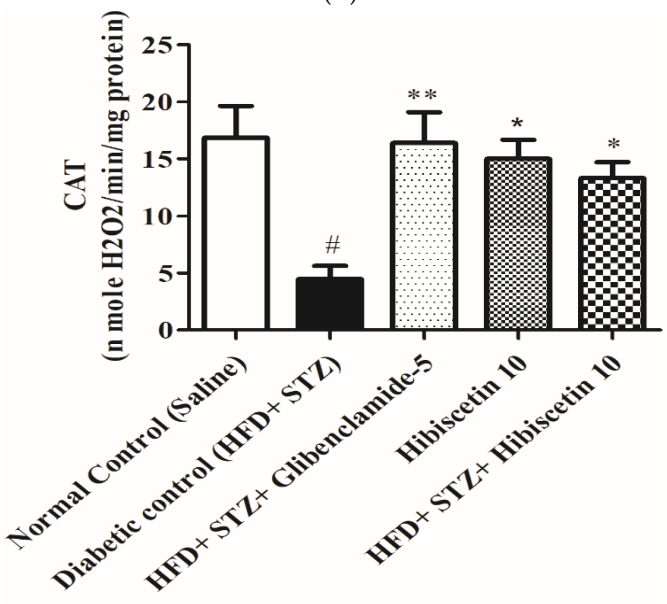
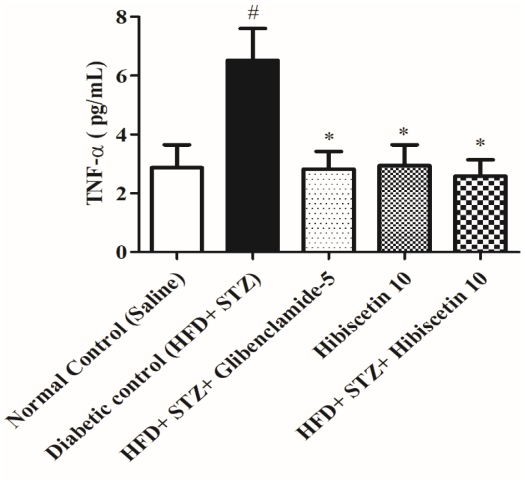


(**D**)

Figure 4. (**A**–**D**) Effect of hibiscetin on MDA, SOD, GSH, and CAT (n = 6). The mean SEM is used to express the data; ($^{\#}$ $p < 0.05$) saline vs. HFD+STZ; (*** $p < 0.001$, ** $p < 0.01$, and * $p < 0.05$) HFD+STZ vs. treatment group.

3.5. Effects of Hibiscetin on Proinflammatory Cytokines

To ascertain the mechanism through which the test medication hibiscetin exerts anti-inflammatory activity in rats. Figure 5A–C depicts the levels of pro-inflammatory cytokines, such as TNF-α, IL-1β, and IL-6, in different research group of rats. TNF-α, IL-1β, and IL-6 levels were investigated in disease control and healthy control rats, and there was a clear increase in TNF-α, IL-1β, and IL-6 in diseased animals. When the rats treated with hibiscetin and the conventional medicine, glibenclamide, were compared to their untreated counterparts, the TNF-α, IL-1β, and IL-6 levels were importantly attenuated. Surprisingly, these elevations in inflammatory markers were greatly reduced after treatment.



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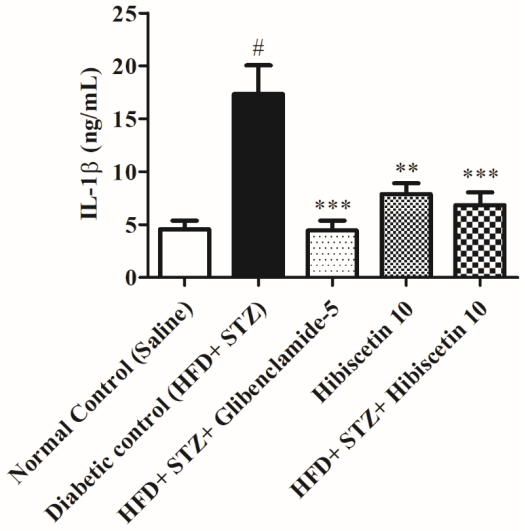

