Lamiaceae Species in Diabetes

Subjects: Plant Sciences

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Diabetes is one of the most dangerous metabolic disorders, with high rates of mortality worldwide. Since ancient times, medicinal plants have been used in traditional medicine to treat many diseases, including diabetes and its related complications. Plants are widely accepted, affordable, and perceived to have minimal adverse side effects. The Lamiaceae family is a potential source of therapeutic agents for the management of metabolic disorders, including diabetes.

Lamiaceae species | diabetes mellitus | oxidative stress | secondary metabolites

1. *Ajuga iva* (L.) Schreb

In vitro and in vivo biological investigations revealed that the methanolic extract of *A. iva* has antidiabetic activity [1] [2]. *A. iva* possesses hypoglycaemic and hypolipidemic activities [2]. The bio-evaluation of the alpha-amylase and alpha-glucosidase inhibitory activities of the aqueous and methanolic extracts of the aerial parts of *A. iva* showed a good inhibition of alpha-amylase, with IC_{50} values of 0.210 ± 0.003 and 0.180 ± 0.005 µg/mL, as well as of alpha-glucosidase, with IC_{50} values of 0.172 ± 0.012 and 0.130 ± 0.008 µg/mL, respectively [3].

The whole plant of *A. iva* has been reported to increase the hepatic glycogen concentration and prevent diabetic complications in the kidneys, pancreas, and liver. Additionally, the extract of *A. iva* showed a preventive effect against the deleterious effects of diabetes on oxidative stress [4]. The administration of the extract of *A. iva* significantly reduced the plasma glucose concentration and consequently resulted in the rapid normalization of glucose levels in diabetic animals [4]. The aqueous extract of *A. iva* significantly decreased the plasma glucose level in STZ-diabetic rats, with no effect on insulin production. Additionally, *A. iva* upgraded the glycaemic value (41%) in hyperglycaemic rats and lessened the glycosylated haemoglobin (HbA1c) [2]. The lyophilized aqueous extract of *A. iva* (whole plant) displayed significant hypoglycaemic activity and was relatively non-toxic to normal (normoglycemic) and streptozotocin (STZ)-diabetic rats [2]. An aqueous extract of the whole plant of *A. iva* showed hypolipidemic and hypoglycaemic effects in both normoglycemic and diabetic rats [2]. Additionally, the aqueous extract of *A. iva* is a rich source of phytoecdysteroids, which are potential therapeutic candidates for alloxan-induced diabetic male albino rats [5].

A. iva aqueous extract demonstrated significant hypolipidemic activity after a single dose and repeated treatments on STZ-diabetic rats [6].

2. *Ballota nigra* L.

A 70% ethanol extract of *Ballota nigra* has been reported to possess hypoglycaemic, insulin-releasing, and cholesterol-lowering effects in rats [7].

3. *Becium grandiflorum* (Lam.) Pic. Serm.

The hydroalcoholic extract of *B. grandiflorum* has been reported to exhibit significant antihyperglycemic activity ($p < 0.05$) in STZ-induced diabetic mice. It also showed a considerable amelioration in oral glucose tolerance and body weight, which justified this species' potential usage in managing diabetes mellitus complications in Ethiopian folk medicine [8].

4. *Calamintha officinalis* Moench

The bio-evaluation of the aqueous extract of *C. officinalis* showed significant hypoglycaemic activity in normal and streptozotocin-induced diabetic rats without modifying the concentrations of basal plasma insulin [9]. Additionally, the aqueous extract of *C. officinalis* demonstrated remarkable hypoglycaemic activity in normal and STZ diabetic rats without influencing the basal plasma insulin concentrations [10]. The antidiabetic and antioxidant activities of the crude extract and its isolates (rosmarinic and caffeic acids) from the aerial parts of *C. officinalis* revealed that both rosmarinic and caffeic acids are prominent natural agents for controlling diabetes [10].

5. *Coleus forskohlii* (Willd.) Briq

The leaves of *Coleus* have been reported to have a wide range of pharmaceutical applications, including diabetes and weight loss [11]. The extract of *Coleus* has been reported to attenuate/reduce the hypoglycaemic action of tolbutamide via a hepatic CYP2C-mediated mechanism [12]. Forskolin, the main predominant constituent of *C. forskohlii,* has been reported to stimulate glucose-induced insulin secretion in the in vitro model [13][14].

6. *Coleus forskohlii* (Willd.) Briq

The 50% aqueous ethanolic extract of *H. suaveolens* has been reported to possess significant antihyperglycemic activity in streptozotocin-induced diabetic rats and decrease the cholesterol and triglyceride levels in a significant manner [15]. The aerial part of *H. suaveolens* has been reported to possess antidiabetic and antioxidant properties [16].

7. *Lavandula angustifolia* Mill

A bio-evaluation of the methanolic extract of *L. angustifolia* regarding the management of diabetic dyslipidaemia demonstrated that *L. angustifolia* can inhibit HSL and PL activities in a dose-dependent manner, with IC_{50} values of 175.5 and 56.5 µg/mL, respectively. The inhibitory activity demonstrated by *L. angustifolia* could be attributed to the presence of rosmarinic acid with IC_{50} values of 125.2 and 51.5 µg/mL for PL and HSL, respectively, and gallic acid

with IC_{50} values of 10.1 and 14.5 µg/mL for PL and HSL, respectively, which are the major compounds of *L. angustifolia* [17].

