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Evaluation of Solasodine in High Fructose Diet-Induced Metabolic Syndrome in Rats

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ABSTRACT

The present study was designed to determine the effect of solasodine in high-fructose diet-induced metabolic syndrome in rats.Metabolic syndrome in rats was induced by high fructose diet administered to all animals daily for 40 days. Animals were divided into 6 groups. Group-I was treated as normal control and Group-II was given high fructose diet plus vehicle, Group-III was treated with standard drug (pioglitazone) and other three groups were treated with solasodine 25, 50 and 100mg/kg of body weight by oral route for 40 days. Effect of this treatment on various parameters of metabolic syndrome like Body weight, abdominal circumference, BMI, abnormal levels of lipids (triglyceride, cholesterol, HDL-C), changes in blood pressure, blood glucose, serum insulin, HOMA-IR, Serum leptin, antioxidants (GSH, SOD, Catalase, AST/ALT) were evaluated. Abnormal changes in body weight, blood pressure, blood glucose and insulin, blood lipids has confirmed induction of metabolic syndrome in the animals. Treatment with standard drug pioglitazone and solasodine in all three doses have shown protective role in the animal models of metabolic syndrome. In conclusion, the effects in high-fructose diet-induced metabolic syndrome in rats has shown that solasodine offers protective role in ameliorating the parameters of metabolic syndrome.

INTRODUCTION

Metabolic syndrome, obesity, and diabetes mellitus are globally increasing to epidemic. The global impact of these disorders is immense in terms of human agony and economic burden. Insulin resistance along with atypical adipose deposition and function in one of the important risk factor for metabolic syndrome (Alberti 2005). There are several alternative definitions of the metabolic syndrome, most of which include insulin resistance, central obesity, dyslipidemia (increased TG and low HDL-cholesterol concentrations) and elevated blood pressure.

Insulin resistance is postulated as underlying cause of metabolic syndrome (Volek and Feinman, 2005). Globally it is on rising in both types of countries. Data from the third National Health and Nutrition Examination Survey (NHANES III) presented by Ford GS (2002), shown that approximately ¼ of the US adults 20 years or older have metabolic syndrome. In adult population samples the worldwide prevalence of metabolic syndrome has been shown to vary from 8 to 24 percent (Cameron AJ et al, 2004). Many studies (Dhurandhar NV, 1992; Gupta A et al., 2003) from India also show high prevalence of metabolic syndrome which varies from 15 to 45 per cent.

Ayurveda describes a set of complex clinical disorders, collectively called Prameha. The clinical conditions associated with Prameha correlate in many ways with obesity, metabolic syndrome, and diabetes mellitus. Xia X (2010) proposed hyperglycemia, hypertriglyceridemia, hypertension, and central (or upper body) obesity as the fatal Quartet of Metabolic syndrome

There is need for a more effective understanding of metabolic syndrome disease processes and its management through affordable and efficacious natural strategies. Ayurveda in its literature has explained several pharmacologic and non-pharmacologic methods for the prevention and management of obesity, hyperglycemia and hyperlipidemia. The food and drinks which alleviates vata, reduces kapha and fat are recommended. In Ayurveda, numbers of plants and its extracts have been suggested to be used to balance the disorders of metabolic syndrome. Number of alternative (herbal) medications have been examined for their role in various underlying parameters of metabolic syndrome (Marles RJ, 1995; Ernst E.1997; Nammi S et al. 2009; Shanmugasundram KR, 1983; Baskaran K ET AL 1990). For e.g Plant extracts from *Zingiber officinale* rhizome (Nammi S, 2009), *Gymnemasylvestre* (Baskaran K et al. 1990) *Solanum*

xanthocarpum (Jalali et al. 2014), plant metabolites from Bitter melon, *Zingiber officinale*, Tea and/or ingredients like flavonoids, polyphenols, and resveratrol have been used in animal models of metabolic syndrome.The extensive literature survey has shown that *Solanum xanthocarpum* is an important source of number of pharmacologically important entities, especially solasodine and also other chemicals like solasonine, campestrol, campeferol, diosgenin and other useful alkaloids. The solasodine is the most studied chemical constituent of *Solanum xanthocarpum* which has a role in the production of sex hormones. The plant is extensively studied for the several pharmacological activities like antiasthmatic, hepatoprotective, cardiovascular, hypoglycemic and mosquito-repellent properties. *Solanum xanthocarpum* has been used in traditional Indian medicines for its antioxidant, anti-inflammatory, and antiasthmatic properties. (Joseph et al. 2012; Jalali et al. 2014).

There is no published evidence on the role of solasodine in metabolic syndrome. Proposed research work will help to confirm the role of solasodine in metabolic syndrome, through its effect on lipid profile, cardiac parameters and blood glucose levels.There is no single drug treatment for metabolic syndrome. It is obvious because metabolic syndrome is a cluster of disorders which involves irregular and improper levels blood lipid and blood glucose, change in BMI, and change in blood pressure levels and so on. There is a need of drug which can take care of all probable pathologies that can lead to metabolic syndrome. Proposed research work will help to elucidate the role of solasodine in high-fructose induced rat model of metabolic syndrome by showing its activity on lipid levels, thereby obesity and cardiovascular function, and on blood glucose levels.

MATERIALS AND METHODS

Wistar rats of both sexes weighing between 150-180 g were obtained and kept individually in polypropylene cages in an environmentally controlled room of the animal house and maintained at temperature of 25 ± 2^{0}C with a 12-hrs dark/light cycle. The animals had free access to food and water. Rats were fed with standard rat chow diet or special high fructose diet according to the protocol. Experiments were carried out after a week of acclimatization. The animal studies were approved by the Institutional Animal Ethics Committee (IAEC/CPD/415/05), constituted for the purpose of control and supervision of experimental animals by Ministry of Environment and Forests, Government of India, New Delhi, India. Animals were naive to drug treatments and

experimentation at the beginning of all studies. All tests were conducted between 08:00 and 14:00 hrs.

