**Macrotyloma uniflorum** (Lam.) Verdc. improves glucose metabolism and proinflammatory parameters in high fructose fed rats

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Diabetes mellitus (DM) is the most common chronic metabolic disease and its complications constitute major health problems in heart, kidneys, eyes and nerves. The high fructose fed diet (HFFD) induces insulin resistance (IR), hyperinsulinaemia, hyperglycaemia, alterations in lipid metabolism, and oxidative stress which plays a vital role in pathology associated with insulin resistance. Here, we explored the possible role of common pulse, horsegram (*Macrotyloma uniflorum*) as a therapeutic adjunct in a metabolic state of insulin resistance. Male adult Wistar strain albino rats (160-180 g) were divided into four groups of six rats in each. It was observed that the levels of Corticosterone (GC) and protein-bound sugars were higher and activities of liver mitochondrial enzymes were altered in HFFD rats, as compared to control animals. With the administered with *M. uniflorum* as adjunct in treatment of IR treatment which are functioned by increased GC in liver and adipose tissue and by stimulated liver mitochondrial enzymes activities and IR with reduce fructose.

**Keywords:** Adiponectin, Fructose diet, Glucocorticoid, Horsegram, Insulin resistance, Leptin, Mitochondrial enzymes

Diabetes mellitus (DM), the most common ‘group of metabolic disorders’ of modern era characterized by hyperglycaemia, is a serious health crisis and a global societal catastrophe¹². Prolonged diabetes leads to complications viz., retinopathy, nephropathy and neuropathy, increased risk of other diseases including heart, peripheral arterial and cerebrovascular disease, obesity, cataracts, erectile dysfunction, non-alcoholic fatty liver disease, and some infectious diseases, such as tuberculosis, HIV/AIDS and malaria¹². As per the latest report of International Diabetes Federation, the global burden of diabetes is currently >425 million people, of which one-third are aged >65 years³. It is estimated to rise to 629 million in 2045. While three quarters of them are from low and middle income countries, two-thirds (279 million) represent urban areas. Currently, China and India alone has 121 and 74 million cases of diabetes, respectively¹. Diabetes prevalence in India has been reported to be 8.8% of its population which is likely to increase to 11.4% by 2045¹. Type 2 diabetes is the most common form of diabetes, accounting 90% of all over the world¹. Type 1 diabetes is also reported to be increasing worldwide and an estimate of children and adolescents below age 20 has now risen to over a million¹.

Fructose, the common fruit sugar, acts as major component of sweeteners, such as table sugar, honey, and high-fructose corn syrup (HFCS). Its consumption has significantly increased, partly with HFCS consumption in the food industry³. Intake of more fructose can lead to increase in blood lipids⁴, development of insulin resistance (IR)⁵, increase in inflammatory biomarkers and oxidative stress, risk on development of obesity, and comorbidities, such as hypertension and DM type II⁶. The liver acts as the primary site for both fructose metabolism and extraction, and hence chronic high fructose load impairs hepatic glucose metabolism⁷. IR is a pathophysiological state in which the hepatic and peripheral tissues are less sensitive to the insulin⁸.

Glucocorticoid (GC) hormones play an important role in regulating carbohydrate and lipid metabolism in the liver. Independent of their circulating concentrations, higher production of local GC have a negative impact on various mechanisms involved in the development of diet induced metabolic
disturbances. IR is associated with chronic excess of GCs, where reduction of GCs improves insulin sensitivity. For example, increased GC production induces hypercortisolism mediated IR through activation of the glucocorticoid receptor. Leptin is a multifunctional hormone which helps in controlling energy exchange and body weight. Adipocytes secrete two important cytokines namely tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) as well as anti-inflammatory cytokines such as adiponectin that play an important role in the immune response and inflammation during IR. Increased levels of TNF-α and IL-6 with reduced level of adiponectin induces IR, an inflammatory disorder. Fructose feeding induces the TNF-α and IL-6 production and initiate chronic inflammation. Therefore, the interaction between glucocorticoid metabolism and proinflammatory signalling pathway may represent an important mechanism which is involved in the regulation of inflammation and insulin action in the liver.

