

## REVIEW ARTICLE

# HYPOLIPIDEMIC AND HYPOGLYCEMIC ACTIVITY OF MEDICINAL PLANTS IN STZ (STREPTOZOTOCIN) INDUCED HYPERLIPIDEMIC RATS AND THEIR ROLE IN HEALTH AND DISEASE

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## ABSTRACT

This study aims to evaluate various medicinal plants for anti-diabetic and hypolipidemic activity in rats. Diabetes mellitus is one of the most common non-communicable diseases present globally and its most lethal complication is the development of cardiovascular disease. Since ancient times plants have been the source of medicines. Literature mentioned the use of plants in the treatment of various diseases. This review covers the anti-diabetic and antihyperlipidemic effects of medicinal plants. Investigation of phytochemicals present in medicinal plants and their biological activities are reported. The hypolipidemic activity which is present in most medicinal plants is strongly associated with new drug development which will be used for high lipid profiles and cardiovascular disease.

**KEY WORDS:** Medicinal Plants; Anti-Diabetic; Hypolipidemic; Cardiovascular Events; Stz (Streptozotocin).

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## INTRODUCTION

Diabetes mellitus is a very common and very prevalent disease that affects people of both developed and developing countries. This syndrome is characterized by an abnormality in carbohydrate metabolism which is due to low insulin level and ultimately cause hyperglycemia, change in lipid metabolism and ultimately cause the development of cardiovascular disease.<sup>1</sup> Defects in carbohydrate metabolism cause the efforts of the physiological system of the body to maintain glucose and electrolyte imbalance and it causes overexertion on the endocrinal system and ultimately causes hyperglycemia. Diabetes mellitus occurs due to many important factors including poor diet intake, hormonal imbalance, and also endocrinal and genetic disorders.

The signs and symptoms of this disease are fatigue, polyuria, weight loss, polydipsia, blurred vision, an increase in urine glucose level etc.<sup>2-4</sup> There are almost more than 150 million people with diabetes mellitus around the world which seems to reach almost 300 million by 2025.<sup>5</sup>

Diabetes mellitus is mainly classified into two different types depending upon the cause and signs and symptoms. Insulin-dependent diabetes mellitus also called type 1; the main cause is genetic and diabetes which does not depend upon insulin is called type 2 and it occurs in late adulthood.<sup>6</sup> Diabetes is a very predominant disease that affects people of different classes and races all over the world. Diabetes mellitus is also considered a main and important cause of disability and hospitalization and its result pose significant financial burden.<sup>7</sup>

Nowadays the main treatment of diabetes mellitus is insulin use and hypoglycemic drug use these have very large adverse effects.<sup>8</sup> In the last 300 years despite the availability of antidiabetic management the DM is still not controlled because of some important disadvantages like drug resistance, adverse effects and side effects, and toxicity of drugs. For example sulfonylureas' effectiveness is lost after six years of treatment in 44% of patients and these glucose-lowering drugs are not able to control hyperlipidemic conditions.<sup>9</sup>

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Medicinal plants have been used for a long time for various diseases.<sup>10-13</sup> There are many reasons for increasing medicinal plant use because herbal formulations show very efficient effects and have very little or no side effects.<sup>14</sup> World health organization (WHO) reported different medicinal plants for treatment based upon their low cost, efficacy, and little or no side effects.<sup>15-16</sup>

Another condition hypercholesterolemia is the main reason for cardiovascular and its associated diseases, and atherosclerosis in major and minor arteries.<sup>17,18</sup> Many studies clearly showed the correlation between high LDL cholesterol and atherosclerosis.<sup>19</sup> However, HDL cholesterol is an antiatherogenic factor.<sup>20</sup> Another strong relationship between high triglycerides level and cardiovascular diseases are seen.<sup>21</sup> Daily lifestyle and dietary habits are important in the prevention of diseases and there is a negative correlation between dietary intake of fruits and vegetables and the development of cardiac diseases.<sup>22</sup>