Drugs and solutions

Solasodine, isolated from dried, ripe fruits of *Solanum xanthocarpum* by method described by Gawande A et al. (1991). All other agents used were of analytical grade. The doses were selected as Solasodine (25, 50, 100 mg/kg, p.o.) on the basis of previous reports and dose-finding study performed in this work.

Experimental groups

Animals were divided into six groups consisting of six wistar rats of either sex in each group, were studied. Group I, as control received normal diet, while the rest five groups were fed with high fructose diet [60% w/w fructose; supplied by Central Drug House (P) Ltd., New Delhi, India] for 20 days *ab libitum*. The High fructose diet provided 60 percent of the calories from fructose. Group II continued to receive High Fructose diet and vehicle solution, while group III received High Fructose diet (HFD) and pioglitazone 10 mg/kg body weight orally for the next 20 days. The other three groups (Group IV to VI) continued to receive High Fructose diet and solasodine at a dose of 25, 50 and 100 mg/kg orally for the next 20 days. All the drugs were administered once time in a day by gavage in 1 percent suspension of carboxymethyl cellulose (CMC).

Rats were sacrificed at the end of study. A portion of liver (50 % of the largest hepatic lobe) was rapidly excised, dipped in liquid nitrogen and stored at -80^{o}C for biochemical estimations. The remaining 50 % of liver was kept in 10 % formalin for histopathological study (Pankaj Prabhakar, 2015).

Biochemical estimation

After overnight fast (12 ± 1 hrs), blood sample was collected and was centrifuged at 3,000 RPM for 10 min at 4^{0} C for the separation of plasma. The levels of fasting plasma glucose, total cholesterol, triglycerides and HDL-C were estimated as per procedure is given by the manufacturers of the kits (Vital Diagnostics Pvt. Ltd, India), it was analyzed using a semi-autoanalyser (Minitecno, India). The indirect tail cuff method was used for measurement of blood

pressure (Powerlab) as described by Kim HY (2010) and Prabhakar P (2015). Oral Glucose tolerance test (OGTT) was performed at the end of the experiment in all the four group animals by oral administration of 2g/kg body weight. Serum level of Advanced Glycated End-products (AGEs) were determined by the method described by Sampathkumar et al. (2005). Serum Leptin level in serum was estimated using ELISA kits based on a quantitative sandwich enzyme immunoassay technique. (Considine R, 1996). Serum ALT and AST levels were estimated with help of standard kit available in the market. Glycosylated hemoglobin levels were estimated by method given by Liu IM et al (2007).For serum Insulin level we have used the method suggested by Mahmoud AAA et al (2014). Further, Insulin resistance was determined using the homeostasis model assessment index for insulin resistance (HOMA-IR). This method was described by Matthews et al. (1985). Following formula was used to calculate HOMA-IR index.

HOMA-IR index = [fasting glucose (mmol/L) X fasting insulin (microU/ml)]/22.5

Liver tissue samples were thawed once and homogenized in 10 % w/v ice-cold 0.1 M phosphate buffer (pH 7.4). The homogenates were used for estimation of thiobarbituric acid reactive substances (TBARS) as a marker of lipid peroxidation and endogenous antioxidants such as reduced glutathione (GSH) level, superoxide dismutase (SOD) and catalase activities. Protein was estimated using Bradford's reagent.

Histopathological analysis:

Liver tissue samples were fixed in 10 % formalin and embedded in paraffin. 5-lm-thick paraffin sections were cut from the paraffin-embedded tissue blocks and stained with hematoxylin and eosin and picrosirius red. The paraffin sections were deparaffinised by immersing in xylene and rehydrated through a series of graded alcohols (100, 95 and 75 %), for 15 min each. The slides were stained with hematoxylin and eosin as well as picrosirius red and mounted with coverslip using distyrene plasticizer and xylene (DPX). The slides were examined under light microscope by a pathologist blinded to the study groups. Images were taken at magnification 9 20 (Maulik SK, 2012).

STATISTICAL ANALYSIS

Values were expressed as mean ± standard error. The results were statistically analyzed for significant differences using one-way ANOVA followed by Dunnets post-test to compare control group with other groups. Analysis of results and plotting of graphs were carried out using Graph Pad Prism (version 5.01 for windows).

RESULTS

Effect on body weight:

The baseline weight of rats in different groups was not significantly different from each other. Administration of High Fructose diet for a period of initial 20 days resulted in an increase in body weight of more than 10 percent in all the groups and reached to significance in all the groups. While rats fed on normal diet (control group) gained 3 percent increase in body weight which was insignificant as compared to the group which has been administered high fructose diet. After treating study animals with pioglitazone and different doses of solasodine day 20 onwards in respective groups, it had shown significant change in body weight (Table 1).

Effect on blood pressure:

The baseline systolic blood pressure in all the groups was similar. After administration of high fructose diet for a period of 20 days resulted in about 40 percent increase in systolic blood pressure in all the groups. The groups which were treated with pioglitazone and different doses of solasodine statistically reduced the systolic blood pressure (Figure 1).

Effect on blood glucose levels:

The baseline fasting plasma glucose was similar in all groups. After administration of high fructose diet for a period of 20 days resulted in a significant increase in fasting plasma glucose of about more than 40 percent in all the groups. Administration of pioglitazone 10mg/kg and solasodine at all dose level caused a statistically significant decrease in fasting plasma glucose level at day 40 (Figure 2).

Effect on plasma insulin:

The baseline fasting levels of plasma insulin were similar in all the groups. After administration of high fructose diet for 20 days significantly increased fasting plasma insulin in all groups as compared to baseline. Pioglitazone 10 mg/kg and Solasodine 25, 50 and 100mg/kg, doses significantly lowered fasting plasma insulin levels at day 40 (Figure 3).