Herbal and other plant derived medicines are preferred as they are potentially safer compared to synthetic drugs. Horsegram [Macrotyloma uniflorum (Lam.) Verde.] is an important rainfed minor pulse crop, used in Indian ayurvedic system to treat various diseases. It is a potential grain legume having significant nutritional and remedial properties with better climate resilience to adapt harsh environmental conditions, grown almost all over the world including East and Northeast Africa, India, China, Philippines, Bhutan, Pakistan, Sri Lanka and Queensland in Australia. These seeds are used to treat heart conditions, asthma, kidney stones, bronchitis, leukoderma, urinary discharges, hepatoprotective role and obesity.

Aqueous extract of Macrotyloma uniflorum seeds has been reported to possess various pharmaceutical properties including analgesic, anticholelithiasis, antidiabetic, antihelminthic, antihistaminic, antihypercholesterolemic, antihypertensive, anti-inflammatory, antimicrobial, antiobesity, antioxidant, antipeptic ulcer, antiulotihsliasis, diuretic, hemolytic and hepatoprotective properties. In the present study, we investigated the effect of M. uniflorum seeds on glucocorticoid, pro inflammatory cytokines (Leptin, Adiponectin, TNF-α, IL-6), gluconeogenic enzymes and liver mitochondrial enzymes in rats with high fructose diet induced insulin resistant model.

Materials and Methods

Animals

Twenty four male adult Wistar strain albino rats, weighing 160-180 g were purchased from “Sri Venkateswara Enterprises”, Bangalore, Karnataka, India, and were housed in clean sterile polypropylene cages under the constant environmental and nutritional conditions throughout the period of experiment. During the course of experiments, the temperature was maintained between 22±2ºC. The rats were fed on a standard pellet diet and high-fructose fed diet (HFFD) during experimental period and water ad libitum. All the animal handling and experimental procedures were approved by the Institutional Animal Ethics Committee of Bharathidasan University and animals were cared for in accordance with the Indian National Law on Animal Care and Use. ((BDU/IAEC68/2013)

Chemicals

Fructose, bovine serum albumin, G-6-P, γ-glutamyl paranitroaniline, nicotinamide adenine dinucleotide (NAD+, NADH) nicotinamide adenine dinucleotide phosphate (NADP+, NADPH), reduced glutathione, oxidized glutathione, adenosine triphosphate, adenosine monophosphate and 1,2,4-aminonapthol sulphonic acid were obtained from Sigma Chemical Company, ST. Louis, MO, USA. All other chemicals and reagents used were of highest purity and of analytical grade marketed by Glaxo Laboratories, Mumbai, SD Fine Chemicals, Mumbai and Sisco Research Laboratories, Pvt. Ltd., India.

Experimental design

After one week of acclimatization, the animals were divided into two batches. One batch was provided with a control diet containing starch as the source of carbohydrate (Groups I and II) and the other was fed a fructose enriched diet for 45 days (Groups III and IV). Different composition of diet (Table 1) was given to all the rats for 45 days followed by horsegram (Macrotyloma uniflorum) @ 1000 mg/kg orally for 15 days. The M. uniflorum dose was selected based on our previous study. Blood samples from all the groups of animals were collected from the tail vein on the 10th, 20th and 30th days and estimated for glucose levels to ensure diabetic status. Groups and treatment details were as follows: Group I, control rats (for 45 days); Group II, control rats fed with M. uniflorum seeds (1000 mg/kg) twice daily for
15 days; Group III, high fructose fed rats (>60% fructose for 45 days); and Group IV, HFFD+ M. uniflorum seeds (1000 mg/kg) twice daily for 15 days.

**Collection of samples**
At the end of the 45th day, all the rats were fasted overnight and sacrificed by cervical decapitation under mild ether anesthesia. Blood was collected tube with heparin and plasma was separated by centrifugation. The liver, heart and kidney tissues were immediately removed and washed in ice-cold saline to remove blood. The tissues were sliced and homogenized in 0.1 M Tris-HCl buffer (pH 7.0). The homogenates were centrifuged at 1000 rpm for 10 min at 4°C in a cold centrifuge.