Many herbs are important for the reduction of hyperlipidemic conditions. The lipid-lowering effects of many herbal plants are important for phytochemical analysis and drug development. Work is increasing for the preparation of drugs that decreases lipids level from plant sources because traditional medicinal plants are more effective for many drugs preparations for dyslipidemia.<sup>23</sup>

#### **Status of diabetes and dyslipidemia in Pakistan**

Almost 150 million people are affected worldwide with diabetes mellitus and in 2025 this number is going to increase to 300 million.<sup>24</sup> Pakistan at this moment is on 7<sup>th</sup> number in the whole world with more population suffering from diabetes and it is expected to reach on 4<sup>th</sup> number after 20 years.

Almost six million are suffering in Pakistan and it will reach up to 11 million in 2025.<sup>25</sup> Males are more affected as compared to women among the age group 40-59 years. To fight this disease more effort is required from all sectors of health, including the public and private sectors.

Dyslipidemia is closely associated with CHD and it is the major, modifiable and independent risk factor for CHD.<sup>26</sup>

#### **Scope and need of herbal remedies for diabetic and dyslipidemic condition**

There are different methods that are used to treat diabetes mellitus and dyslipidemia like insulin therapy, monoclonal antibody, and different type of statins for dyslipidemia. Metformin is the drug of choice for diabetes mellitus mainly type 2 but chronic use of metformin causes malabsorption of Vit. B12 and lactic acidosis.<sup>26</sup>

Prolong use of sulfonylureas cause hypoglycemic effects and increase the chances of cardiovascular disease.<sup>27</sup> Each drug has some disadvantages like

the development of any other disease and these are expensive drugs. Statins are most commonly used for dyslipidemia but the main side effects of statins are disturbed liver function tests. There are many benefits of medicinal plants which contain active ingredients like tannins, flavonoids, alkaloids.

Tannins cause increase insulin secretion from beta cells and also improve the function of insulin and quercetin work as an antioxidant and prevent lipid peroxidation. In our country, the poverty level is above 24 percent and diabetic and dyslipidemia treatments are expensive. So as a developing country herbal treatment is the cheapest source of drugs for preventable diseases like diabetes and dyslipidemia.

#### **PLANTS WITH ANTI-DIABETIC EFFECT**

**1. *Acacia Arabica*:** One of the studies was conducted to show the hypoglycemic effect of plants in streptozotocin-induced Wistar diabetics rats for three weeks period. 200mg/kg, 100mg/kg oral extracts of acacia arabicabark were induced. As a result glucose level decreased, insulin resistance decreased, and lipid profile improved. The presence of anti-oxidant substances polyphenol, tannins, and flavonoids is an explanation for anti-diabetic activity.<sup>28</sup> In another study chloroform extracts of Arabica leaves were used in diabetic rats for 14 days and there was a markedly decrease in blood sugar and improvement in lipid profile.<sup>29</sup>

**2. *Asperaachyanthes*:** *AchyranthesAsperaleaves* extracts which were made in ethanol markedly reduced blood glucose level when 1000mg/kg was given in STZ induced diabetic rats. This affect is due to glucose absorption inhibition from the intestine.<sup>30</sup>

**3. *Acosmiumpanamense*:** Butanoic extracts of *Acosmiumpanamense* decreased plasma glucose level in Wistar rats which were made diabetic with streptozotocin in 5 to 6 hours duration with a dose of 100/20mg/kg. The hypoglycemic effects are the same as glibenclamide.<sup>31</sup>

**4. *Allium sativum (garlic)*:** Oral administration of ethanolic extracts of *Allium sativum* showed a decrease in serum glucose level, renal function tests, liver function tests, and total cholesterol. This treatment was given for 14 days in rats in both groups normal and diabetic. The hypoglycemic activity of this extract is compared with the antidiabetic drug in a dose of 600mg/kg demonstrating more effectiveness as compared to the drug.<sup>32</sup>