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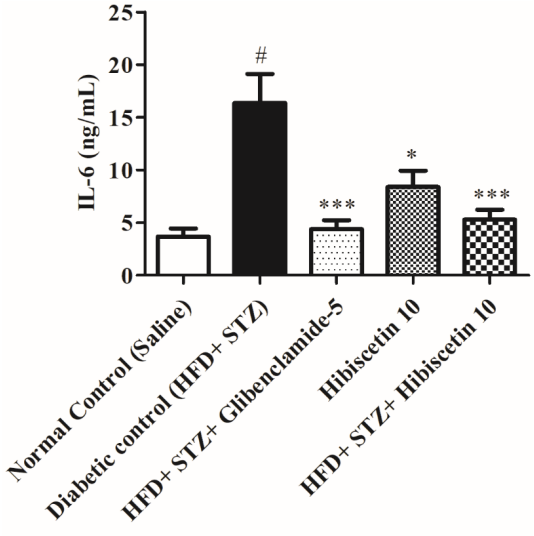
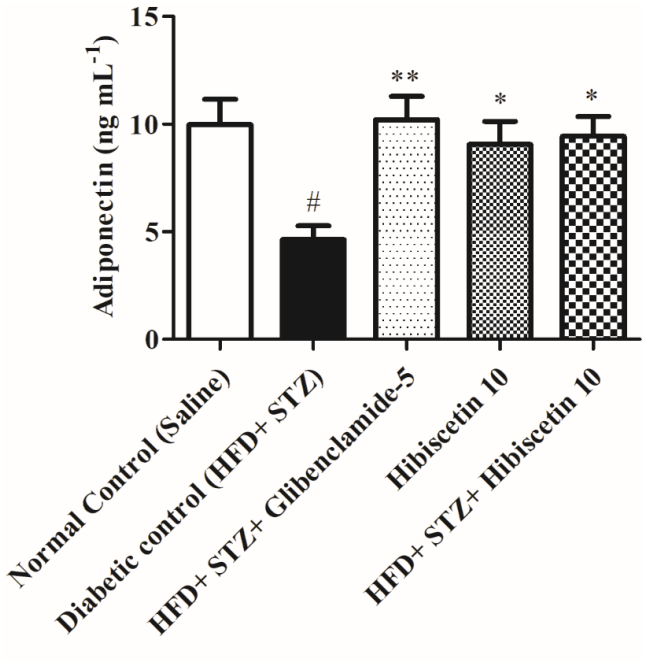


(**C**)

Figure 5. (**A**–**C**) Effect of hibiscetin on proinflammatory cytokines (n = 6). The mean SEM is used to express the data; ($^{\#}$ $p < 0.05$) saline vs. HFD+STZ, (*** $p < 0.001$, ** $p < 0.01$, and * $p < 0.05$) HFD+STZ vs. treatment group.

3.6. Effects of Hibiscetin on Leptin, Resistin, and Adiponectin

In HFD/STZ-induced diabetic animals, hibiscetin affects leptin, adiponectin, and resistin levels (Figure 6A–C). The trial's findings revealed a considerable drop in adiponectin and leptin levels in HFD/STZ-induced experimental animals, but a large increase in resistin levels when compared to saline-treated rats. The glibenclamide 5 mg/kg and the hibiscetin 10 mg/kg were given to HFD/STZ-induced rats, resulting in a fundamental rise in adiponectin and leptin levels compared to the untreated animals, but a significant drop-off in resistin levels after therapy in contrast to the untreated rats. The test medication had a positive impact on leptin, adiponectin, and resistin levels.



