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Original Article

Prophylactic and Curative Effect of Boswellia Serrata on Blood Glucose Level and Architecture of Pancreas in Diabetic Mice Induced by Alloxan

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ABSTRACT

Background and objectives. *Herbal medicines have gained significant attention from the scientific community for treating and managing diabetes in both developing and developed countries. Boswellia serrata, known for its anti-inflammatory and antioxidant properties, has been historically used to treat various diseases. This study aimed to determine the effect of Boswellia serrata on body weight, blood glucose level, and pancreas architecture in alloxan-induced diabetes in albino mice.* ***Methods***. *Forty albino male mice, aged 10 to 12 weeks and weighing between 24 and 34 grams, were divided into four groups of ten each. The first group was the negative control group, and the second group was the diabetic positive control group that received 120 mg/kg alloxan intraperitoneally. The third group received a single injection of alloxan at a dose of 120 mg/kg bw and was treated with Boswellia serrata macerated at a dose of 150 mg/kg bw for four weeks. The fourth group received orally Boswellia serrata extract at a dose of 150 mg/kg for two weeks, followed by a single injection of alloxan at a dose of 120 mg/kg, and were left for two weeks.* ***Results***. *This study found that Boswellia serrata has antidiabetic properties in diabetic mice, as it significantly reduced blood sugar levels compared to the diabetic group. Additionally, histological analyses of the groups treated with B. serrata showed a significant improvement in the harmful effects of alloxan on pancreatic islet cells.* ***Conclusion***. *Boswellia serrata has shown a notable improvement in the detrimental effect of alloxan on pancreatic islet cells, and its curative effect has been proven to be better than its prophylactic effect. This is supported by the improved blood glucose levels and the histological changes that were more pronounced.*

Keywords: Alloxan, Diabetes, Histopathology, Boswellia Serrata, Mice

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INTRODUCTION

Diabetes mellitus is a metabolic endocrine disease associated with high blood glucose levels and interferes with the metabolism of carbohydrates, proteins, and fats [1]. It affected about 463 million people in 2019 and is expected to affect 700 million people by 2045 [2]. The rising incidence of diabetes mellitus is significantly correlated with an unhealthy lifestyle, including an unbalanced diet., inactivity, and smoking [3].

Many traditional plant remedies for diabetes have gained popularity in both industrialized and

developing nations in recent years because they have comparably fewer negative effects than synthetic medications. Boswellia (B) is one such plant that belongs to the family Burseraceae. There are over 30 species, 16 of which grow in tropical Africa and Asia in the genus Boswellia, but only five species, *B. serrata*, *B. carterii*, *B. sacra*, *B. papyrifera*, and *B. frerana* are well known [4, 5]. Boswellia serrata (B. serrata) commonly known as frankincense [6], has been known since ancient times to treat digestive disorders, cancer, asthma, and joint inflammation [7]. The oleogum resin of frankincense was found to include more than 200 different chemical constituents, including penta- and tetracyclic terpenoids, saponins, alkaloids, polyphenols, tannins, essential oils, mucus, sugars, and other substances, according to phytochemical investigations [8]. The pentacyclic boswellic acids are primarily responsible for the oleogum resin's pharmacological action

According to recent research, the resin of B. serrata has several potential health benefits and can be used as a substitute for conventional medications. Studies show that the active components of B. serrata resin have anti-diabetic [9], antioxidant, and peptic ulcer healing [10], and anticancer [11]. Moreover, Boswellia extracts have been shown to effectively cure several ailments, include non-alcoholic fatty liver disease and renal fibrosis [12], autoimmune encephalomyelitis and multiple sclerosis [13] and rheumatoid arthritis [14]. Based on these findings, B. serrata can be a potent alternative treatment for a variety of health conditions.

Furthermore, previous studies found that B. serrata was typically safe in vivo experiments, with doses below 1000 mg/kg body weight without producing alterations in biochemical or histopathological markers [15]. Additionally, the lowering of oxidative stress was one of the phenotypic changes seen after treatment with frankincense and its components. It has been shown that membrane lipid peroxidation and the production of reactive oxygen and nitrogen species are reduced [16].