Effect on HOMA-IR:

The baseline HOMA-IR in all the groups was similar. After administration of high fructose diet for a period of 20 days resulted in significant increase in HOMA-IR in all the groups. Pioglitazone and solasodine treatment in the doses of 25, 50 and 100 mg/ kg has shown significant decrease in HOMA-IR at day 40 (2, 1.7 and 1.6 respectively).

Effect on OGTT:

The baseline AUC for glucose was similar in all the groups. Administration of high fructose diet daily for 20 days resulted in significant increase of AUC for glucose. Pioglitazone and solasodine (25, 50 & 100 mg/kg) treatment caused a significant lowering in AUC for glucose in all groups at day 40 (Figure 4).

Effect on lipid parameters:

Daily administration of high fructose diet led to an increase in triglyceride, total cholesterol and decrease in HDL-cholesterol level at day 20. Treatment with solasodine at a dose 25, 50 & 100 mg/kg resulted in significant decrease in triglyceride (Figure 5) and total cholesterol level (Figure 6). The solasodine at all dose levels shown significant alteration in HDL-cholesterol (Figure 7).

Effect on oxidative parameters

Free radical scavenging enzyme (SOD, catalase and GSH) activity in serum was reduced and serum MDA level was increased significantly in high fructose rat compared to normal rats. Solasodine treatment significantly enhanced levels of antioxidant enzyme and reduced MDA in treated group of rats (Figure 8)

Serum ALT & AST levels:

The ALT & AST levels were significantly increased in group-II whereas these levels were significantly decreased in solasodine treated groups. The effect on ALT & AST was more in high dose as compared to low dose solasodine (Figure 9).

Effect on Glycosylated Haemoglobin &AGEs:

Solasodine treated rats showed significant reduction in glycosylated hemoglobin (Figure 10) and advanced glycated end products (Figure 11) increased due to high fructose diet.

Serum leptin levels:

The serum leptin was significantly increased in group-II which was significantly decreased in solasodine treated groups. The effect on serum leptin with solasodine was found to be dose-dependent (Figure 12).

Liver histology

High Fructose diet caused micro and macrovesicular fatty changes of hepatocytes and also infiltration of inflammatory cells or necrosis was observed in disease control group. Pioglitazone and solasodine (25, 50 and 100mg/kg) lead to protection of micro and macrovesicular fatty changes of hepatocytes caused by high fructose diet.

DISCUSSION

Metabolic syndrome is a cluster of abnormal conditions like high blood glucose, insulin resistance, high fat and obesity, and high lipid levels. These abnormal conditions lead to development of diabetes mellitus type-2, hyperlipidemia and hypertension.

Our results showed that the groups which had received high fructose diet (60%) for 20 days induced the classic symptoms of the metabolic syndrome. Rats from these groups showed significant increase in weight gain, abdominal circumference and BMI as compared to the control group rats. They have shown impaired glucose tolerance, significantly higher levels of blood glucose, total cholesterol, triglycerides, higher SBP, and DBP compared to control group which was not fed high fructose diet. In addition to this, it was found that high fructose diet has induced

insulin resistance as seen by significant increase in HOMA-IR index. There was increased hepatic oxidative stress change seen in rats, which was indicated by high levels of hepatic thiobarbituric acid reactive substances (TBARS) and decreased endogenous antioxidant levels (GSH, SOD and catalase). Together, these all changes confirmed the proper induction of metabolic syndrome in our study.

High fructose diet disrupts the normal hepatic carbohydrate metabolism which leads to abnormality in glycolytic pathway. There was significant increase in serum triglycerides and cholesterol levels in animals who were fed only high fructose and not given any treatment. HDL-C levels were drastically reduced in this animals, whereas the drug treated animals have prevented substantial change in HDL-C levels. In present study, pioglitazone (10 mg/kg) prevented an increase in levels of triglycerides and total cholesterol and further decrease in HDL-C caused by high fructose diet. Similarly, solasodine helped to prevent the increase in triglycerides and total cholesterol as well as decrease in HDL-cholesterol caused by consumption of high fructose diet. High dose solasodine (100mg/kg) has shown numerical superiority over other doses. Suzuki M (1997) earlier reported that pioglitazone has shown effect against an increase in triglycerides in fructose-induced insulin resistance.Solasodine in all dose levels (25mg, 50mg and 100mg/kg) and pioglitazone had shown the reducing effect on fasting plasma insulin levels as compared to high fructose diet group. This may be due to control of increased glucose levels by solasodine in this model. In our study, high fructose diet also caused hyperglycemia,impaired glucose tolerance and alteration in insulin sensitivity. Solasodine prevented the increase in fasting plasma glucose, impaired glucose tolerance and change in insulin sensitivity. The anti-hyperglycemic effect of alcoholic extract of *Solanum xanthocarpum* has been reported earlier in streptozotocin(STZ)–nicotinamide-induced diabetic rats [Gupta et al. (2005); Kar et al. (2006)],this study is showing anti-hyperglycaemic effect of solasodine in a high fructose diet model of metabolic syndrome. Even solasodine helped to protect hemoglobin from glycosylated and also shown effect to control advanced glycated end products.

Serum leptin is an important adipose tissue–derived hormone that has been shown to be involved in pathways that influence the risk of cardiovascular disease and diabetes. (Wannamethee SG et al. 2007). In current study except for disease control group all drug-treated groups has shown to prevent increase in serum leptin levels. Solasodine has shown dose-dependent decrease in serum

leptin levels. Thus solasodine may aid in prevention of pathways that may prove to be risk factor for diabetes and cardiovascular disease, which are part of metabolic syndrome.

