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Antihyperglycemic effect of *Ocimum* plants: A short review

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ABSTRACT

This present review provides information on the antihyperglycemic effect of the plants belonging to the genus *Ocimum*. The species of this genus which mostly show significant antihyperglycemic effects are *Ocimum tenuiflorum* L., *Ocimum basilicum* L., *Ocimum gratissimum* L. and *Ocimum canum* L. The results were shown in both *in vitro* and *in vivo* studies. The anti-hyperglycemic activities of different extracts from all these species are reported here. Aqueous extracts are common to show a satisfactory result for all the species. The results for ethanol, methanol, ethyl-acetate, petroleum ether extracts, chloroform and hexane fraction of ethanol extract are also presented here. Some of the results showed a better effect than the standard medicine. Eugenol is the most important bioactive compound among all the components for reducing blood glucose level. Other components include polyphenols, caffeic acid, p-coumaric acid compound and chichoric acid, which are reportedly found in these species. There are fewer studies performed to identify the phytochemical components which are responsible for these plants blood glucose, serum glucose and plasma glucose lowering effect. This review presents the studies which have been done lately to establish the antihyperglycemic effects of these plants with a view to identify the core components responsible for this activity in near future.

1. Introduction

Diabetes mellitus is one of the most common metabolic disorders [1]. It is an increasing health problem throughout the world which can lead to grave complications in the body over time like nephropathy, neuropathy, retinopathy, cardiovascular diseases and dyslipidemia [2,3]. It is mainly characterized by a loss of glucose homeostasis with an interruption in carbohydrate, fat and protein metabolism and defects in insulin secretion or insulin action, or both [4]. With insulin deficiency, the body tissues, the liver, muscular and adipose tissues fall short in taking up and using glucose from the blood circulation. This results in elevation of blood glucose level, which is known as hyperglycemia [5].

During the last few years an increase in the use of medicinal plants in curing various health problems has been observed as they are from natural origin and have less side-effect [6]. Plants have been the primary source of medication since ancient times and many drugs have been directly or indirectly derived from different plants [7]. At least 12 000 plants in the world are used for medicinal purposes, but less than 10% of them are investigated from pharmacological point of view [8]. Among all the medicinal plants, the plants under the genus of *Ocimum* belonging to family Lamiaceae have strong therapeutic potentials [9]. This genus has about 150 species of aromatic annual and perennial herbs and shrubs which grow widely around the tropical and subtropical regions in the world [10,11]. As reported by another researcher, various *Ocimum* species have been used in food and perfumery industry traditionally for a long time and the aerial parts of the plants have been used as native medicine [12,13]. Some species of the genus *Ocimum* reportedly have strong anti-hyperglycemic effects such as *Ocimum tenuiflorum (O. tenuiflorum)* or *Ocimum sanctum (O. sanctum)* [14,15], *Ocimum canum (O. canum)* [8], *Ocimum basilicum (O. basilicum)* [16] and *Ocimum gratissimum (O. gratissimum)* [17]. The current review focuses on different studies done with these four *Ocimum* species in hypoglycemia management both *in-vitro* and *in-vivo*.

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2. Phytochemical component responsible for anti-hyperglycemic effect

Different chemical components in *Ocimum* species have been found to have antihyperglycemic effects. Various chemical compounds were characterized and evaluated, among which eugenol has the highest potentials [18]. Eugenol (l-hydroxy-2-methoxy-4-allylbenzene) is a phenolic compound of the essential oils which can be found in different *Ocimum* species with the largest proportion in *O. tenuiflorum* L. (84%) followed by *O. gratissimum* (74.80%) [19]. *O. basilicum* contains almost 10% eugenol [20]. Eugenol has been found to lower the blood glucose level [21]. A diabetic study was done *in vivo* [18] showing that eugenol can reduce blood glucose levels by 38% by inhibiting α-glucosidase while insulin and glycated hemoglobin levels were the same. The polyphenols, caffeic acid, p-coumaric acid of aqueous extracts of *O. sanctum* leaves show anti-diabetic effect [22] as reported. Chicoric acid, one phenolic component found in *O. gratissimum* significantly reduced the glycemic level by 53% after 120 min of treatment [23].

