Effect of Boswellia species on the metabolic syndrome: A review

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**Abstract**

The metabolic syndrome, a cluster of metabolic disorders, includes abdominal obesity, hypertension, dyslipidemia, and hyperglycemia leading to insulin resistance, development of diabetes mellitus, and cardiovascular diseases. For the treatment of metabolic syndrome, traditional herbal medicines such as frankincense or Boswellia species have been used due to their anti-inflammatory, anti-oxidant, anti-obesity, anti-diabetic, anti-hypertensive, and hypolipidemic properties. Based on the literature, published evidence up to 2020 about the therapeutic effects of Boswellia species on the metabolic disorder among Medline, Scopus, and Google Scholar were precisely evaluated by keywords such as obesity, diabetes, hyperglycemia, hypertension, blood pressure, dyslipidemia, metabolic syndrome, frankincense, and Boswellia. According to the results, Boswellia species have beneficial effects to control metabolic syndrome and its related disorders such as hyperglycemia, dyslipidemia, hypertension, obesity, diabetes, and its complications. Boswellia species by reducing the resistance to insulin and restoring pancreatic beta cells decrease blood glucose. Also, Boswellia species have antithrombotic and anti-agulant properties that regulate blood pressure. The anti-oxidant properties of Boswellia species modulate the blood lipid profile via reducing TNF-α, IL-1β levels, and increasing the adiponectin level. The therapeutic and protective effects of Boswellia species on metabolic disorders were remarkably confirmed regarding decreasing hyperglycemia, hyperlipidemia, hypertension, and obesity.

**Keywords:** Boswellia, Dyslipidemia, Frankincense, Hyperglycemia, Hypertension, Metabolic syndrome, Olibanum

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**Introduction**

The metabolic syndrome is defined as abdominal obesity, dyslipidemia (DL), hypertension (HTN), insulin resistance with or without glucose tolerance, pro-inflammatory and pro-thrombotic state (1, 2). Moreover, metabolic syndrome is a serious problem and challenge with an ascending trend throughout the world that is caused by excessive calorie intake, urbanization, and inactive lifestyles (3). Systemic HTN that is also known as high blood pressure (HBP) and abnormal lipid profile can be observed because of the resistance to insulin, which results in atherosclerotic vascular disease. Hence, metabolic syndrome enhances myocardial infarction (MI) and stroke risks (4).

Today, studies have been focused on supplementary and substitute medicine (5-7) due to inadequate efficiency and significant complications from recent treatments for hyperlipidemia (HLP) and diabetes (8-11). Recently, researchers have paid attention to the use of medicinal plants due to the reduced complications and different efficient compounds in the herbs as recommended by the World Health Organization (WHO) (12).

Concerning the important clinical consequences of the metabolic syndrome, investigators have mainly attended to study the values of herbal medicines or herbalism. Boswellia internationally known as Indian frankincense or olibanum has been used to treat various diseases. The frankincense or olibanum, a yellowish-brown oleo-resin, is prepared from Boswellia species such as Boswellia serrata (13). Boswellia genus contains about 25 different species. A number of the prominent species consist of B. frereana, B. sacra, B. ovalifoliolata, B. carterii, B. papyrifera, B. rivae, B. neglecta, and so forth (14-17). Recent research indicated the anti-inflammatory, anti-ulcerous function, and anticancerous impacts of this plant (18). Of course, some studies demonstrated the antihyperglycemic and antihyperlipidemic impacts of Boswellia in streptozotocin-induced diabetic rats (19). Also, one of the studies indicated the protective impacts of B. serrata gum on diabetic side effects in animal models (20, 21). Moreover, this plant has useful impacts on the low-density lipoprotein (LDL), blood glucose, and high-density lipoprotein (HDL) of patients with diabetes who had received B. serrata gum at a dosage of 900 mg every day with no significant complications (22).

Numerous animal research projects demonstrated the anti-oxidant features of gum resin extracts of B. serrata (23, 24). Pandey et al. showed that the extracts of B. serrata gum resin resulted in a reduction in serum cholesterol and the enhancement of HDL in the rats (25). Another research indicated that patients with type 2 diabetes who have been supplemented with gum resin of B. serrata for six weeks experienced a remarkable decline of fasting blood glucose and the augmentation in plasma insulin level (26).
Pharmacognostical features of *Boswellia*

*Boswellia* belongs to the family Burseraceae, which is a deciduous tree. In general, it reaches a moderate height (4 to 5 m). As other moderate to big size trees with branches, this tree possesses a circumference of 2.4 m (average 1.5 m). The color of the thin barks of the tree changes from greenish-gray, yellow, or reddish to ash color that its peeling may be readily done. The papery barks, when peeled off or cut, release translucent lumps, tear, or droplets of white to yellow color gummy oleoresin (26).