Oxidative stress is an important characteristic of diet-induced metabolic syndrome in animals as well as humans (Pakdeechote P, 2014). Vincent and Taylor (2006) reported that even the alteration of insulin sensitivity leads to increase in rate of glucose oxidation and more production of hydroxide free radical. Ogihara T et al. (2004) has shown that the oxidative stress induces the expression of NF-kB (Nuclear factor KB) which directly or indirectly may contribute to the insulin resistance. Hence, antioxidants can be used in the treatment of oxidative stress-induced insulin resistance. Pioglitazone (and other thiazolidinediones) are known to agonize the transcription factor peroxisome proliferator activated receptor-γ (PPAR-γ) and thus currently used in the treatment of Type 2 diabetes. In current study, solasodine has reduced the insulin resistance but the mechanism is not clear. This can be studied further separately.Kim JH (2014) shown that oxidative stress can be one of the important predictive parameters for metabolic syndrome. Sharma T et al. has recently shown the potential antioxidant effect of solasodine to protect rat brain from ischemia/reperfusion injury. In this study, there is increased hepatic TBARS and decrease in GSH, catalase as well as SOD levels which may lead to oxidative stress on liver. This oxidative stress in liver may lead to be induction of metabolic syndrome. Solasodine effectively helps to arrest the changes in oxidative stress markers at all dose levels. Pioglitazone and solasodine administration reduced the hepatic lipid peroxidation and prevented decrease in reduced GSH, catalase, ALT/AST and SOD levels in the liver in present study. It is possible that solasodine, by virtue of its reported antioxidant effect, might be playing an important protective role in metabolic syndrome.

In our study, HFD caused an elevation in systolic blood pressure as also reported earlier (Shahataa MG et al. 2016). Hypertension is one of the component of human metabolic syndrome, the exact mechanism of which is not understood. This is in similar line of earlier findings by Krayer and Briggs (1951), they have reported anti-accelerator effect of solasodine and some of its derivatives in heart-lung preparation of the dog. In our study, solasodine at all dose levels shown significant decrease in systolic blood pressure compared to normal group (normal control) and high fructose diet group [(disease control) ($p< 0.05$)]. Thus we can say that solasodine helps to prevent the increase in systolic blood pressures caused by HFD.

Pioglitazone and solasodine (25, 50 and 100mg/kg) helped to protect the hepatocytes against micro and macrovesicular fatty changes that are caused by high fructose diet. Additionally, histopathological changes were also seen liver tissue.

Solasodine has helped to control body weight, abdominal circumference and BMI. Weight gain or obesity is one of the important factor which leads to development of metabolic syndrome. Current data suggests a possible role of solasodine in reducing the high levels of blood glucose and lipid levels.The administration of solasodine prevented metabolic and microscopic changes caused by high fructose diet. Current study has attempted to evaluate as many parameters which are linked to metabolic syndrome.Solasodine has shown considerable effect on parameters of metabolic syndrome.

CONCLUSION

In conclusion, the present study demonstrates that high fructose diet consumption caused metabolic syndrome in rats, which was associated with hepatic oxidative stress, body weight and abdominal circumference, blood pressure, blood lipid and blood glucose changes. Earlier studies have shown that extract of *Solanum xanthocarpum* has shown effect on some of the parameters of metabolic syndrome. Current study went one step ahead, which included evaluation of the effect of isolated solasodine from *Solanum xanthocarpum* on parameters high-fructose-induced animal model of metabolic syndrome. This protective effect of solasodine further can be evaluated in terms of real human metabolic syndrome.

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CONFLICT OF INTEREST

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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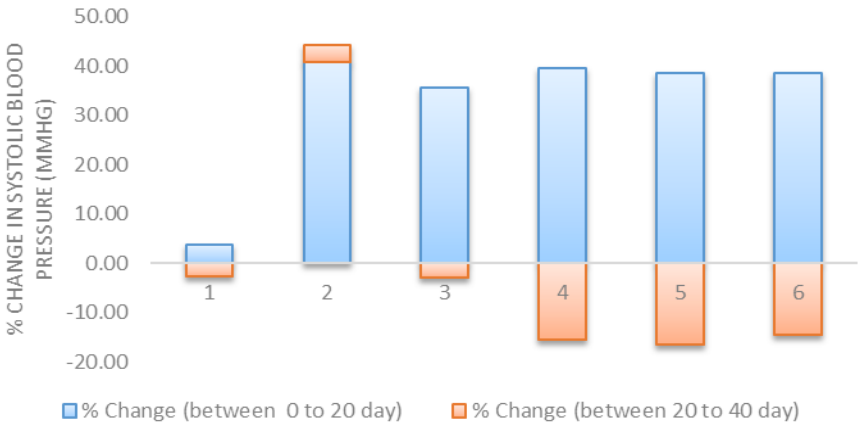
Table 1: Effect of Solasodine on body weight (g) in High Fructose diet-induced rat model

Group	Treatment	Day 0	Day 20	Day 40	% increase (between 20 to 40 day)
Group-I	Normal	160.34±12.46	163.26± 10.02	168.36±13.17	3.12
Group-II	High Fructose Diet + Vehicle	163.43± 9.45	187.76± 6.86*#	216.04± 7.26*#	15.06
Group-III	High Fructose Diet + Pioglitazone (10 mg/kg)	158.92±10.56	189.31±10.27*#	196.82± 7.43*$	3.97
Group-IV	High Fructose Diet + Solasodine (25mg)	159.67±9.64	186.71± 11.20*#	193.75±11.27*$	3.77
Group-V	High Fructose Diet + Solasodine (50mg)	157.38±12.41	188.17± 10.04*#	195.83±8.16*$	4.07
Group-VI	High Fructose Diet + Solasodine (100mg)	162.50±6.72	190.73± 13.55*#	199.16±12.21*$	4.42

Each value expressed as Mean ± S.E.M. Data were analyzed by one way analysis of variance (ANOVA) followed by Tukey's test (n=6).