**Analytical methods**
Plasma and tissue corticosterone levels were determined by the fluorometric procedure. The hepatic gluconeogenic enzymes glucose-6-phosphatase (glucose-6-phosphate phosphohydrolase, EC 3.1.3.9) and fructose-1,6-bisphosphatase (fructose-1,6-bisphosphate 1-phosphohydrolase, EC 3.1.3.11) were assayed by the methods. Glycogen content in liver tissue was estimated by the previous researcher method followed.

**Estimation of Liver mitochondrial enzymes activity**
LDH (EC: 1.1.1.27), ICDH (EC: 1.1.1.41), SDH (EC: 1.3.99.1) and MDH (EC: 1.1.1.37) activity levels were estimated according to the method as described earlier.

**Pro- and anti-inflammatory adipocytokines**
Levels of TNF-α, IL-6, leptin and adiponectin were measured in plasma using ELISA method.

**Statistical analysis**
Values or mean ± SD for six rats in each group and statistically significant differences between mean values were determined by one way analysis of variance (ANOVA) followed by DMRT values of $P < 0.05$ was considered to be significant. Statistical Package for Social Studies (SPSS Inc., Chicago, IL) 19.0 versions were used for this analysis.

**Results**
A significant increase in the body weight of the animals was observed in HFFD fed group at the end of the experimental period. The final body weight of group I and III was: CON 178.1±15. g and FRU 236.1±16.8 g. (Table 2)

Corticosterone levels in liver and adipose tissue were higher in HFFD animals as compared to control rats (Fig. 1). The levels were reduced liver and adipose tissues in the HFFD+ M. uniflorum group as compared to the HFFD group. There was no significant difference between control and M. uniflourm alone treated rats.

Fig. 2 shows the activity of glycogen in the liver and skeletal muscle. The values were lower in fructose-fed rats as compared to the normal rats.

**Table 1**—Composition of diets fed to rats for determination of insulin resistance

<table>
<thead>
<tr>
<th>Ingredient (g/100 g)</th>
<th>Control diet</th>
<th>High-fructose diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corn starch</td>
<td>60</td>
<td>-</td>
</tr>
<tr>
<td>Fructose</td>
<td>-</td>
<td>60</td>
</tr>
<tr>
<td>Casein</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Methionine</td>
<td>0.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Groundnut oil</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Wheat bran</td>
<td>10.6</td>
<td>10.6</td>
</tr>
<tr>
<td>Salt mixture†</td>
<td>3.5</td>
<td>3.5</td>
</tr>
<tr>
<td>Vitamin mixture‡</td>
<td>0.2</td>
<td>0.2</td>
</tr>
</tbody>
</table>

[†Composition of the mineral mix (g/kg): MgSO$_4$7H$_2$O, 30.5; NaCl, 65.2; KCl, 105.7; KH$_2$PO$_4$, 200.2; 3MgCO$_3$Mg (OH)$_2$, 38.8; Fe$_3$H$_4$O$_7$,5H$_2$O, 40.0; CaCO$_3$, 512.4; KI, 0.8; NaF, 0.9; CuSO$_4$,5H$_2$O, 1.4; MnSO$_4$, 0.4; and CONH$_3$, 0.05. ‡One kilogram of vitamin mix contained: thiamine mononitrate, 3 g; riboflavin, 3 g; pyridoxine HCl, 3.5; nicotinamide, 15 g; d-calcium pantothenate, 8 g; folic acid, 1 g; d-biotin, 0.1 g; cyanocobalamin, 5 mg; vitamin A acetate, 0.6 g; α-tocopherol acetate, 25 g; and choline chloride, 10 g]

**Table 2**—M. uniflorum on glucose in plasma of control and experimental rats

<table>
<thead>
<tr>
<th>Body wt.</th>
<th>Control</th>
<th>Control+MUF (1000 mg/kg)</th>
<th>HFFD</th>
<th>HFFD+MUF (1000 mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial (g)</td>
<td>162.8±14.5</td>
<td>162.9±14.7</td>
<td>163.1±13.7</td>
<td>153.6±10.8</td>
</tr>
<tr>
<td>Final (g)</td>
<td>178.1±15.2</td>
<td>174.9±15.9</td>
<td>178.5±15.3</td>
<td>236.1±16.8</td>
</tr>
</tbody>
</table>

[Each value is mean ± S.D. for six rats in each group. Values not sharing a common superscripts (a, b and c) differ significantly at $P < 0.05$ (DMRT)]
Administration of *M. uniflorum* significantly increased the activity of glycogen content.