**5. *Aloe barbadensisMiller*:** This plant also called Aloe vera and is used in many medicines. The ethanolic extracts of leaf gel resulted in decreased blood glucose levels in 42 days with a dose of 500 and 300 milligrams in streptozotocin given Wistar rats. The effects of this drug are compared with standard antidiabetic drugs glibenclamide and metformin.<sup>33</sup>

**6. *Artemisia herba*:** Aqueous extracts of the aerial portion of this tree for 14 days in a dose of 0.39g per kg bodyweight cause a marked decrease in the blood glucose. It also stabilized glycosylated hemoglobin concentration in hyperglycemic rats and rabbits. This plant extract also has a hypoliposis effect.<sup>34</sup>

**7. *Averrhovabilimbi*:** The ethanolic extracts of *Averrhovabilimbi* leaves (ABE) showed antihyperglycemic and antihyperlipidemic activity when given in diabetic rats. Comparison of distilled water, ABE, and metformin were studied for 14 days of metformin (500mg) and ABE (125 mg/kg). ABE markedly decrease glucose level in blood by 50% and triglycerides by 130% when compared with distilled water and also increased HDL cholesterol by 60%. The extracts didn't affect cholesterol and LDL cholesterol levels. The study revealed that ABE has anti-lipidperoxidative, hypoglycemic, hypotriglyceridemic effects in diabetic Wistar rats.<sup>35</sup>

**8. *Biophytumsensitivum*:** The plant contains steroids, flavonoids, amino acids, essential oils, pectin, and polysaccharides. When given in oral form with a dose of 200 milligrams for 4 weeks showed markedly lowering of blood sugar level and HbA1c in Wistar hyperglycemic rats. Studies showed an increase in hemoglobin level and decrease in fructose 1 6 biphosphate level in hyperglycemic rats and this is due to the synthesis of the hormone insulin from the pancreas.<sup>36</sup>

**9. *Brassica Nigra*:** Treatment of aqueous extracts of plant in streptozotocin-induced hyperglycemic rats for 4 weeks showed a decrease in plasma glucose level and a very mild change in HbA1c and lipid level.<sup>37</sup>

**10. *Citruscolocynthis*:** Aqueous extracts of seed of *Citruscolocynthis* caused a decrease in glucose level, increased in insulin level while hydroalcoholic extracts of peel caused an increase in glucose level and decreased in insulin level with dose 200mg/kg. The peel is harmful to diabetes and seed is most effective in treating diabetes.<sup>38</sup>

## **PLANTS WITH HYPOLIPIDEMIC EFFECT**

**1. *Allium porrum*:** On hypercholesterolemic diet in rabbits *Allium porrum* extract was studied. The extract was given in 3 different doses, 250, 500, 1000 milligrams according to total body weight in Wistar rats. Cholesterol levels showed positive effects with all different doses. This extract also exerted anti-platelet aggregation activity.<sup>39-41</sup>

**2. *Allium sativum*:** Serum cholesterol, triglycerides, and LDL cholesterol levels reduced significantly when allium sativum was administered in hyperlipidemic Wistar rats.<sup>42</sup> Daily consumption of 10 grams garlic for two months significantly reduced (15-28.5%) serum cholesterol level among hypercholesterolemic patients.<sup>43</sup>

The use of garlic oil caused a decrease in low-den-

sity lipoprotein, very low-density lipoproteins, and increased high-density lipoproteins levels.<sup>44</sup> Enteric-coated garlic powder (400 mg) twice daily has markedly decreased the lipid profile and increased the level of HDL.<sup>45</sup>

**3. *Aleo Vera*:** Its gel reduced triglycerides levels in the blood and liver. On slide examination size of adipocyte is reduced with the use of gel. *Aloe verin* decreased fasting and postprandial sugar level, decreased total cholesterol and triglycerides level, and increased HDL level.<sup>46</sup>