METHODS

Animals

Adult male albino mice were reared in the animal house of the Department of Zoology / Faculty of Science/ Tripoli University. Mice were housed in plastic cages in an air-conditioned room and maintained at 25°C and natural daylight, with free access to drinking and food

Induction of diabetes

After about two weeks of acclimatization, mice were given intraperitoneally (i.p) a single injection of 120 mg/kg body weight (bw) of freshly prepared alloxan in distilled water to induce diabetes. Four days following the injection, diabetes was identified by checking the blood glucose level in the tail vein using an Accu-Check Sensor Comfort glucometer. Animals with a blood glucose level of more than 200 mg/dl were chosen for the investigation.

Preparation of B. serrata macerated

The B. serrata used in this study was purchased from the local market and verified by a qualified taxonomist from the Department of Botany /Faculty of Science/University of Tripoli. B. serrata was prepared by soaking 3 grams of B. serrata in 10 ml of distilled water overnight to give a stock solution of 300 mg/ml and administrated to the mice orally at a dose of 150 mg/kg bw

Experimental design

Forty albino male mice with body weights ranging from 24 to 34 grams and ages between 10 and 12 weeks were divided into four groups of ten mice each (n=10) as follows:

Group I (G I): Negative control group (untreated mice administered distilled water).

Group II (G II): positive control mice (diabetic) injected with a single dose of alloxan at a dose of 120 mg/kg/bw.

Group III (G III): (Alloxan+ B. serrata) injected (i.p) with a single dose of alloxan at a dose of 120 mg/kg

bw, then received orally B. serrata macerated at a dose of 150 mg/kg bw for four weeks.

Group IV (G IV): (B. serrata +Alloxan) received orally B. serrata macerated at a dose of 150 mg/kg for two weeks. Afterward, injected with a single dose of alloxan at a dose of 120 mg/kg and left for two weeks. The weights of the mice and blood glucose levels in all groups were measured weekly throughout the experimental period.

At the end of the experiment, mice were killed by cervical dislocation. The mice were dissected, and the pancreases were removed and immediately fixed for 24 hours in 10% formalin buffered with phosphate buffer solution pH 7.4. The samples were washed twice with 70% alcohol. In a sequence of increasing concentrations of alcohol from 70% to 100%, the fixed tissues were dehydrated and cleared in xylene embedded in paraffin wax. On a rotating microtome, the pancreas is sectioned into 5µ thick slices. Hematoxylin-eosin was used to stain the prepared sections according to standard procedures.

Statistical analysis

All results are expressed as mean ± SD (standard deviation). Data were analyzed using SPSS software (version 20). One-way analysis of variance (ANOVA) followed by post hoc Duncan's test was applied for comparisons between treated groups and control. ($P<0.05$) was considered statistically significant.

RESULTS

In this study, the effect of administering B. serrata on blood glucose level, body weight, and the pancreas's architecture in alloxan-induced diabetes in albino mice was investigated. The average body weight of each experimental group is displayed in Table 1. The results of the current investigation made it abundantly evident that the mean body weight in the positive control group (diabetic, G II) was significantly lower ($p<0.001$) than that of the non-diabetic control group (negative control, G I). Also, when compared to the duration, the weight significantly decreased in group II from 24±1.5 g to 21±0.82 g in the second week then to 18 g and 16.3±0.47 g in the third and fourth week, respectively ($P=0.000$). When compared to the positive control group (G II), the body weight of the B. serrata -treated diabetics (G III) has significantly improved ($p<0.001$) from 29.3±0.47 g in the first week to 34.1±0.83 g in the fourth week.

The study discovered that the highest mean value of blood glucose was observed in mice injected with 120 mg/kg alloxan (G II) in the second, third and fourth weeks, 580±14.14, 533±12.47 and 516.67±4.96 mg/dl respectively, followed by group III (Alloxan+ B. serrata) 203±34.5 in the second week and 152.8±11.24 in the third week as shown in Table 2. When compared with the negative control group (G I), alloxan-treated mice (positive control, G II) had significantly higher serum glucose levels on weeks 2, 3, and 4 ($P<0.001$). However, there was a considerable decrease ($P<0.05$) in blood glucose levels in the second, third, and fourth weeks, when alloxan and B. serrata were given together (G III) compared to the first week. Also, there was a highly significant difference in the level of blood glucose in this group when compared to the positive control group ($p<0.001$) as presented in Table 2. Treatment of mice with B. serrata for two weeks followed by alloxan decreased serum blood glucose insignificantly ($P>0.05$) on weeks 2, 3, and 4 compared to the first week. However, when compared with the positive control group (G II), there was a statistically substantial difference ($P<0.001$) in group IV.