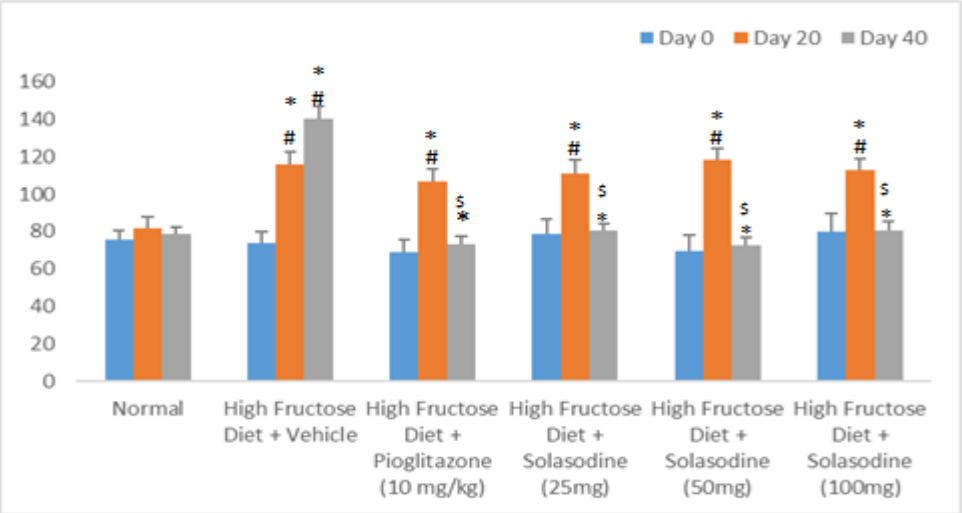
* $p < 0.05$ compared to baseline, # $p < 0.05$ compared to Normal Group (Normal Control), $ $p < 0.05$ compared to High Fructose Diet(Disease Control) 40 day, @ $p < 0.05$ compared to High Fructose Diet (Disease Control)

Figure 1: Effect of Solasodine on percentage change in Systolic pressure (mmHg) in High Fructose diet-induced rat model



1: Normal Control; **2:** High Fructose Diet + Vehicle; **3:** High Fructose Diet + Pioglitazone (10 mg/kg); **4:** High Fructose Diet + Solasodine (25mg); **5:** High Fructose Diet + Solasodine (50mg); **6:** High Fructose Diet + Solasodine (100mg)

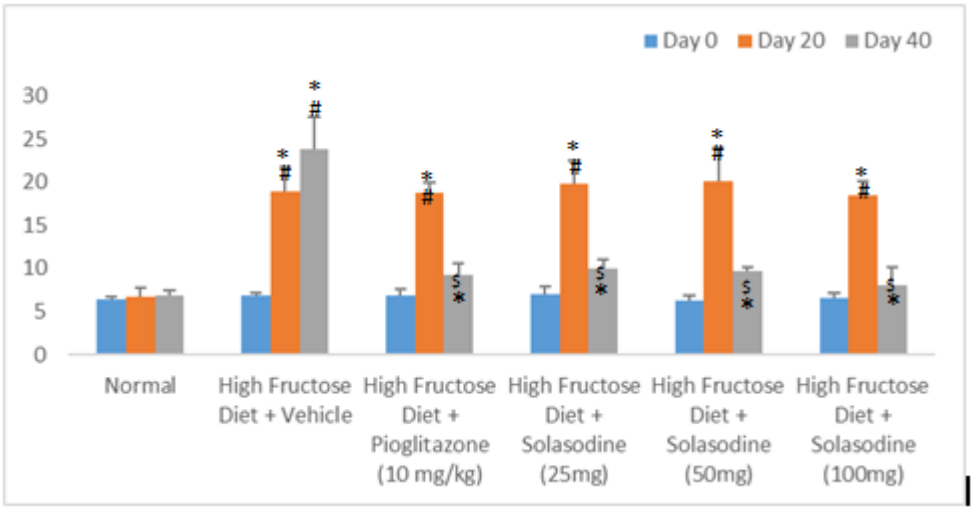
Figure 2: Effect of Solasodine on Fasting plasma glucose (mg/dl) in High Fructose diet-induced rat model



Each value expressed as Mean ± S.E.M. Data were analyzed by one way analysis of variance (ANOVA) followed byTukey‘s test (n=6).

* p< 0.05 compared to baseline, # p < 0.05 compared to Normal Group (Normal Control), $ p < 0.05 compared to High Fructose Diet (Disease Control) 40 day

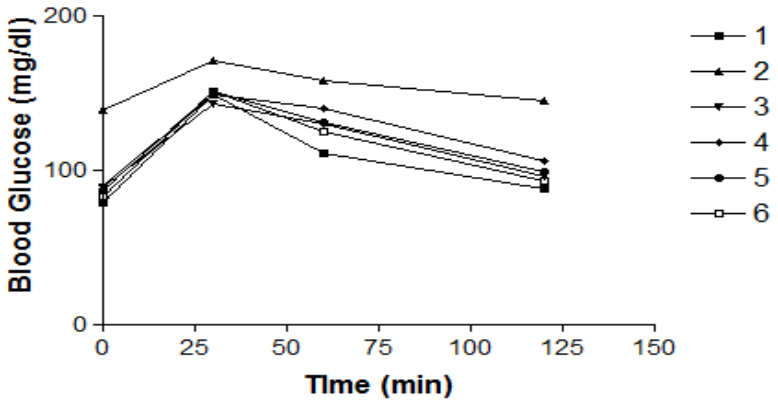
Figure 3: Effect of Solasodine on Fasting plasma insulin (µU/ml) in High Fructose diet-induced rat model



Each value expressed as Mean ± S.E.M. Data were analyzed by one way analysis of variance (ANOVA) followed by Tukey's test (n=6). HOMA-IR: Homeostasis model assessment - Insulin Resistance