3. Anti-hyperglycemic study of *Ocimum* plants

3.1. O. tenuiflorum L. or sanctum L.

O. tenuiflorum L. which is also known as Tulsi or Holy basil is cultivated in many parts of the world, such as Asia and Africa [24]. The leaf extracts of *O. tenuiflorum* L. (formerly known as *O. sanctum* L.) have been shown to have anti-hyperglycemic effects by increasing the insulin secretion from isolated islets, perfused pancreas and clonal pancreatic β–cells [25,26]. It is highly recommended and stated as one of the most potent traditional plants to manage diabetes [27].

According to studies, *O. tenuiflorum* L. extracts have the capability of decreasing plasma glucose level in type-2 diabetic rats which has been consistent throughout the 10 weeks duration of therapy as both low and high doses (200 mg/kg and 400 mg/kg) decreased plasma glucose levels significantly from 2 weeks onwards. A 70% ethanol extract of *O. sanctum* L. leaves have shown a significant decrease in blood sugar in both normal and streptozotocin induced diabetic model rats which was dose dependant [14]. *In vivo* studies with ethanol extract have also showed blood glucose decreasing and plasma insulin increasing activity in type 2 diabetes mellitus [26]. Though in another study [28] it has been described that, in a milder form of diabetes the ethanol extract of *O. sanctum* L. showed a greater anti-hyperglycemic effect than in moderate form of diabetes.

Another study showed that aqueous extract of *O. sanctum* L. exhibited a significant decrease in the blood glucose level ($P < 0.000\ 1$). The blood glucose level was 345 mg/dL before treatment and after treatment it reduced to 263 mg/dL [29]. Aqueous extract of *O. tenuiflorum* L. leaves was also used for the treatment of hyperglycemic tilapia. During the treatment the serum glucose level of hyperglycemic tilapia was dropped and got back to the level same as control [30]. A treatment with *O. sanctum* leaves was done on fasting and post-prandial blood glucose level, which was assessed through a randomized placebo controlled crossover single blind trial in type 2 diabetes patients. The result indicated a significant reduction in both fasting and post-prandial blood glucose level as compared to placebo. The levels of fasting and post-prandial blood glucose fell by 21 mg/dL ($P < 0.001$) and 15.8 mg/dL ($P < 0.02$) respectively [31]. Hypoglycemic and hypolipidemic effects were confirmed [32] in a randomized placebo-controlled, single blind trial performed on type 2 diabetes patients.

Antidiabetic effects of different fractions of ethanol extract (ethyl acetate, chloroform and petroleum-ether) of the *O. sanctum* leaves were investigated. Significant rise in liver glycogen was observed, which resulted from the administration of these fractions in normal and alloxan induced diabetic rats. In alloxan induced diabetic rats, significant elevations were observed in both SGOT (Serum Glutamate Oxaloacetate Transaminases) and SGPT (Serum Glutamate Pyruvate Transaminases) levels but reduced after *i.p.* administration of these fractions. According to the result, different fractions of *O. sanctum* leaves were able to reduce the severity of diabetes as well as hepatoprotectivity [33]. Methanolic extracts of various *Ocimum* species leaves were compared for antidiabetic activity and the result showed antidiabetic activity at 0.5 mg/kg concentration for all extracts is better than other *Ocimum* species as well as standard drug [34].

The leaf powder of *O. sanctum* L. has also shown a reduction in fasting blood glucose (21%) and glycated protein (11%), low density lipoprotein (LDL) (14%), very low density lipoprotein (VLDL) (16%), total cholesterol (11%), and triglyceride (TG) (16%). It has been done with 27 patients having type 2 diabetes mellitus [35]. Another study [36] showed a significant decrease in various diabetic symptoms (polydypsia, polyphagia and tiredness) in 30 type 2 diabetic patients who were consuming leaf powders of *O. sanctum* L. Two grams per day for 3 months.

Oral glucose tolerance was studied by a researcher and stated that it has been improved and potentiated by the activity of exogenously injected insulin [37]. The isolated tetracyclic triterpenoid compounds from the aerial parts of *O. sanctum* L. was studied and stated that they have strong antihyperglycemic potential [38]. The results of another study [39] indicated that ethanolic extract of *O. sanctum* L. has substantial oral hypoglycaemic activity which was comparable with the anti-hyperglycemic effect of standard drugs like glibenclamide and sulfonylurea.