The current study revealed that administration of B. serrata with alloxan (G III) showed the lowest glucose levels (121.2±10.78 mg/dL) in the fourth week compared to the G IV (156.1±9.68mg/dL) which was given B. serrata for two weeks followed by alloxan. This indicated that the protective effect of B. serrata given with alloxan was greater than that given before alloxan.

Table 1. Body weights for the experimental groups

Groups	1st week	2nd week	3rd week	4th week
G I:	25.5±2	27.7±1.7^{ns}	29±2.9^{ns}	30.3±3.4^{c,d}
G II:	24±1.5	21±0.82^{c}	18±0.009^{a}	16.3±0.47^{a}
G III:	29.3±0.47	31±1.6 ^{ns}	35.1±2.19^{b}	34.1±0.83^{c,d}
G IV:	34±0.24	33±0.83 ^{ns}	34.1±0.61	31.2±0.82^{b,d}

Values are presented as means ± SD (n = 10). The mean difference is significant at the *P*≤0.05. significant differences: ^{a}P<0.001, ^{b}P<0.01, ^{c}P<0.05, ns (non-significant) compared with the first week in each group. ^{d}P<0.001, compared with the positive control group.

Histological examination of the negative control mice (untreated, G I) revealed that the pancreatic acini and Langerhans islets cells had a typical shape. The normal appearance of the islets of Langerhans cells can be seen through the clear borders separating them from the secretory cells, as their nuclei are round and their cells contain an amount of acidophilic cytoplasm. The secretory glands take a pyramidal shape and their nuclei are located near the base as seen in Figure 1.

Table 2. Fasting blood glucose levels in experimental groups

Groups	Serum glucose level (mg/dl)			
	1st week	2nd week	3rd week	4th week
G I	145.4±2.8	146.3±8.99^{ns}	145.7±4.92^{ns}	146±2.94^{ns}
G II	146.3±4.98	580±14.14^{a}	533±12.47^{a}	516.67±4.96^{a,d}
G III	146.87±13.8	203.4±34.5^{c}	152.8±11.24^{ns}	121.2±10.78^{ns,e,f}
G IV	146.2±7.64	140.9±2.57^{ns}	161±2.45^{ns}	156.1±9.68^{ns,f}

Values are presented as means ± SD (n = 10). The mean difference is significant at the *P*≤0.05. significant differences: ^{a}P<0.001, ^{b}P<0.01, ^{c}P<0.05, ns (non-significant) compared with the first week in each group. ^{d}P<0.001, ^{e}P<0.05, compared with the negative control group. ^{f}P<0.001 versus the positive control group.

On the other hand, mice injected intraperitoneally with 120 mg/kg/day alloxan (G II) showed many histological abnormalities in the structure of the pancreas like acute necrotic changes in islets of Langerhans cells, and severe acinar cell modification compared to the negative control group. Moreover, the cells of the secretory glands lose their distinctive pyramidal shape, and their nuclei disappear, changing from their typical shape and appearing in some areas of pale color. The thickness of the septa separating the pancreatic lobes from one another is also noted (Figures 2 I and II).

However, B. serrata significantly reduced all of these degenerative alterations in the pancreas.

The architecture of the pancreas in the Alloxan+ B. serrata group (G III) treated mice was similar to normal morphology. The majority of the pancreatic secretory glands are pyramidal, and their nuclei are near the base, giving them a more typical appearance. The borders of the Langerhans islets looked to be distinct as shown in Figure 3. In G IV (B. serrata + Alloxan), the islets of Langerhans appear to be shrunken and have slightly irregular borders with dense nuclei, also there is a variation in the normal pattern of gland cells (Figure 4)