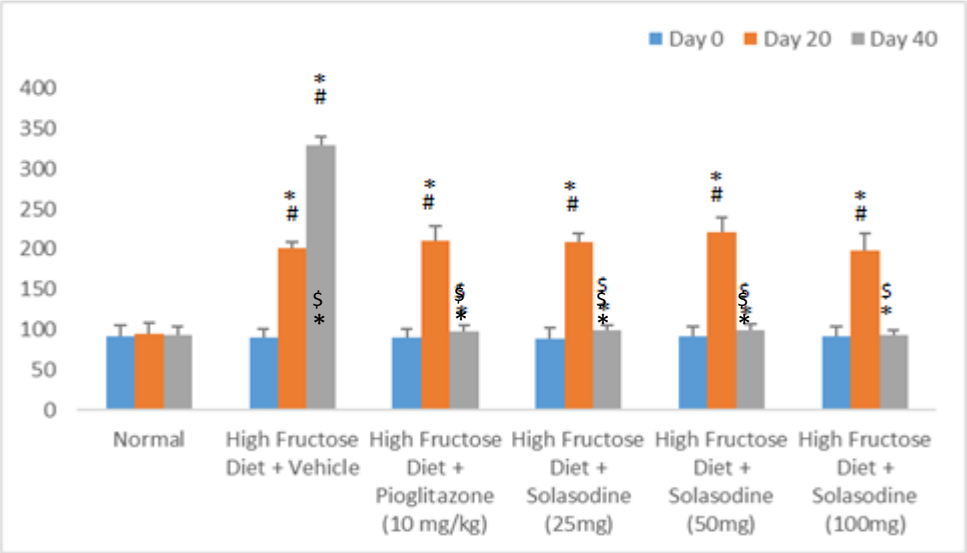
* p< 0.05 compared to baseline, # p < 0.05 compared to Normal Group (Normal Control), $ p < 0.05 compared to High Fructose Diet (Disease Control) 40 day

Figure 4: Effect of Solasodine on OGTT in High Fructose diet-induced rat model



1: Normal Control; **2:** High Fructose Diet + Vehicle; **3:** High Fructose Diet + Pioglitazone (10 mg/kg); **4:** High Fructose Diet + Solasodine (25mg); **5:** High Fructose Diet + Solasodine (50mg); **6:** High Fructose Diet + Solasodine (100mg)

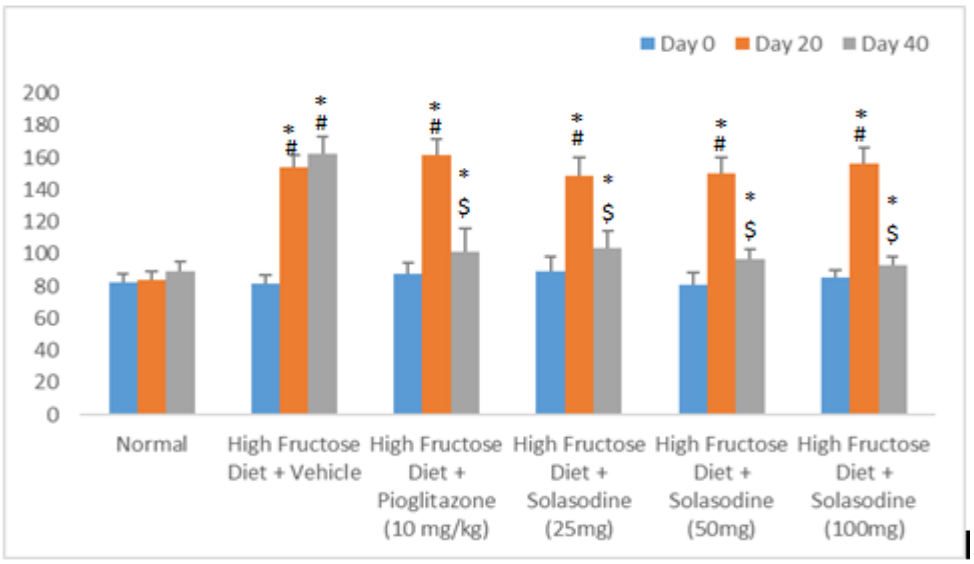
Figure 5: Effect of Solasodine on Serum Triglyceride (mg/dl) in High Fructose diet-induced rat model



Each value expressed as Mean ± S.E.M. Data were analyzed by one way analysis of variance (ANOVA) followed by Tukey's test (n=6).

* p< 0.05 compared to baseline, # p < 0.05 compared to Normal Group (Normal Control), $ p < 0.05 compared to High Fructose Diet (Disease Control) 40 day

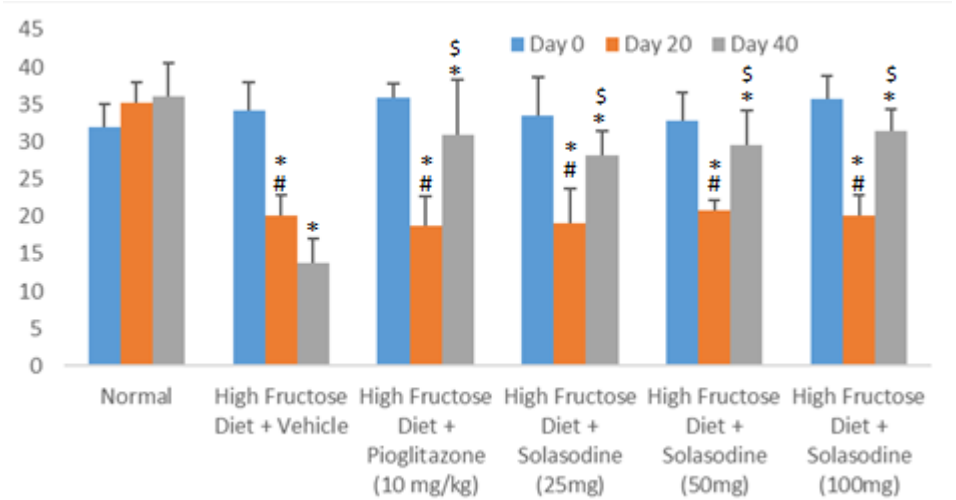
Figure 6: Effect of Solasodine on Serum Cholesterol (mg/dl) in High Fructose diet-induced rat model



Each value expressed as Mean ± S.E.M. Data were analyzed by one way analysis of variance (ANOVA) followed by Tukey's test (n=6).