The activities of glucose-6-phosphatase, fructose-1,6-bisphosphatase and glucose-6-phosphate dehydrogenase in liver, kidney and skeletal muscle are presented in Table 3. In fructose fed rats, significant increase in glucose 6-phosphatase, fructose-1,6-phosphatase and significantly decreased level of glucose-6-phosphate dehydrogenase was observed compared to the control rats. Supplementation of *M. uniflorum* prevented the increase in the level of glucose 6-phosphatase, fructose-1,6-phosphatase as well as decrease in the level glucose-6-phosphate dehydrogenase in HFFD + *M. uniflorum* (1000 mg/kg) as compared to control rats. No significant differences were observed between Group I and II.

The effect of *M. uniflorum* on activity levels of liver carbohydrate metabolizing enzymes in different experimental groups is depicted in Table 4. In HFFD rats, activity levels of ICDH, SDH and MDH were significantly decreased while LDH activity level was significantly decreased as compared to control rats. Administration of 1000 mg/kg *M. uniflorum* seeds resulted in a significantly higher ICDH, SDH and MDH activity levels and lower LDH activity levels as compared to the HFFD rats.

**Activation of inflammatory cytokine signals and its suppressor**

The levels of TNF-α, IL-6 and leptin were increased in liver of HFFD fed rats indicating inflammation and possibly leptin resistance. Adiponectin levels were decreased in HFFD fed rats. Individual and combination administration of *M. uniflorum* fed rats increased adiponectin levels and decreased the levels of TNF-α, IL-6 and leptin (Table 5).

Administration of *M. uniflorum* seed (1000 mg/kg of body wt.) was significantly effective for all parameters in HFFD + *M. uniflorum* induced rats as compared to HFFD rats. *M. uniflorum* alone did not show any significant change compared to control rats.

![Image](50x200 to 301x318)

**Table 3—Effect of *M. uniflorum* on Activities of G6Pase, F1,6pase and G6PDH in tissues of control and Experimental rats**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Control + MUF</th>
<th>HFFD</th>
<th>HFFD + MUF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G6pase*</td>
<td>4.04±0.31</td>
<td>3.96±0.30</td>
<td>6.38±0.42</td>
<td>4.10±0.30</td>
</tr>
<tr>
<td>F1,6pase*</td>
<td>3.89±0.36</td>
<td>3.78±0.33</td>
<td>12.05±0.74</td>
<td>3.96±0.30</td>
</tr>
<tr>
<td>G6PDH*</td>
<td>4.88±0.42</td>
<td>4.96±0.39</td>
<td>3.42±0.24</td>
<td>4.81±0.41</td>
</tr>
<tr>
<td>Kidney</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G6pase*</td>
<td>3.92±0.28</td>
<td>3.84±0.27</td>
<td>5.07±0.41</td>
<td>3.99±0.20</td>
</tr>
<tr>
<td>F1,6pase*</td>
<td>4.14±0.33</td>
<td>4.06±0.32</td>
<td>13.78±0.93</td>
<td>4.20±0.87</td>
</tr>
<tr>
<td>G6PDH*</td>
<td>3.38±0.25</td>
<td>3.40±0.26</td>
<td>2.29±0.18</td>
<td>3.32±0.24</td>
</tr>
<tr>
<td>Skeletal muscle</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G6pase*</td>
<td>5.01±0.46</td>
<td>4.96±0.39</td>
<td>5.98±0.47</td>
<td>5.08±0.29</td>
</tr>
<tr>
<td>F1,6pase*</td>
<td>4.21±0.39</td>
<td>4.16±0.22</td>
<td>11.96±0.85</td>
<td>4.26±0.34</td>
</tr>
<tr>
<td>G6PDH*</td>
<td>4.80±0.34</td>
<td>4.76±0.35</td>
<td>3.34±0.27</td>
<td>4.74±0.31</td>
</tr>
</tbody>
</table>