3.2. O. basilicum L.

O. basilicum L. is also known as great basil or Saint-Joseph's-wort [40], sweet basil with a strong flavor similar to aniseed and used in flavoring curries and stir-fries [11]. This plant is mainly native to India [41]. The leaves and flowers of basil are used in folk medicine and basil tea is good for treating dysentery, nausea and flatulence. The oil of the plant is used for the alleviation of rhinitis mental fatigue, cold, spasm and as a first aid treatment for snakebites and wasp stings [42].

Different studies showed that aqueous extract of *O. basilicum* has *in-vitro* anti-hyperglycemic activity. Significant dose-dependent inhibition was observed against rat intestinal sucrose, maltose and porcine pancreatic α-amylase. The inhibition was observed against maltose as compared to sucrose. The results showed via α-glucosidase and α-amylase inhibiting activities, offered a significant response to control diabetes from the aqueous extracts of the plant [16]. Another study showed that methanol-dichloromethane leaf extract (MDE) and different fractions of *O. basilicum* L. has anti-hyperglycemic effects. Hypoglycemic and glucose tolerance effects were also evaluated in normal rats. The result showed a decrease in blood glucose of alloxan diabetic rats.

Methanol-dichloromethane leaf extract showed highest reduction (48.70%) followed by *n*-hexane fraction (44.74%), methanol fraction (42.28%) and dichloromethane fraction (31.88%). The extracts did not work in normal rats, but postprandial blood glucose rise was controlled after glucose load [43]. The methanol, hexane and dichloromethane extracts of the aerial parts of *O. basilicum* were used to evaluate the role of glucose transporter-4 (GLUT4) in anti-hyperglycemic effects. During the study 17 new compounds were found and in the result the observed anti-hyperglycemic properties were possibly because of one or more of the 17 new identified compounds [44].

An advanced study [45] on the silver nanoparticles derived from *O. basilicum*, displayed an inhibitory effect against Bacillus stearothermophilus α-glucosidase enzyme model, which indicates enhanced biocatalytic potential compared to the crude extracts and the control.

3.3. O. gratissimum L.

O. gratissimum, also known as Clove Basil [11], contains various therapeutic potentials such as antibacterial [46], antidiabetic [47], antitumor, anti-cancer [48], hepatoprotective [49] and analgesic activity [50]. The methanol and aqueous leaf extracts from *O. gratissimum* were studied *in vivo* and evidenced to have hypoglycemic activity [17,51,52].

A study was done to observe the anti-hyperglycemic effects of aqueous extract of *O. gratissimum* leaves in streptozocin-induced diabetic rats. A dose of 500 mg/kg significantly ($P < 0.05$) lower the blood glucose level after 24 h of administration and the blood glucose lowering rate was 81.3% [53]. The response of aqueous extract of the leaves in decreasing the fasting blood glucose level of pregnant and non pregnant rats was observed in which the result showed a significant reduction in fasting blood glucose level in diabetic pregnant rats and in non-diabetic pregnant rats there was no significant reduction [54]. A researcher investigated anti-hyperglycemic effect of leaf extract of *O. gratissimum* in alloxan-induced diabetes in rats. Extracts were given orally for 7 day at various doses. The result showed significant ($P < 0.05$) reduction in plasma glucose level which indicates that an oral dose of this plant leaves have potential plasma glucose lowering effect. In a recent study [55], researchers used standard method to evaluate the hypoglycemic effect of the aqueous extract compared to insulin treatment which showed that percentage recovery of the leaf extracts after treatment is higher than insulin. Besides this, another result showed that addition of NaCl or lime water to the aqueous extract may reduce its anti-hyperglycemic and antioxidant potentials [56].

Hypoglycemic effect of the methanolic extracts of *O. gratissimum* leaves was investigated in normal and alloxan-induced diabetic rats, which showed a decreased blood sugar level for both alloxan-induced diabetic and normal rats with the rates of 69% and 56% respectively [51]. In another study [51], it was evaluated that at equal doses the aqueous extracts of *O. gratissimum* leaves show a greater degree of blood glucose reduction than the ethanol extract.