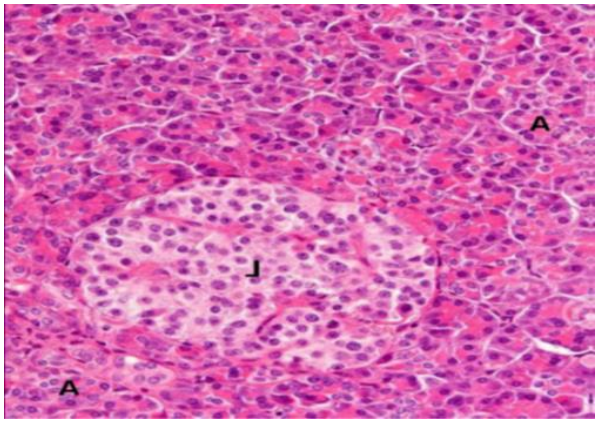

Figure 1. *Photomicrograph of pancreas tissues in the mice of group I (negative control). A- shape of the pancreatic exocrine glands (Acinar cells); L- the cells of the islet of Langerhans, Hematoxylin and Eosin 400x*

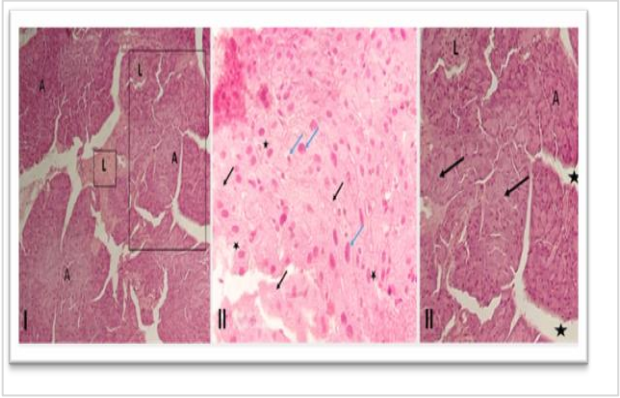

Figure 2. *Photomicrograph of pancreas tissues in the mice of group II (injected with Alloxan) shows degeneration and necrosis in Langerhans islet cells (black arrows); difference in the size and shape of the cells (star); difference and multiplicity of the shape of the nuclei (blue arrows). I (100x), II (400x) Hematoxylin and Eosin dye.*

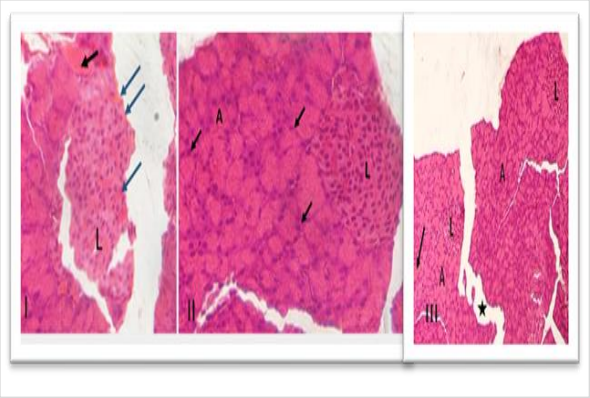

Figure 3. *Photomicrograph of pancreas tissues in the mice of group III (Alloxan + B. serrata) shows the pancreatic exocrine glands (Acinar cells), where most of the glands appear close to the normal pyramidal shape (A) and their nuclei are near the base (black arrows); the normal features of the islets of Langerhans, which appear with distinct boundaries and dense nuclei that were close to that of normal mice (L); septum between the pancreatic lobes (star); blood vessels (blue arrows). Hematoxylin and Eosin 400X (I and II), 100X (III).*

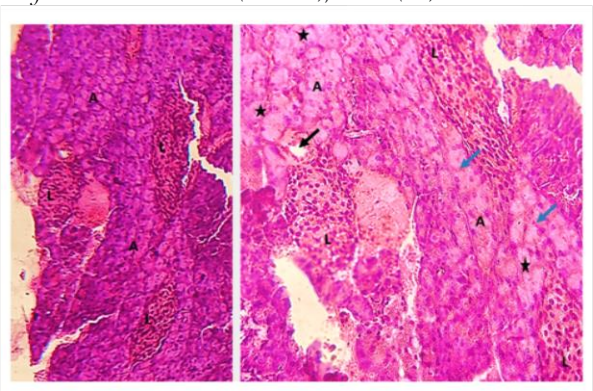

Figure 4. *Photomicrograph of pancreas tissues in mice of group IV (B. serrata + Alloxan) shows the shape of the pancreatic exocrine glands, Acinar cells(A); the shape of the cells of the islets of Langerhans, which appear to be shrunken and have slightly irregular borders with dense nuclei (L); a variation in the normal pattern of gland cells (blue arrows); blurred cell boundaries (star); blood vessel (black arrow). Hematoxylin and Eosin dye 400X*