[Each value is mean ± S.D. for six rats in each group. Values not sharing a common superscripts (a, b and c) differ significantly at P < 0.05 (DMRT)]

**Table 4—Effect of *M. uniflorum* on the activities of mitochondrial enzymes in liver in control and Experimental rats**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Control + MUF</th>
<th>HFFD</th>
<th>HFFD + MUF</th>
</tr>
</thead>
<tbody>
<tr>
<td>SDH</td>
<td>4.43±0.03a</td>
<td>4.45±0.03a</td>
<td>2.01±0.02b</td>
<td>4.40±0.03c</td>
</tr>
<tr>
<td>ICDH</td>
<td>0.70±0.06b</td>
<td>0.71±0.04c</td>
<td>0.49±0.03c</td>
<td>0.68±0.04b</td>
</tr>
<tr>
<td>MDH</td>
<td>0.67±0.05a</td>
<td>0.69±0.05a</td>
<td>0.28±0.04c</td>
<td>0.64±0.04b</td>
</tr>
<tr>
<td>LDH</td>
<td>0.98±0.07a</td>
<td>0.99±0.06c</td>
<td>1.83±0.9a</td>
<td>101.3±0.08c</td>
</tr>
</tbody>
</table>

[Each value is mean ± SD of six rats in each group. Values not sharing a common superscripts (a, b and c) differ significantly at P < 0.05 (DMRT)]

**Table 5—Effect of *M. uniflorum* on Levels of adipocytokines in plasma and Experimental rats**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Control + MUF</th>
<th>HFFD</th>
<th>HFFD + MUF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leptin (ng/mL)</td>
<td>0.33±0.01a</td>
<td>0.32±0.01a</td>
<td>1.99±0.07b</td>
<td>0.37±0.02c</td>
</tr>
<tr>
<td>Adiponectin (μg/mL)</td>
<td>4.71±0.32a</td>
<td>4.9±0.3a</td>
<td>1.76±0.51b</td>
<td>4.99±0.3c</td>
</tr>
<tr>
<td>TNF-α (pg/mL)</td>
<td>19.4±0.72a</td>
<td>18.1±0.68a</td>
<td>61.28±3.5b</td>
<td>21.15±0.61c</td>
</tr>
<tr>
<td>IL-6 (pg/mL)</td>
<td>76.83±4.55a</td>
<td>75.91±4.45a</td>
<td>216.5±13.25b</td>
<td>79.87±6.25c</td>
</tr>
</tbody>
</table>

[Each value is mean ± S.D. for six rats in each group. Values not sharing a common superscripts (a, b and c) differ significantly at P < 0.05 (DMRT)]
Discussion

High dosage of fructose in the diet (60/100 g diet) is known to induce insulin resistance (IR) accompanied by deleterious metabolic consequences including hyperglycemia and hyperinsulinemia in animals26. Inspite of glucocorticoids are known for including hyperglycemia and hyperinsulinemia in tissues could be due to reduced synthesis or increased breakdown of glucose. Also, depletion of hepatic glycogen concentration in liver has been reported infructose fed rats32. Glycogen synthesis is proportional to the insulin sensitivity. Consequently, the decreased insulin stimulated the glycogen synthesis and glucose transport activities are observed during IR35. On administration of M. uniflorum, the levels of glucose-6-phosphatase, fructose-1,6-bisphosphatase and glucose-6-phosphate dehydrogenase in liver, kidney and skeletal muscle are lowered and level of glycogen is raised in Group IV compared to Group I. M. uniflorum contains alpha amylase inhibitor, which can also reduce glucose-6-phosphatase and fructose-1,6-bisphosphatase activities in HFFD rats. This could be responsible for increased glycolytic activity and reduction of blood glucose.