3.4. O. canum L.

O. canum L. is a native plant of tropical Africa and an annual herb with white or lavender flowers. The medicinal purpose is the major one among its various uses. It contains different volatile oils, phytosterols, flavonoids, tannins, carbohydrates and fixed oils. Aqueous extracts of *O. canum* L. leaf extract observed to have anti-hyperglycemic activity [57].

In vivo, the aqueous extract of both fresh and dried leaves of *O. canum* lowered fasting blood glucose levels as well as body weight of genetically diabetic mice and their non-diabetic lean littermates. A mirabetic plant extract was also prepared for an investigation which did not prevent the rise in plasma glucose level and also the *in vitro* studies on the freeze dried extracts of *O. canum* fresh leaves significantly increased insulin release from pancreatic β-islet cells. It was a concentration-dependent effect which was a concentration up to 0.03 mg/mL and then decreased [58]. In another study [59], researchers had done both *in vitro* and *in vivo* modulations to evaluate the antihyperglycemic effect of *O. canum* L. The result for *in vivo* studies using the aqueous extract of *O. canum* L. showed a decrease in fasting blood glucose level in both diabetic and non-diabetic C57BL/KsJ mice. The *in vitro* study showed a notable increase in insulin release with aqueous extract of the plant from isolated rat pancreatic β-islet cells. The result depended on glucose concentration and an increase was observed in insulin release with increased level of *O. canum* L. aqueous extract concentration in the incubation medium. The optimum extract concentration was found out to be 0.03 mg/mL. Investigation of anti-hyperglycemic activity of the aqueous extract of *O. canum* leaf was done on Wister Albino rats by administration of streptozotocin (45 mg/kg, *i.p.*) for inducing diabetes. It was given for 28 d at the doses of 100 mg/kg and 200 mg/kg body weight and the result showed a significant reduction in blood glucose level ($P < 0.01$) [60]. One more study [8] on aqueous extracts of the leaves and stems was conducted by oral administration of the extract in alloxan induced diabetic mice using a glucometer which also proved its anti-hyperglycemic potential.

In another study [61], petroleum ether extract of *O. canum* leaves was evaluated for antihyperglycemic and antioxidant properties in streptozotocin-induced diabetic rats. After three days of streptozotocin induction, Ocimum extract was given in 100 mg/kg and 200 mg/kg body weight daily for 28 d. Glibenclamide (600 mg/kg) was served as reference. In every 7th day blood glucose levels were measured during 28 d. The result showed that the extracts caused a significant ($P < 0.01$) decrease in blood glucose levels and also improved other altered biochemical parameters which were associated with diabetes. Moreover, histopathological changes of the pancreas were also observed in streptozotocin-induced diabetic rats.

4. Conclusion and future prospects

Plants of *Ocimum* species have great medicinal values for treating various health problems and were used throughout the world. *O. tenuiflorum*, *O. basilicum*, *O. gratissimum* and *O. canum* have reportedly shown antihyperglycemic potentials in both *in vitro* and *in vivo* studies. Other than that *Ocimum kilimandscharicum* also shows some antidiabetic properties [11] but there are few reports on this plant. Usually the leaves have shown the most anti-hyperglycemic potentials but studies also showed some effects in the stems and inflorescence. This present review gives an overview on anti-hyperglycemic effects of different extracts such as aqueous, ethanolic, methanolic and ethyl acetate extracts of these 4 species which has been done in

previous years. *O. tenuiflorum* showed positive effects for both aqueous and hydro-alcoholic extract while *O. basilicum*, *O. gratissimum* and *O. canum* showed significant results in aqueous extracts. There have been few studies done on the components which are responsible for anti-hyperglycemic properties of these 4 species but more studies can be done in future regarding this area which can give a clear conception about the active component in *Ocimum* species responsible for its anti-hyperglycemic potentials. Furthermore, some new methods of extraction and solvents which have not been used yet can be used to look for some new results in this area.

Conflict of interest statement

We declare that we have no conflict of interest.

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