DISCUSSION

One of the endocrine disorders that is quickly spreading and has serious implications that affect people all over the world is diabetes mellitus. Consequently, efforts are being made to find a better form of treatment. In light of this, individuals with diabetes have been using a variety of plants with anti-diabetic properties for the past few years, such as Persea Americana, Mangifera odorata [17], Portulaca oleracea [18], Boswellia carterii [19] and Boswellia dalzielii [20]. Therefore, the purpose of this study was to investigate the possible effect of B. serrata on blood glucose level, body weight, and architecture of the pancreas in alloxan-induced diabetes in albino mice.

Our findings demonstrated that alloxan caused a considerable body weight decrease in the G II ($p<0.001$). These findings are in agreement with earlier research reported by Kherouf *et al*. [21]. According to Tebboub and Kechrid [22], this may be caused by the breakdown of structural proteins and the body's inability to use carbohydrates and lipids as a source of energy.

In contrast, treatment of mice with B. serrata (G III and IV) increased significantly ($p<0.001$) body weight in comparison to diabetic mice (G II). This result is consistent with previous studies that showed diabetic rats treated with Boswellia carterii [19] and B. serrata [23] for four weeks had considerably higher body weights. Additionally, according to Al-Amoudi *et al*. [24], the possible hypoglycemic effects of Boswellia carterii aqueous extract may be responsible for the improvement in body weight of diabetic rats.

The results of the current study indicate that the administration of B. serrata significantly reduced the level of serum glucose in both groups (G III and IV), compared to the diabetic group, as shown in Table 2 ($P=0.000$). These results are similar to those reported by Azemi *et al*. [25], who found that administering B. serrata at a concentration of 200, 400, and 600 mg/kg in diabetic rats reduced the level of blood glucose. Similarly, Al-Mehdar and Albattah [19] reported a significant decrease in glucose levels in rats after receiving 100 mg/kg of Boswellia carterii for four weeks. Ahangarpour *et al*. [26] also showed that administering B. serrata at a dose of 300 mg/kg to diabetic patients for 45 days produces a positive change in blood glucose and lipids.

The antidiabetic effects of B. serrata may be attributed to several mechanisms, including decreased intestinal glucose absorption, increased peripheral glucose uptake, stimulation of Langerhans beta cell renewal, and reduction of oxidative stress [27]. Additionally, Khamchan *et al.* [28] found that the activity of

antioxidant enzymes was decreased in diabetic rats, but treatment with an extract of Syzygium samarangense led to a decrease in blood glucose levels and an increase in body weight and antioxidant enzymes.

In terms of histological findings, alloxan-induced diabetic mice showed a notable decrease in the size of the islet cells, varying degrees of degeneration, and acute necrotic cells. These results were consistent with those of Kherouf *et al*. [21], who similarly reported a decrease in the number of islet cells. However, the administration of B. serrata concurrently with alloxan significantly reduced these degenerative alterations in the pancreas. The architecture of the pancreas in the Alloxan+B. serrata group (G III) treated mice was similar to normal morphology. Histological images of the G III showed increased vasculature in pancreatic islets to levels approaching those seen in normal mice. On the other hand, administering B. serrata fifteen days before alloxan (G IV) resulted in a slight improvement. The Langerhans cells appeared shrunk and had slightly irregular borders, and the shape of the secretory gland cells had not completely returned to their normal shape. The study showed that administering B. serrata with alloxan (G III) improved the histological structure of the pancreas significantly when compared to the group that was given B. serrata before alloxan (G IV). This indicates that B. serrata has a better therapeutic effect rather than a preventive one. any part of its essential substance, tables, or figures has been or will be published in another journal or is simultaneously submitted to another journal.

CONCLUSION

This study provides evidence that the administration of B. serrata has a protective effect on the architecture of the pancreas and significantly reduces blood glucose levels. These findings are promising and suggest that B. serrata may be a potential natural remedy for diabetes management.

Conflict of Interest

There are no financial, personal, or professional conflicts of interest to declare.