8. *Lavandula dentata* L

L. dentata has been reported to exhibit hypolipidemic, antioxidant, and hypoglycaemic activities. It has also been reported to reduce blood sugar levels ($p < 0.05$) [18].

9. *Lavandula mul[19]ifida* L

L. multifida has been reported to possess antioxidant and antihypolipidemic activities [58]. Additionally, it has been also reported for its potent hypoglycaemic activity [20].

10. *Lavandula stoechas* L

L. stoechas has been reported to reduce blood glucose levels [19][21]. The aerial parts of *L. stoechas* effectively protect against increases in the blood glucose level, and a decrease in the antioxidant activities was observed [19].

11. *Leonotis leonurus* (L.) R.Br

L. leonurus has been reported to lower the blood glucose level in streptozotocin-induced diabetic rats. Additionally, *L. leonurus*' aqueous extract has antihyperglycaemic and antilipidemic activities. Its aqueous leaf extract induced a significant ($p < 0.05$-0.001) hypoglycaemic effect in rats, which was ascribed to different diterpenoids, polyphenolics, flavonoids, and other phytochemical constituents of the plant extract [22].

12. *Leonotis nepetifolia* (L.) R.Br

The bio-evaluation of the ethanolic extract of the whole plant of *L. nepetifolia* exhibited a potent antidiabetic activity in diabetic rats [23].

13. *Marrubium vulgare* L

Scientific studies on *M. vulgare* have demonstrated through in vivo research the hypoglycaemic effect of *M. vulgare*, which supports its traditional use in controlling diabetes mellitus [24]. *M. vulgare* has been reported to possess hypoglycaemic and antioxidant activities. The 80% ethanolic extract of *M. vulgare* showed a moderate alpha-glucosidase inhibitory activity, with an IC_{50} value of 12.66 µg/mL [25][26]. The methanolic extract exhibited a considerable decrease in blood glucose and a significant increase in plasma insulin and tissue glycogen contents [27]. The administration of an infusion from the aerial parts of *M. vulgare* significantly decreased the blood glucose level in a dose-dependent manner in alloxan-induced diabetic rats [28]. The ethanolic extract from the root

considerably suppressed the increase in the plasma glucose level in healthy rats [28]. Moreover, *M. vulgare* shows an antidiabetic effect by suppressing the carbohydrate absorption from the intestine and thereby reducing the postprandial increase in the blood glucose level [29]. The oral administration of the aqueous extract induced significant antidiabetic and antihyperlipidemic dose-dependent effects in treated animals [30]. *M. vulgare* significantly lessen the blood glucose level, pancreatic levels of interferon-gamma and nitric oxide, total cholesterol, low-density lipoprotein (LDL), and very LDL cholesterol and triglycerides compared with diabetic mice [31]. The methanolic extract was found to have PPARγ agonist activity in a luciferase reporter assay. PPARγ adjusts the glucose and lipid metabolism and its synthetic agonists such as pioglitazone ameliorate insulin resistance, thus it is clinically employed for diabetes therapy [32].

14. *Ocimum gratissimum* L

The methanolic and aqueous extracts of the leaves showed hypoglycaemic activity. Additionally, the aqueous extract at the dose of 500 mg/kg significantly decreased the blood glucose level ($p < 0.05$) of diabetic rats by 81.3% after 24 h of extract administration [33]. The leaf extract was reported to have antidiabetic activity in streptozocin-induced diabetic rats [34] *O. gratissimum* decreased the baseline blood glucose levels in normal and alloxan-induced rats [35]. The leaf extract showed a potential plasma glucose lowering effect [36].

The aqueous extract showed anti-hyperglycaemic and antioxidant potentials. The hypoglycaemic effect of the methanolic extracts showed a decrease in the blood glucose level of 69% and 56% for alloxan-induced diabetic and normal rats, respectively [37].

15. *Ocimum sanctum* L

The aqueous suspension considerably decreases the blood glucose level ($P < 0.0001$) and oxidative stress with a significant increase in glycogen and protein in diabetic rats [38][37]. A 70% ethanol extract of the leaves of *O. sanctum* has been reported to significantly decrease the blood glucose level in both normal and streptozotocin-induced diabetic rats [37]. In vivo studies of the ethanolic extract have also shown a decrease in the blood glucose level and an increase in the plasma insulin activity in type 2 diabetes mellitus. Another study showed a significant decrease in diabetic symptoms (polyphagia, polydipsia, and tiredness) in type 2 diabetic patients who consumed the leaf powders of *O. sanctum* [37]. Additionally, the ethanol extract activates insulin production from the perfused pancreas, isolated islets, and clonal pancreatic cells [39]. The leaf extracts of *O. sanctum* have been shown to have anti-hyperglycaemic effects by increasing the insulin secretion from isolated islets, perfused pancreas, and clonal pancreatic β–cells [37][40].