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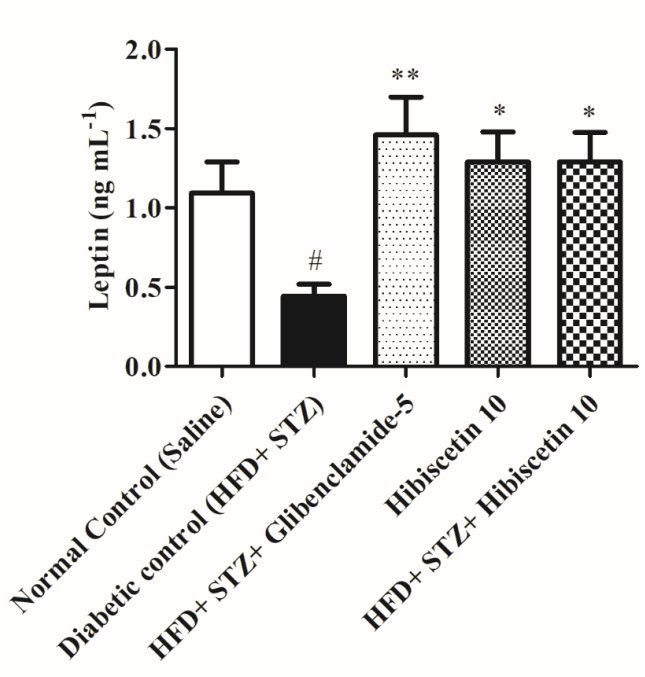

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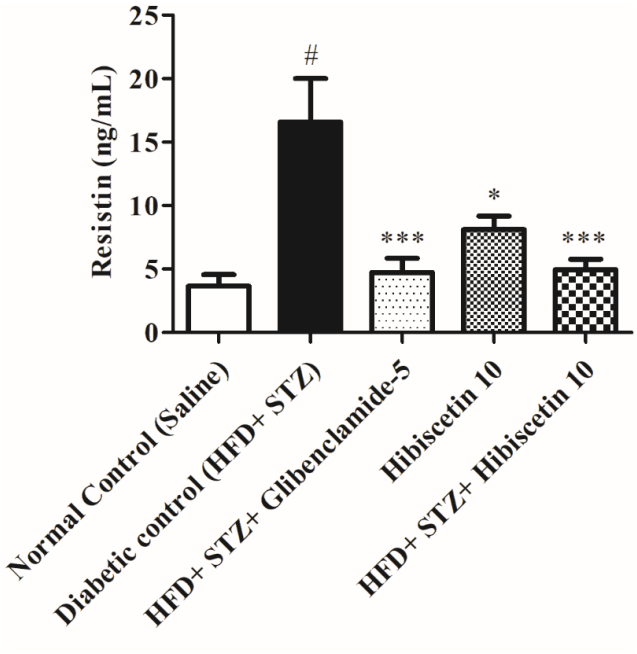
Figure 6. *Cont.*

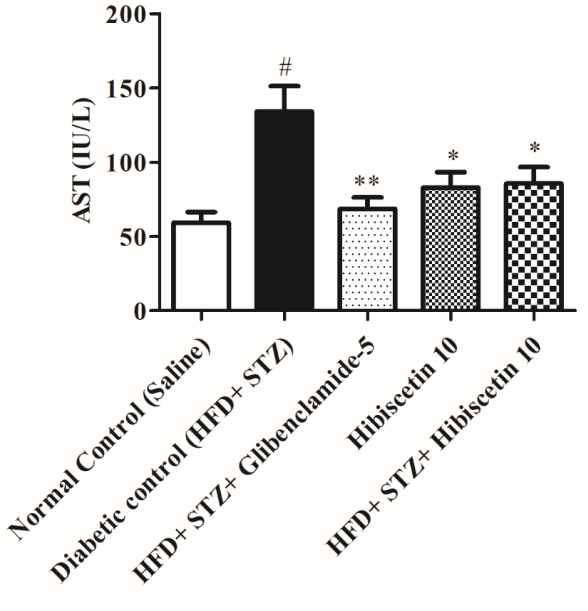


(**C**)

Figure 6. (**A**–**C**) Effect of hibiscetin on resistin, leptin, adiponectin and resistin (n = 6). The mean SEM is used to express the data; ($^{\#}$ $p < 0.05$) saline vs. HFD+STZ, (*** $p < 0.001$, ** $p < 0.01$, and * $p < 0.05$) HFD+STZ vs. treatment group.

3.7. Effect of Hibiscetin on Liver Functions

Figure 7A, B represents the impact of hibiscetin on hepatic functions. Diabetic animals had higher ALT and AST levels compared to the saline-treated group. Furthermore, when compared to the disease animals, treatment with glibenclamide and hibiscetin in disease experimental rats and hibiscetin in healthy rats resulted in evidential decreases in the aforementioned parameters, indicating their significant protective potential against diabetes-induced hepatic impairment. Significant hepatoprotection was observed with the standard drug glibenclamide in the HFD/STZ model.