* p< 0.05 compared to baseline, # p < 0.05 compared to Normal Group (Normal Control), $ p < 0.05 compared toHigh Fructose Diet (Disease Control) 40 day

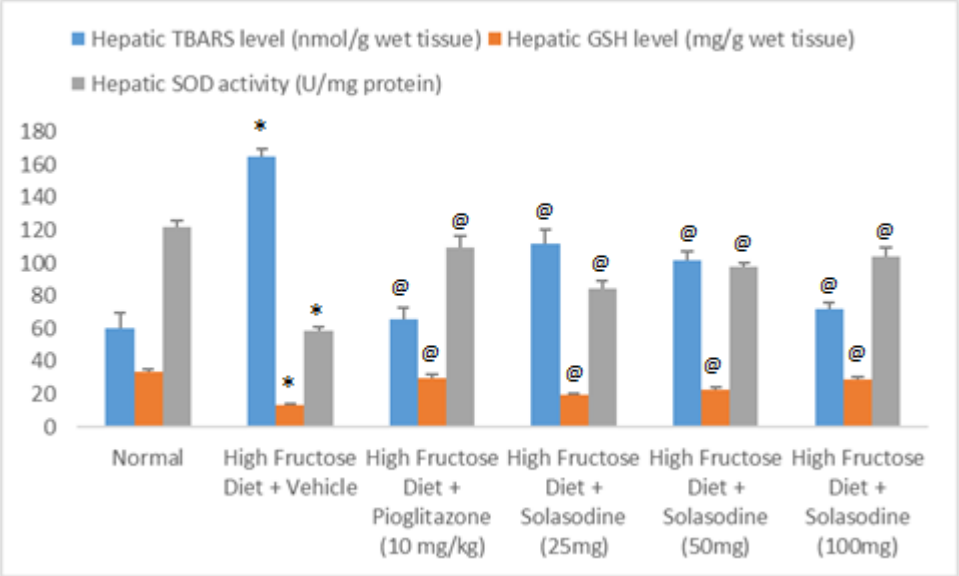
Figure 7: Effect of Solasodine on Serum HDL-C (mg/dl) in High Fructose diet-induced rat model



Each value expressed as Mean ± S.E.M. Data were analyzed by one way analysis of variance (ANOVA) followed by Tukey's test (n=6). HDL-C: High-density cholesterol level

* p< 0.05 compared to baseline, # p < 0.05 compared to Normal Group (Normal Control), $ p < 0.05 compared to High Fructose Diet (Disease Control) 40 day

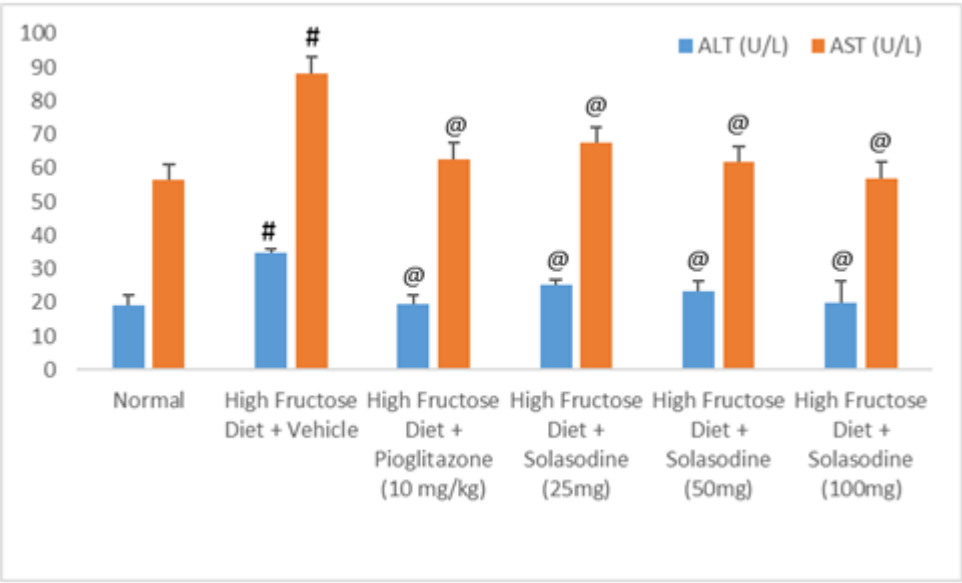
Figure 8: Effect of Solasodine on Oxidative parameters in High Fructose diet-induced rat model



Each value expressed as Mean ± S.E.M. Data were analyzed by one way analysis of variance (ANOVA) followed by Tukey's test (n=6).