REFERENCES

1. Adeshara KA, Diwan AG, Tupe RS. Diabetes and complications: cellular signaling pathways current understanding and targeted therapies. Curr Drug Targets. 2016; 17(11):1309–1328. DOI: 10.2174/1389450117666151209124007
2. IDF: The International Diabetes Federation International Diabetes Federation Diabetes Atlas. 2019; 9th ed. IDF, Brussels (Available from diabetesatlas.org)
3. Dos Santos JM, Tewari S, Mendes RH. The role of oxidative stress in the development of diabetes mellitus and its complications. J Diabetes Res. 2019; 4189813. DOI: 10.1155/2019/4189813
4. Hamidpour, R., Hamidpour, S., Hamidpour, M., and Shahlari, M. Frankincense (Rǔ Xiāng; *Boswellia* Species): From the Selection of Traditional Applications to the Novel Phytotherapy for the Prevention and Treatment of Serious Diseases. Journal of Traditional and Complementary Medicine. 2013; 3: 221-226. DOI: 10.4103/2225-4110.119723
5. Efferth T, Oesch F, Anti-inflammatory and anti-cancer activities of frankincense: Targets, treatments and toxicities, Seminars in Cancer Biology. 2020 doi: https://doi.org/10.1016/j.semcancer.2020.01.015
6. Schmiech M, Lang S, Werner K, Schmidt CQ, Syrovets T, and Simmet T. Boswellic acid composition of frankincense dietary supplements and correlation to cytotoxic efficacy against treatment resistance triple negative breast cancer cells. The FASEB Journal. 2019; 33(S1):816. https://doi.org/10.1096/fasebj.2019.33.1_supplement.816.5
7. Assimopolou AN, Zlatanos SN, Papageorgiou VP Antioxidant activity of natural resins and bioactive triterpenes in oil substrate. Food Chemistry. 2005; 92(4): 721-727 https://doi.org/10.1016/j.foodchem.2004.08.033
8. Morikawa T, Matsuda H, Yoshikawa M. A Review of anti-inflammatory terpenoids from the Incense gum resins frankincense and myrrh. J Oleo Sci. 2017; 66:805-814. DOI: 10.5650/jos.ess16149
9. Mehrzadi S, Tavakolifar B, Huseini HF, Mosavat SH, and Heydari, M. The Effects of Boswellia serrata Gum

Resin on the Blood Glucose and Lipid Profile of Diabetic Patients: A Double-Blind Randomized Placebo-Controlled Clinical Trial. Journal of Evidence-Based Integrative Medicine. 2018; 23: 1-7. DOI: 10.1177/2515690X18772728