Composition

There are nearly 200 phytochemicals in the oleo-gum-resin mix in various species of *Boswellia*. These compounds contain pure resin, mucus, and essential oil (27, 28).

The essential oil compositions of each species are different and change concerning the environment, harvest condition, and geographic areas (29, 30). The gum portion is composed of pentose and hexose sugar containing a couple of oxidation and digestive enzymes. The essential oil is a mix of mono-terpenes, diterpenes, and sesquiterpenes. β-boswellic acid (Bas) is the main constituent of each species of the genus *Boswellia* (Figure1). There are 6 main Bas, including α- and β-BA (10 to 21%), acetylated α- and β-BA (0.05–6%), 11-keto-β-boswellic acid (KBA, 2.5 to 7.5%), and 3-O-acetyl-11-keto-β-boswellic acid (AKBA, 0.1– 3%), which are found in each *Boswellia* species with variable amounts. The contents of BA, which can be found in the market as the standardized extracts, change from 37.5-65% (31, 32).

Review literature

The search was performed by keywords such as diabetes or hyperglycemia, *Boswellia*, frankincense, olibanum, boswellic acid, elevated BP or HTN, hypertensive or antihypertensive, DL, and metabolic syndrome using Google Scholar, Scopus, and Medline databases. In fact, in the current research, most of the papers about the effects of *Boswellia* on metabolic disorders have been precisely evaluated. To better review, irrelevant or duplicated papers have been disregarded. Publications have been specified from their admission up to August 2020.

Dosing

*Boswellia* species are usually administered as a capsule, pill, or bark decoction orally. The respective dose is suggested based on historical practices or existing trials. Today, there is ambiguity on the optimum dosage for balancing a safe and efficient method. Each producer has their production method of *Boswellia*, and these results are too inconsistent to provide a standardized product. Notably, several trials applied different products manufactured by different producers. For this reason, clinical impacts cannot be compared (33).

Hypoglycemic effect of the *Boswellia species* in diabetic patients and animal models

*Boswellia* species tree and the corresponding gummy resin are completely known due to their useful impacts on several diseases such as diabetes mellitus (DM) (39). Azemi *et al.* showed that the extract of *B. serrata* has antidiabetic impacts and can prevent the microvascular complications of diabetes in the kidney and liver (40). Investigators showed that herbal formulations with *B. serrata* oleo-gum-resin generated considerable antidiabetic activities via influencing the hepatic gluconeogenesis, pyruvate carboxylase, and phosphoenolpyruvate carboxykinase (41). Shehata *et al.* studied AKBA contribution to the prevention of inducing auto-immune reaction, insulins, and hyperglycemia in a model of multiple low dose streptozotocin (MLD-STZ) diabetes. The induction of hyperglycemia or high blood sugar has been done via injection of IP 40 mg/kg STZ in male mice for five days every day, whereas the second treatment group has been administered KBA with STZ for ten days. In STZ treated rats, a considerable burst of pro-inflammatory and anti-inflammatory cytokines in the blood, infiltrating lymphocytes (CD3) into pancreatic islets, and emerging peri-insular apoptotic cells have been registered. A significant increase in plasma glucose has been observed (124.4±6.65 versus 240.2±27.36 mg/dl, P<0.05). Nonetheless, concurrent treatments with AKBA and KBA indicated a significant decrease in pro-inflammatory and anti-inflammatory cytokines. Moreover, the detection of infiltrating lymphocytes into pancreatic islets and emerging peri-insular cells has not been reported (42).

Ahangarpour *et al.*, clinically studied patients with type 2 diabetes supplemented with extract of *B. serrata* gum resin for six weeks and compared them to type 2 diabetic patients. A considerable reduction of fasting blood glucose and a decrease in insulin levels have been reported (22). The researchers were satisfied with the findings, and thus developed the research and examined antidiabetic, hypolipidemic, and hepatoprotective impacts of the supplement *B. serrata* in 60 patients with type 2 diabetes from both genders. Treating diabetic patients with the extract of *B. serrata* gum resin (orally, 900 mg) for six weeks led to a considerable enhancement of the levels of HDL and significant decline of cholesterol, LDL, as well as the amounts of fructosamine SGPT and SGOT. The research indicated that the administration of 900 mg of *B. serrata* supplement daily is one of the healthy and efficient options for decreasing hazardous agents related to type 2 diabetes. Diabetic patients who receive *B. serrata* can keep fructosamine level, hepatic enzyme activity, and lipid profiles close to the standard levels and have a high-quality life (21). Herbal formulations with *B. serrata* oleo-gum-resin as an ingredient of the supplementation led to considerable antidiabetic activities on non-insulin-dependent DM in streptozocin induced diabetic rat model.