In this study, activity levels of liver mitochondrial enzymes (ICDH, SDH and MDH) were evidently reduced in HFFD rats suggesting ATP generation by 36 moles of ATPs per mole of glucose34. Two Krebs cycle enzymes, namely SDH and MDH where the former has the highest activity as compared to other enzymes in the cycle35. In diabetes model, activity of Krebs cycle enzymes was observed lower than control rats36, resulting in impairment of ATP generation. These may compromise the liver biosynthetic, degradation, and detoxification functions. Even though the diabetes decreased the activity levels of liver Kreb cycle enzymes, LDH activity level was concretely increased. Similar findings were reported by others37. LDH is the terminal glycolytic enzymes which interconvert the pyruvate to lactate for produce energy under anaerobic condition38. The factor of significant LDH increasing in diabetes is unknown; however, this could be related to lower amount of insulin as insulin has been reported to affect the activity of LDH38. Ramalingam & Kim39 have indicated that increased in cellular activity of LDH in diabetes was due to increase in peroxide (H₂O₂) levels. Ability of the M. uniflorum seeds to lower the free radical levels in diabetes could explain the decrease in hepatic LDH activity levels as revealed in our study.
Administration of 1000 mg/kg *M. uniflorum* resulted in significantly higher ICDH, SDH and MDH activity levels and lower LDH activity levels as compared to HFFD rats. *M. uniflorum* against deterioration of activity levels of key enzymes involved in liver mitochondrial enzymes in HFFD rats.

Leptin is mainly produced in adipocytes, controlling food intake and energy expenditure. High fructose diet gives rise to leptin resistance in adipose, characterized by down-expression of leptin and leptin receptor in rats 40, possibly affecting autophagy 41. Chronic consumption of high fructose may lead to increased adiposity, which causes elevated circulating leptin levels resulting in leptin resistance. Leptin resistance is associated with induction of diet-induced obesity. In our studies, the levels of TNF-α, IL-6 and leptin were increased and adiponectin level decreased in the liver of HFFD fed rats as compared to the control rats. Adiponectin, a 30 kDa protein, is an anti-inflammatory, antiatherogenic and insulin-sensitizing hormone whose levels are found to be reduced in obesity. Adiponectin is mainly produced from white adipose tissue and specifically in mature adipocytes. Three major adipose tissue deposits are recognized as producers of this protein: subcutaneous, visceral and perivascular. 42 Adiponectin favours insulin action, inhibits stress-kinase activation and improves fatty acid oxidation by activating AMPK. Leptin also activates AMPK allowing increased fatty acid oxidation. However, obesity leads to leptin resistance. Adiponectin is structurally related to proteins of the complement system (C1q) and tumor necrosis factor alpha (TNF-α), which are prototype members of a growing family of proteins known as CTRPs (C1q/TNF bonds) 43. High blood levels of leptin, plays a major role in insulin resistance by inducing production of pro-inflammatory cytokines (like IL-6, TNF-α) and vice versa.

TNF-α promotes renal damage by the local generation of reactive oxygen species (ROS) resulting in alterations of the barrier function of the glomerular capillary wall leading to enhanced albumin permeability. These investigations demonstrated a significant role of TNF-α in the development of renal hypertrophy and renal damage. Increased TNF-α production to suppress insulin receptor signal transduction in fructose-fed rats has been suggested as a link between inflammation and IR 37. Experimental studies have consistently reported that both mRNA and the protein levels of TNF-α increase in glomerular and proximal tubule cells from diabetic rats 44. The present study demonstrated that *M. uniflorum* reduced levels of TNF-α and IL-6 in plasma of fructose-fed rats. *M. uniflorum* inhibits cytokine induce over expression of proinflammatory reactions in human brain microvascular endothelial cells. TNF-α interferes with early steps of inflammatory signaling, and causes ubiquitinylination and loss of Akt in the adipocyte. In this case, the administration of *M. uniflorum* to HFFD rats significantly altered the glyconeogenic enzymes and reducing inflammation. This possibly due to the antioxidant potential of MUF.

**Conclusion**

Our findings in this study demonstrated the potential of *Macrotyloma uniflorum* in improving the insulin sensitivity and attenuation of inflammatory parameters as well as carbohydrate metabolism, which protects the body against the adverse effects of insulin resistant. Collectively, our study suggests the possible utility of *Macrotyloma uniflorum* as a therapeutic adjunct in a metabolic state of insulin resistance.

**Conflict of Interest**

The authors declare no conflict of interest.

**Reference**

7. Reddy S, Ramatholisamma P, Karuna R & Saralakumari D, Preventive effect of Tinospora cordifolia against high-fructose