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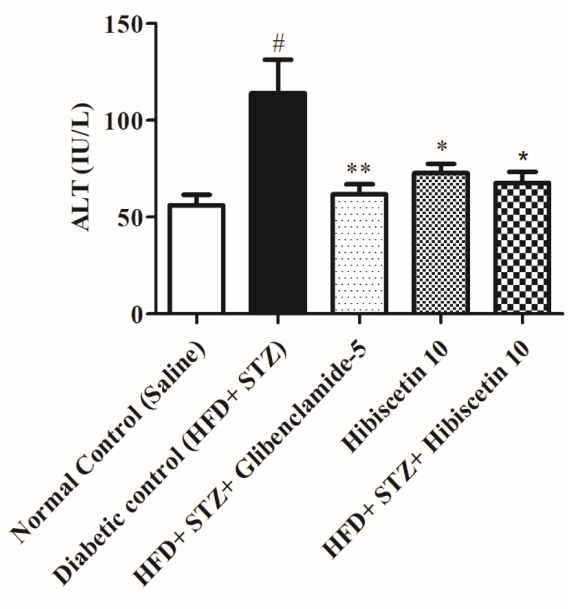

(**B**)

Figure 7. (**A**,**B**) Effect of hibiscetin on AST and ALT (n = 6). The mean SEM is used to express the data; ($^{\#}$ $p < 0.05$) saline vs. HFD+STZ; (** $p < 0.01$, and * $p < 0.05$) HFD+STZ vs. treatment group.

4. Discussion

The use of HFD in conjunction with a low dosage of STZ to produce type 2 diabetes in rats has been extensively described in the literature and has been found to imitate the T2D state and its accompanying metabolic problems in humans [19]. Hibiscetin favorably modulated antidiabetic (blood glucose and insulin), hypolipidemic (favorable lipid profile), anti-inflammatory (TNF-α, IL-6, and IL-1β), oxidative state and antioxidant (MDA, SOD, GSH, and CAT), and liver safety (AST and ALT) parameters in the experimental model of diabetes. Furthermore, the test medicine hibiscetin improved leptin, adiponectin, and resistin levels.

As a model for T2DM, this study employed a rat model of HFD diet followed by low-dosage STZ. Several researchers used the HFD/STZ paradigm to produce momentous weight gain. The treatment of diabetic rats with hibiscetin and the standard drug glibenclamide, on the other hand, reduced body weight; this might be explained by the treatment regimen's ability to regulate blood glucose levels. *Hibiscus sabdariffa* extract has the potential to be used to treat metabolic issues, since it reduces fat formation in white adipose tissue in the therapy groups through the exploitation of different dosages, resulting in weight loss. The current study findings are consistent with earlier research by other writers [20,21].

Hibiscetin was reported to have antihyperglycemic activity in the HFD/STZ diabetes model. The evidential rise in body weight and blood glucose seen in disease experimental rats compared to saline-treated might be attributed to the HFD and STZ administration feeding regimen. In groups treated with treatment, the hyperglycemic state in diabetic control rats was gradually controlled. Furthermore, the insulin levels in the therapy animals were higher than in the sick control rats. Glibenclamide's antidiabetic effectiveness was shown to be superior when compared to other treatment groups. The observed hypoglycemic effects are in agreement with previous reports. In this investigation, the in vitro inhibitory effect of *Hibiscus sabdariffa* extracts on α-amylase enzymes and α-glucosidase may highlight the likely mechanism by which *Hibiscus sabdariffa* extracts influence hypoglycemic activity [22,23]. Such a physiologically connected function may impact the anti-glycemic characteristics of roselle calyces and is pertinent to using this edible flower in T2DM dietary support regimens [24–26]. The protein enzyme PEPCK modulates the triglyceride cycle in adipose tissue and the liver. Understanding lipid homeostasis, glucose homeostasis, and

disease bar requires research into the protein enzyme PEPCK expression and regulation in the triglyceride/fatty acid series. The results demonstrate that four chemical compounds from the *Hibiscus sabdariffa* have a bring-down docking score and a higher potential as inhibitors of PEPCK than the conventional drug metformin. Because *Hibiscus sabdariffa* chemical compounds have a lower docking score, they are more stable and better for drug creation [5].