In a case study report of a male patient diagnosed with Latent Autoimmune Diabetes in Adults, *B. serrata* gum resin during 9 months treatment reduced both the levels of autoantibodies (43). Some results demonstrated the decline of the blood glucose levels in patients with diabetes by orally administrating the aqueous extracts of the leaf and root of *B. glabra*. The continuous application of the extract of the leaf and root for 28 days represented a reduction.
of cholesterol, creatinine, triglyceride, serum glucose, urea, enzyme activity with considerable hypo-glycemic impacts (44). One of the auto-immune diseases is a type 1 diabetes, in which a chronic inflammatory procedure eventually leads to beta-cell mortality and a lack of insulin production. It was indicated that extracts obtained by the gum resin of BS have anti-inflammatory features, especially via targeting agents or mediators associated with auto-immune diseases (39). The recent research demonstrated the antidiabetic impacts of BS extracts and their capability for preventing the side effects of diabetes in the kidney and liver (40).

Hypoglycemic activities in mice with type 1 diabetes have been confirmed by BS oleo-gum and respective active ingredients, KBA and AKBA by suppressing pro-inflammatory cytokines related to inducing auto-immune procedure in pancreatic islets, such as interleukin (IL)-1A, IL-1B, IL-2, IL-6, interferon (IFN)-γ, TNF-α, granulocyte colony-stimulating factor (G-CSF), and granulocyte/macrophage colony-stimulating factor (GM-CSF), and infiltrating lymphocytes into islets. Two of the major antidiabetic mechanisms include suppressing pancreatic islet tissue atrophy and peri-insular apoptotic cells mediated by anti-caspase 3 (39, 45). Rao et al. (2013) revealed the improvement of chronic diabetic side effects by oleo-gum resin and the isolated compound boswellic acid through the inhibition of polyol enzyme aldose reductase and reduction in the developed glycation end product in vivo in rat lens and rat kidneys and in vitro in human recombinant cells (20). Additionally, B. carterii oleo-gum resin showed an antidiabetic capacity by increasing the serum insulin, regenerating β-cells of Langerhans islets, enhancing glycosogenesis, and declining glycogenolysis in rats with alloxan-induced type 1 diabetes (46).

The previous study showed that blood-glucose levels increased significantly (P<0.05) in the control group in comparison to other groups that received 3 g B. serrata/l in drinking water. However, the remaining treated groups showed a significant decrease in comparison with control (47). Also, Al-Daraji et al. (47), reported that the drinking water of broiler chickens supplemented with different levels of B. carteri powder led to a significant decrease in blood glucose concentrations, at levels 0.5, 0.75, and 1 g/l. However, 0.75 and 1 g/l water supplementation reduced the values of blood plasma concentrations of glucose. 6 weeks complementarity of B. serrata to type 2 diabetic patients also produced a very significant decrease in fasting blood glucose and an increase in insulin level (48). Similarly, B. glabra aqueous extract increased the synthesis of secretory granules in the beta-cell and led to an increase in pancreatic enzyme resulting in reduced blood-sugar level (49) (Table 1).

Impact on the elevated blood pressure

Not many authors assessed the positive impacts of Boswellia species on elevated BP which is an important component of the metabolic syndrome. Recent studies have introduced some mechanisms of actions concerning B. serrata gum resin on cardiac health. There is enough knowledge of the relationship between oxidative stresses, inflammation, and thrombosis resulting in cardiovascular diseases (50, 51). Hence, the anti-oxidant and antithrombotic characteristics of B. serrata gum resin were examined. Enriching B. serrata gum resin with triterpenoids showed their anti-oxidant activities based on the respective chemical compositions (52, 54). The experiments of the anti-oxidant activities of B. serrata gum resin suggested antilipid per-oxidation actions in the liver and heart. Researchers studied the phytochemical ingredients of the crude extract of B. serrata and demonstrated that it consists of essential oils, resin, and gum. Boswellic acid, a pentacyclic triterpene, has been recognized as an active moiety of the resin portion (55). Primary phytochemical studies showed the existence of flavonoid and saponin in B. serrata Previous observations showed that several compounds, such as flavonoids, saponins, or organic acids might contribute to the herb diuretic impacts (56). Likewise, some authors revealed that specific flavonoids induce diuretic activities by attaching with adenosine A1 receptors related to the diuretic actions (57). Since B. serrata has a lot of saponins and flavonoids, the diuretic activities of the herb understudy might result from these mechanisms. It has been indicated that sodium is a prominent external agent that plays a role in primary HTN (58). Several research projects demonstrated the adverse effects of higher uptake of sodium adversely on the arterial BP (59). The higher excretion of urinary sodium in the present experimental animals revealed the antihypertensive activity of the B. serrata (Table 1).