# p< 0.05 compared to Normal Group (Normal Control), @ p < 0.05 compared to High Fructose Diet (Disease Control)

Figure 9: Effect of Solasodine on ALT and AST levels (U/L) in High Fructose diet-induced rat model

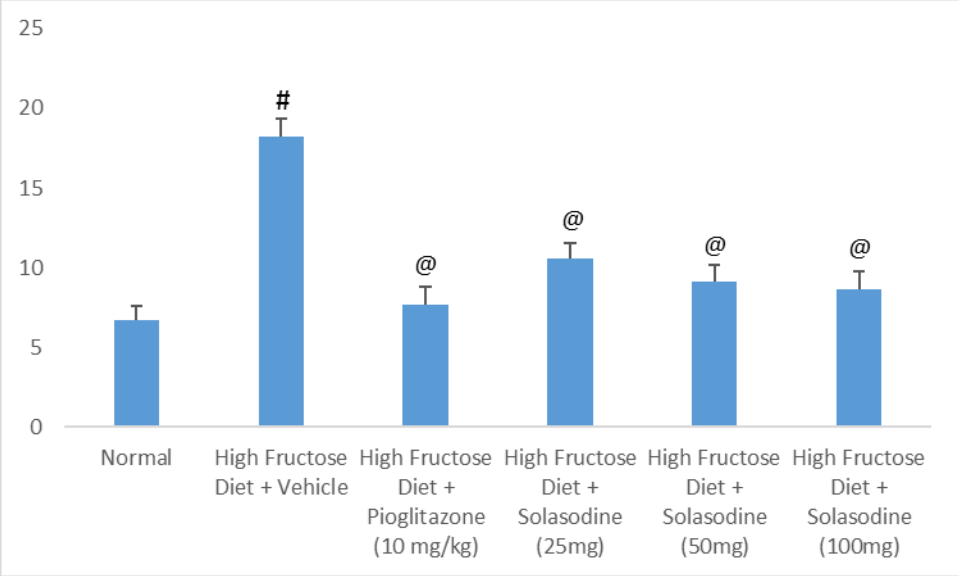


Each Value is expressed as Mean ± S.E.M., Data were analyzed by one way analysis of variance (ANOVA) followed by Tukey‘s test (n=6),

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase

# p< 0.05 compared to Normal Group (Normal Control), @ p < 0.05 compared to High Fructose Diet (Disease Control)

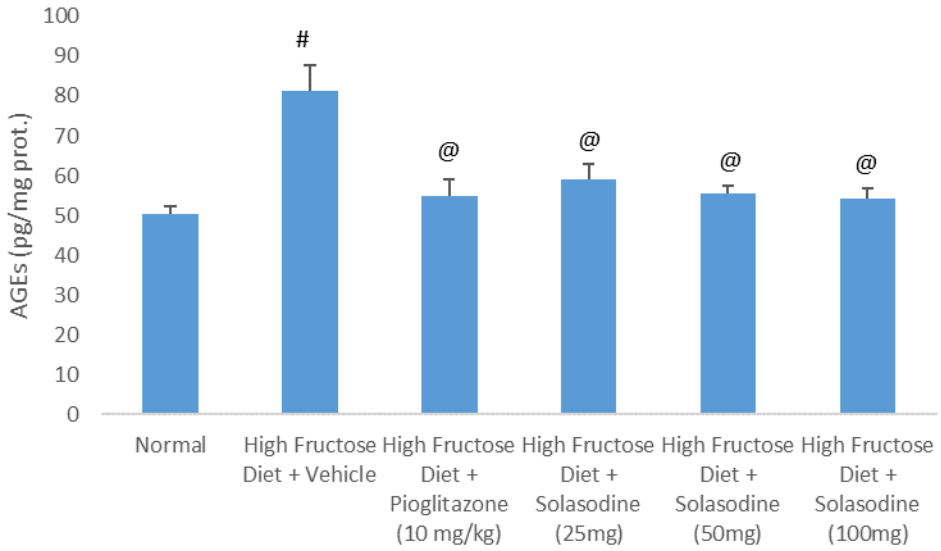
Figure 10: Effect of Solasodine on % Glycosylated Haemoglobin in High Fructose diet-induced rat model (n=6)



Each Value is expressed as Mean ± S E M, Data were analyzed by one way analysis of variance (ANOVA) followed by Tukey‘s test (n=6),

# p< 0.05 compared to Normal Group (Normal Control), @ p < 0.05 compared to High Fructose Diet (Disease Control)

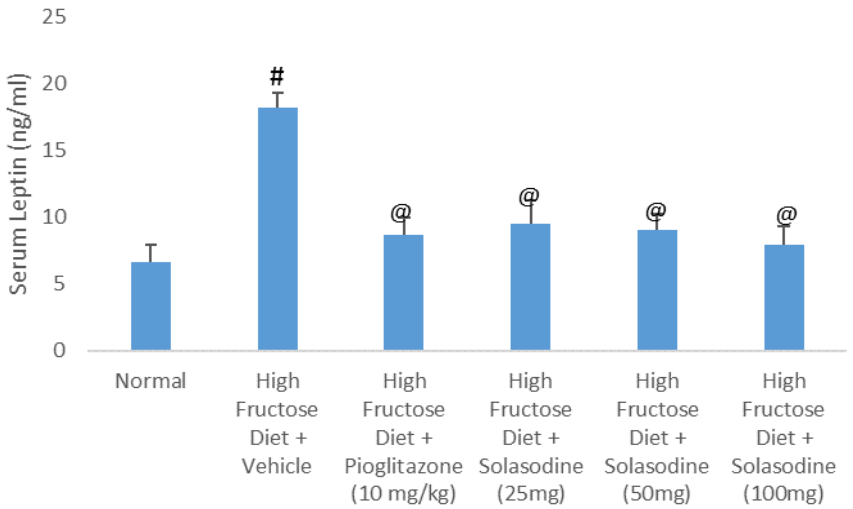
Figure 11: Effect of Solasodine on AEGs in High Fructose diet-induced rat model



Each Value is expressed as Mean ± S.E.M., Data were analyzed by one way analysis of variance (ANOVA) followed by Tukey‘s test (n=6),

# p< 0.05 compared to Normal Group (Normal Control), @ p < 0.05 compared to High Fructose Diet (Disease Control)

Figure 12: **Effect of Solasodine on serum leptin (ng/ml) in High Fructose diet-induced rat model**



Each Value is expressed as Mean ± S.E.M., Data were analyzed by one way analysis of variance (ANOVA) followed by Tukey‘s test (n=6),

# p< 0.05 compared to Normal Group (Normal Control), @ p < 0.05 compared to High Fructose Diet (Disease Control)