In addition to its beneficial effect on serum blood glucose, the hypolipidemic effect of hibiscetin was also evaluated in the present study. Deficiencies in insulin production or sensitivity have been linked to lipid abnormalities that contribute to illnesses including atherosclerosis and fatty liver disease [27]. The high-fat diet STZ was found to cause dyslipidemia by increasing total cholesterol and triglycerides and decreasing HDL cholesterol, while the therapy groups had the opposite outcomes. According to several studies, anthocyanin is a lipase pancreatic inhibitor. As a result, the anthocyanin-rich *Hibiscus sabdariffa* extract may slow the digestion of a high-fat meal in the intestinal lumen, resulting in lower plasma triglyceride and cholesterol levels [28,29]

Further exploring the antioxidant effects of hibiscetin in HFD/STZ-induced diabetes mellitus. The antioxidant and antihyperglycemic properties of *Hibiscus sabdariffa* extracts were also found to be consistent with a previous study that looked at the antioxidant potency of six Algerian propolis ethyl acetate extracts and the effectiveness of an ethyl acetate part from *Hibiscus sabdariffa* in reducing diabetes-related cognitive deterioration in experimental animals [30]. TNF-α, IL-1β, and IL-6 indicators were used to validate the anti-inflammatory benefits of hibiscetin in this investigation. Another putative mechanism implicated in *Hibiscus sabdariffa* anti-inflammatory actions is the downregulation of pro-inflammatory genes and proteins. Several in vivo and in vitro investigations have shown that *Hibiscus sabdariffa* or known *Hibiscus sabdariffa* components can suppress the countenance of proinflammatory genes, such as interleukins, NF-B, and iNOS [31,32]. The precise mechanism of pro-inflammatory gene downregulation is unknown, but mounting evidence shows that *Hibiscus sabdariffa* may influence one or more of the upstream components of the inflammatory genomic pathway. One example is the *Hibiscus sabdariffa*–induced decrease of Ang II and AT1 receptor levels that inhibits downstream NF-B and facilitates the production of the pro-inflammatory gene [33,34].

Low adiponectin levels have been associated with obesity-related metabolic disorders, and low adiponectin levels have been demonstrated to be under-expressed in people with T2DM. Adiponectin prevents atherosclerosis, inflammation, endothelial dysfunction, T2DM, and obesity-related cardiovascular diseases [35]. In comparison to diabetic rats that were not given any treatment, hibiscetin significantly increased adiponectin levels. This study distinctly demonstrated that, in the disease rats, adiponectin and leptin levels are significantly lower, and there is also improved resistin, when compared to the saline-treated animals, and this hypothesis was clinically supported in the current research, where the experimental rats that received hibiscetin effectively altered adipokine profiling. According to another study, roselle extract can enhance the sensitivity of insulin by lowering leptin resistance, oxidative stress, and inflammation in obese animals [20]. Resistin was first defined as an adipocyte-secreted peptide that was proposed to be related to obesity and diabetes. Recently, in vivo and in vitro documents have disclosed that resistin is involved in the inflammation process. Resistin has been shown to stimulate the IL-12 and TNF-α secretion from macrophages; and TNF-α and IL-1 β, IL-6, or lipopolysaccharides strongly induce resistin expression [36].

Roselle has an excellent record of safety and tolerability [37]. The considerable rise in blood hepatic enzyme activity (particularly AST and ALP) seen in the diabetic animals in this research might be attributable to the hypertoxic impact of the high-fat meal coupled with STZ administration. Elevated ALP activity might indicate cell membrane peroxidation, resulting in cell membrane integrity loss. ALT has been demonstrated to participate in amino acid transamination, and insulin inhibits its transcription. Exaggerated ALT activity may be caused by impaired insulin action [38]. ALP and AST levels were more importantly

brought down in the hibiscetin-treated rats than in the untreated rats. The same may be stated about glibenclamide's impact. The putative hepatoprotective and antioxidant actions of the extracts might explain the reduction in hepatic enzyme activity seen in diabetic rats treated with hibiscetin.

5. Conclusions

The outcome of the study shows the antihyperglycemic benefits of hibiscetin exposed to a diet and streptozotocin in diabetic rats. Furthermore, hibiscetin dramatically reduced alterations in biochemical indicators linked with diabetes.

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