Impact on obesity and lipid profiles

Several herbal medicines such as Ginkgo biloba can manage and improve hyperlipidemia or obesity in patients (60). Numerous academic research projects performed during recent years showed that Boswellia species would be efficient hypolipidemic agents. It has been demonstrated that the water-soluble fraction of B. serrata reduces the levels of total cholesterol (38-48%) (61) in experimental animals, which confirms its hypolipidemic potentials. Moreover, Zutshi et al. showed the antihyperlipidemic activities of Boswellia gum (19). Salami gum keeps the levels of serum cholesterol and triglyceride of animals within optimal ranges that would be received on diets with increased cholesterol and saturated fat (61). It was reported that AKBA inhibits NF-κB activity in atherosclerosis (62). Of course, AKBA has anti-adiposity properties, through which it can induce lipolysis in mature human adipocytes that have been observed by Liu et al. in the in vitro study. Moreover, this event has been followed by downregulating the expression of PPAR-γ2 and losing phenotypic markers (63). The study of Al-Yasiry et al. (46) showed that Boswellia species (3 g B. serrata/l in drinking water) reduced the cholesterol level in broiler chicken. Their findings were in agreement with those of Pandey et al (64). In this study, they showed that the supplementation of BS gum resins extract 15 mg/100 g body wt for 90 days caused a significant decrease in serum cholesterol and increased HDL in rats. It has also been reported by Al-Daraji et al. (65) that B. carterii (0.5, 0.75, and 1 g/l in drinking water) decreased significantly cholesterol, triglycerides, and LDL levels. The results of this study suggest the probability that B. serrata supplementation restores β-cells function for insulin secretion, and that insulin helps to reduce
Table 1. The efficacy of *Boswellia* species on different animal models composed of the metabolic syndrome

| Study type  | Metabolic syndrome component                                      | Reference |
|-------------|-------------------------------------------------------------------|-----------|
| Animal studies | ↓ Blood insulin levels                                           | 39        |
| Animal studies | ↓ Hyperglycemia                                                   | 42        |
| Human studies | ↓ Fasting blood glucose                                          | 22        |
|              | ↓ Insulin levels                                                  |           |
| Animal studies | ↓ Hepatic gluconeogenesis, ↓ Blood glucose                       | 41        |
| Human studies | ↓ Diabetic, Hypolipidemic, ↑ Levels of HDL                        | 21, 65, 66|
|              | ↓ Total cholesterol, triglycerides, LDL                           | 44, 49, 50, 61, 62, 46 |
| Animal studies | ↓ Cholesterol, creatinine, triglyceride, serum glucose, urea, enzyme activity |           |
| Animal studies | ↓ Diabetic                                                        | 39, 45    |
|              | ↓ Pancreatic damages                                              |           |
|              | ↓ Infiltration of lymphocytes into pancreatic islets              |           |
| Animal studies | ↓ Polyol enzyme aldose reductase                                 | 20        |
|              | ↓ The developed glycation                                         |           |
|              | ↓ Blood glucose                                                   |           |
| Animal studies | ↓ Blood insulin levels                                            | 40        |
| Animal studies | ↓ Blood insulin levels                                            | 36        |
| Animal studies | ↓ The serum insulin                                               | 46        |
|              | ↑ Glycogenesis                                                    |           |
|              | ↓ Glycogenolysis                                                  |           |
| Animal studies | Adjusts the lipid profile                                         | 38        |
| Animal studies | ↑ Anti-oxidant defense                                            | 53, 55, 57, 58 |
|              | ↑ Anti-oxidant and Anti-thrombolic effects                        |           |
|              | ↑ Antilipid peroxidation actions in liver and heart               |           |
|              | ↑ Diuretic activities                                             |           |
|              | ↑ Antihypertensive factor                                          |           |
|              | ↓ High sodium absorption                                          |           |
| Animal studies | Modulates vascular tones                                          | 37        |
| Animal studies | ↓ Obesity                                                         | 72, 75, 76|
|              | ↓ Food intake                                                     |           |
|              | ↓ Concentration adiponectin                                       |           |
|              | ↓ Hyperlipidemia                                                  |           |
|              | ↓ Oxidative stress and inflammation                               |           |
|              | ↓ TNF-α, IL-1β                                                    |           |
|              | ↓ Leptin resistance                                               |           |
| Animal studies | ↓ Oxidative stress and inflammation                               | 75, 73    |
|              | ↓ TNF-α, IL-1β                                                    |           |
|              | ↓ Leptin resistance                                               |           |
| Human studies | ↓ Obesity                                                        | 78        |