16. *Ocimum basilicum* L

The aqueous extract significantly lowered both plasma triglycerides (TG) and cholesterol in acute hyperlipidaemia induced by Triton WR-1339 in rats [41]. The aqueous extract of the whole plant exhibited a hypoglycaemic effect in

normal and streptozotocin diabetic rats[42]. Furthermore, the methanol-dichloromethane extract of the leaves has anti-hyperglycaemic effects [37]. The extracts have been reported to possess different pharmacological effects, including blood glucose-lowering and hepatoprotective properties [43]. The extract of the aerial parts possessed antidiabetic effects, which might be mediated by limiting glucose absorption through the inhibition of carbohydrate metabolizing enzymes and the enhancement of hepatic glucose mobilization [43].

The extract demonstrated significant dose-dependent inhibition against rat intestinal sucrose, maltose, and porcine pancreatic alpha-amylase. The ethanolic extract of the leaves exhibited hepatoprotective effects against H_2O_2- and CCl_4-induced liver damage [44].

17. *Ocimum canum* L.

L. canum has been reported to inhibit the growth of cataracts in diabetic patients. Aqueous extract of the leaves showed anti-hyperglycaemic activity [45].

The total extract demonstrated a significant ($P < 0.01$) decrease in blood glucose levels and ameliorated other altered biochemical parameters, which were related to diabetes. Moreover, histopathological modifications of the pancreas were also observed in streptozotocin-induced diabetic rats [37].

18. *Rosmarinus officinalis* L

Rosemary extract and its polyphenols (carnosic and rosmarinic acids) have been reported to possess significant antidiabetic effects in different in vivo models of type 2 diabetes and insulin-like effects in insulin target cells in in vitro models [46].

The aqueous extract has been reported to potentially reduce the oxidative stress induced by streptozotocin and blood glucose levels [47]. Rosemary was found to demonstrate significant alpha-glucosidase inhibitory activity (60% decreases) [48].

19. *Salvia lavandulifolia* Valh

The bio-evaluation of the hypoglycaemic activity of *S. lavandulifolia* demonstrated that this plant significantly decreases the blood glucose levels in alloxan-diabetic rabbits [49].

20. *Salvia officinalis* L

L. officinalis has been reported to have a wide range of pharmaceutical applications, including hypoglycaemic and hypolipidemic effects. Additionally, *S. officinalis* has been reported to have a hypoglycaemic effect on diabetic animals and be beneficial for type 2 diabetic patients due to its ability to reduce liver glucose production [50][51]. The

methanolic extract of *S. officinalis* has considerably decreased serum glucose levels in type 1 diabetic rats. The aqueous extract of *S. officinalis* has been found to possess insulin-like effects [50].

Infusions (tea) of *S. officinalis* have been reported to reduce liver glucose production and increase insulin action. *S. officinalis* has been demonstrated [52]to be as powerful as metformin, a well-known oral antidiabetic drug utilized for the treatment of type 2 diabetes [50].

21. *Salvia fruticosa* Mill

L. fruticosa has been reported to possess hypoglycaemic activity by reducing the intestinal absorption of glucose [53]. This plant is well known for its antidiabetic activities in Jordan. The oral administration of a 10% leaf infusion of 0.25 g/kg BW caused a significant reduction in blood glucose levels in alloxanized rabbits without exerting any effect on normal ones [6].

22. *Teucrium polium* L

T. polium and its isolates have been reported to have a broad spectrum of pharmacological applications, including hypoglycaemic and hypolipidemic effects. *T. polium* enhanced insulin secretion by nearly 135% after a single dose of the plant extract (equivalent to 0.1 mg plant leaf powder per mL of the culture medium) at a high glucose concentration (16 mmol/L). Its aqueous extract (50 mg/kg) significantly ($p < 0.05$) decreased the serum glucose levels of diabetic Sprague–Dawley male rats from 283.622.1 to 96.211.9 mg/dL [52].

T. polium extract has been reported to reverse the symptoms of streptozotocin-induced diabetes in rats by adjusting the pancreatic transcription factor pancreas/duodenum homeobox gene-1 (Pdx1) and forkhead transcription factor (FoxO1) expressions [54].

T. polium showed a considerable decrease in the blood glucose level of STZ-diabetic rats and demonstrated protective effects on pancreatic tissue in STZ-induced oxidative stress based on its strong oxidative capacity. Furthermore, *T. polium* showed weak alpha-amylase inhibitory activity (5%) [6].

23. *Teucrium cubense* Jacq

The aqueous extract of *T. cubense* has been reported to decrease plasma glucose levels in healthy rabbits. Additionally, 70 µg/mL of *T. cubense* extract activated glucose uptake by 112% (murine) and 54% (human) in insulin-sensitive cells. At the same time, it induced the incorporation of glucose by 69% (murine) and 31% (human) in insulin-resistant adipocytes [55].

According to the scientific databases consulted for this review, twenty-three plant species of the Lamiaceae family, belonging to twelve (12) genera, are reported for their potential antidiabetic activity.

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