**4. *Alpinia galangal*:** The use of ethanolic extracts 20mg/day for four weeks in rats significantly decreased lipoproteins level and increased HDL level.<sup>47</sup>

**5. *Anethumgraveolens*:** The crude extracts showed strong antioxidants effects and reduced lipid peroxidation in the liver and also modulate the oxidant enzyme activity in rats with a high cholesterol feed diet.<sup>48,49</sup> Use of extract 1 ml daily (equal to 500 mg of powder plant) in hyperlipidemic rats reverses the serum cholesterol level as compared to those rats in which only high fat diet was given for 10 days.

It significantly decreased the HMG-CoA mevalonate ratio in hyperlipidemic rats as compared to those Wistar rats in which only a high feed diet was given.<sup>50</sup>

**6. *Apiumgraveolens*:** Use of *Apiumgraveolens* markedly decreased LDL, VLDL, triglycerides, total cholesterol level, and increased HDL level. It decreased absorption of lipids in the intestine, increased cholesterol acyltransferase activity, and increased fecal bile acid excretion. This effect is due to the presence of compound 3n butylphthalide and many studies showed that the presence of sugar and amino acid side chain also exerts hypolipidemic effects.<sup>51-53</sup>

**7. *Arachishypogaea*:** Studies indicate the hypolipidemic activity of water-soluble extract of peanut skin. The use of this extract markedly decreases total body weight and fat deposition on epididymis. Total cholesterol levels, TAG levels also decreased. There is increased excretion of TG and TC in feces. On administration of peanut skin enzyme of fatty acid synthesis, (SREBP) were decreased and PPAR $\gamma$  was increased.<sup>54,55</sup>

**8. *Asparagus officinalis*:** Hypolipidemic effects were studied in rats who were given a high-fed diet. This reduced the body weight, total cholesterol level, LDL level, and significantly increased HDL in rats when different doses 40, 60, and 180 milligrams were administered in Wistar rats. These extracts also decreased the liver enzyme level. Antioxidant activity and superoxide dismutase activity increased and the level of malondialdehyde and lipid droplet distribution were reduced.<sup>56,57</sup>

**9. *Bauhinia variegata*:** This study reported the effects of these extracts on brain serotonin level and lipid profile level. Methanolic extracts of root and stem Wistar female rats that were given a high-fat diet

were observed in a dose of 200 and 400 milligrams of body weight showed hypolipidemic effect by decreasing total cholesterol level, triglyceride level and LDL level and also increased brain serotonin level.<sup>58,59</sup>

**10. *Benincasahispida*:** Supplementation of ash ground (*Benincasahispida*) 100 gram, one gm of curry leaves (ten leaves), 5-gram milk powdered skimmed milk had a significant hypoglycemic and hypolipidemic effect when given to hyperlipidemia and diabetic patient for a period of three months in mid of morning.<sup>60</sup>

## CONCLUSION

Diabetes mellitus and hyperlipidemia prevalence are very high all over the world and the treatment with hypoglycemic and anti-hyperlipidemic drugs have many side effects and have huge monetary expenditure. This paper reviewed the effects of medicinal plants on diabetes and hyperlipidemia. Plants have anti-diabetic and hypolipidemic activity and can significantly reduce total lipids level, total cholesterol level, LDL level, and triglycerides and increase in high-density lipoprotein levels. Demand is increasing in the world to use natural plants as medicine with hypoglycemic effects and hypolipidemic effects by patients. We should adopt a new approach to study plants components that are phytochemical active and study their molecular interaction with diseases.

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#### CONFLICT OF INTEREST

Authors declare no conflict of interest.  
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#### AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	FNT, HA
Acquisition, Analysis or Interpretation of Data:	FNT, HA, IT
Manuscript Writing & Approval:	FNT, HA, IT

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.



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