DM: Diabetes Mellitus; NAFLD: Non-Alcoholic Fatty Liver Disease; HLP: Hyperlipidemia; LDL: Low-Density Lipoprotein; HDL: High-Density Lipoprotein; BP: Blood Pressure, OB: Obesity
serum lipid profiles (66). Moreover, *B. carterii* may have a protective effect on pancreatic β cells through its anti-oxidant action (67) (Table1). Obesity, a chronic disease characterized by the storage of excess energy in fat cells, is a result of abnormal metabolism. Obesity is a complex issue and its causes, consequences, and management are an area of considerable debate as a widespread disease. Several studies reported *Boswellia* species exhibited anti-obesity effects by lowering total cholesterols, triglycerides, free fatty acids, LDL concentrations, circulating adiponectin, food intake as well as elevating HDL (68-70). The study performed by Tawfik showed that boswellic acid has a promising anti-aggregatory effect by reducing the enhanced HLP, oxidative stress, and inflammation associated with a high-fat diet (HFD) (71). Gomaa et al. investigated that *B. serrata* extract is as effective as orlistat in preventing obesity, hyperlipidemia, steatosis, and insulin resistance. These actions may be mediated by the suppression of food intake and reducing the levels of TNF-α, IL-1β, and leptin resistance along with increasing adiponectin (72). *B. serrata* extract has anti-obesity effects and can be attributed to the presence of active principles such as phenolic compounds and triterpenoids (73-75). In another study, *B. serrata* extract showed a suppressive effect on cumulative food intake compared to ephedrine used as a standard anorectic drug (76).

The findings of previous studies demonstrated that the use of *B. serrata* appears safe and effective to control obesity (77). The possible mechanism of *B. serrata* reported by Singh et al. consists of the stimulation of the thyroid gland leading to an increase in metabolic rate. Thereby enhancing thyroid efficiency which in turn causes to lose weight. Regarding toxicity, *B. serrata* showed no toxic effect up to 500 mg/kg (78) (Figure1 and Table1).

**The overall mechanism of *Boswellia species* in the metabolic syndrome**

Several features of *Boswellia* species have been explored. The general mechanisms of the *Boswellia* species include anti-oxidant, radical scavenger, glutathione contents regulator, cellular membranes stabilizer, and cell permeability regulator. Moreover, *B. serrata* extracts enhance the regeneration of the liver and delay developing and progressing hepatic fibrosis (34, 35).

Based on numerous research projects, the major classifications of *Boswellia* mechanisms are as following: 1. *Boswellia* gum resin reduces plasma glucose in...
diabetes by decreasing the resistance to insulin and restoring pancreatic beta cells (36) (Figure 2).

2. *Boswellia* gum resin regulates BP in hypertensive conditions by modulation vascular tones, diuretic effects, and suppression platelet aggregations with antithrombotic and anticoagulant properties (37) (Figure 2).

3. *Boswellia* gum resin adjusts the lipid profile via decreasing hepatic steatosis and ameliorates liver dysfunctions tests through its anti-oxidant and cytoprotective impacts (38) (Figure 2).

4. *Boswellia* extracts suppress food intake and reduce TNF-α, IL-1β levels and leptin resistance along with increasing the adiponectin level (72) (Figure 2).

**Conclusion**

According to the broad range of properties of *Boswellia* species, this review described the potential effects of *Boswellia* species in either the treatment or prevention of the metabolic syndrome. The previous studies shed light on new ways of treatment for the metabolic syndrome by the exhibition of the effectiveness of *Boswellia* species in HBP, obesity, DL, and high blood glucose. Nevertheless, a series of effective clinical studies should be conducted in this regard.

**Conflicts of Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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