10. Borrelli F, Capasso F, Capasso R, Ascione V, Aviello G, Longo R, Izzo AA. Effect of Boswellia serrata on intestinal motility in rodents: inhibition of diarrhea without constipation. British journal of pharmacology. 2006; 148(4): 553-560. DOI: 10.1038/sj.bjp.0706740
11. Bertocchi M, Isani G, Medici F, Andreani G, Tubon Usca I, Roncada P, Forni M, Bernardini V. Anti-inflammatory activity of Boswellia serrata extracts an in vitro study on porcine aorta endothelial cells. Oxidative medicine and cellular longevity. 2018; https://doi.org/10.1155/2018/2504305.
12. Zaitone SA, Barakat BM, Bilasy SE, Fawzy MS, Abdelaziz EZ, Farag NE. Protective effect of boswellic acids versus pioglitazone in a rat model of diet-induced non-alcoholic fatty liver disease: influence on insulin resistance and energy expenditure. Naunyn Schmiedebergs Arch Pharmacol. 2015; 388:587-600. DOI: 10.1007/s00210-015-1102-9
13. Wildfeuer A, Neu IS, Safayhi H, Metzger G, Wehrmann M, Vogel U, Ammon HP. Effects of boswellic acids extracted from a herbal medicine on the biosynthesis of leukotrienes and the course of experimental autoimmune encephalomyelitis. Arzneimittelforschung. 1998; 48:668-74.
14. Sengupta K, Kolla JN, Krishnaraju AV, Yalamanchili N, Rao CV, Golakoti T, Raychaudhuri S, Raychaudhuri SP. Cellular and molecular mechanisms of the anti-inflammatory effect of Aflapin: a novel *Boswellia serrata extract*. Mol Cell Biochem. 2011; 354:189-97. DOI: 10.1007/s11010-011-0818-1
15. Singh P, Chacko KM, Aggarwal ML, Bhat B, Khandal RK, Sultana S, Kuruvilla BT. A-90 day gavage safety assessment of *Boswellia serrata* in rats. Toxicol Int. 2012; 19:273-8. DOI: 10.4103/0971-6580.103668
16. Ammon HP. Modulation of the immune system by Boswellia serrata extracts and boswellic acids. Phytomedicine. 2011;18:334. DOI: 10.1016/j.phymed.2010.03.003
17. Sihombing JR, Sidabutar CA, Edy Fachrial E, Almahdy Chaidir Z, Dharma A. Fruit peel extracts of Persea Americana, Cyphomandra betacea, Mangifera odorata and Archidendron pauciflorum as antidiabetic in experimental rats. Res. J. Pharm. Boil. Chem. 2017; sci. 8: 1407-1410.
18. Ramadan BK, Schaalan MF, Tolba AM. Hypoglycemic and pancreatic protective effects of Portulaca oleracea extract in alloxan-induced diabetic rats. Bmc Complementary and Alternative Medicine. 2017; 17:37. DOI: 10.1186/s12906-016-1530-1
19. Al-Mehdar AA and Albattah AM. Evaluation of Hypoglycemic Activity of Boswellia carterii and Cissus rotundifolia in Streptozotocin/Nicotinamide-Induced Diabetic Rats. Yemeni J Med Sci. 2016;10: 31–39. DOI: 10.20428/YJMS.10.1.A4
20. Yakubu J, Mamza UT, Balami VM, Medugu AN, Abdulrahman FI, Sodipo OA. Antidiabetic effects of partitioned methanol extract of Boswellia dalzielii (Frankincense tree) on rats. The Journal of Phytopharmacology. 2020; 9(4): 224-229. DOI: 10.31254/phyto.2020.9402
21. Kherouf A, Aouacheri O, Tichati L, Tebboub I, Kherouf M, Saka S. Potential antioxidant properties and anti-diabetic and hepatic/pancreatic protective effects of dietary *Boswellia serrata* gum resin powder against oxidative damage in streptozotocin-induced diabetic rats. Comparative Clinical Pathology. 2021; 30:891–904. DOI: 10.1007/s00580-021-03284-3
22. Tebboub I, and Kechrid Z. Effect of Curcuma on zinc lipid profile and antioxidants levels in blood and tissue of streptozotocin-induced diabetic rats fed zinc deficiency diet. Arch Physiol Biochem. 2019; 1–8. DOI: 10.1080/13813455.2019.1623820
23. Kamal T, EL-Sayed Nasr N, Fattouh I, Dorgham D Shukry M, Kahilo K. Kigelia Africana and Boswellia serrata ameliorated diabetic nephropathy in streptozotocine – induced diabetic rats. Assiut Vet. Med. J. 2017; 63 (154), 138-145 138
24. Al-Amoudi MO, Al-Nahary HY, Ali SS. Effect of Boswellia Carterii resin supplementation on hematological parameter and lipid profile of streptozotocin-induced diabetic rats. J Med Med Sci. 2019; 14(1):1–8
25. Azemi ME, Namjoyan F, Khodayar MJ, Ahmadpour F, Padok AD, Panahi M. The antioxidant capacity and anti-diabetic effect of *Boswellia serrata* triana and plant aqueous extract in fertile female diabetic rats and the possible effects on reproduction and histological

changes in the liver and kidneys. Jundishapur journal of natural pharmaceutical products. 2012;7(4):168.

26. Ahangarpour A, Heidari H, Fatemeh RA, Pakmehr M, Shahbazian H, Ahmadi I, Mombeini Z, Mehrangiz BH Effect of *Boswellia serrata* supplementation on blood lipid, hepatic enzymes and fructosamine levels in type2 diabetic patients. J Diabetes Metab Disord. 2014; 13(1):29. doi: 10.1186/2251-6581-13-29
27. Kibiti CM, and Afolayan AJ. Herbal therapy: a review of emerging pharmacological tools in the management of diabetes mellitus in Africa. Pharmacogen. Mag. 2015; 11(2):S258-S274. doi: 10.4103/0973-1296.166046
28. Khamchan A, Paseephol T, Hanchang W. Protective effect of wax apple (*Syzygium samarangense* (Blume) Merr. & L.M. Perry) against streptozotocin-induced pancreatic ÃŸ-cell damage in diabetic rats. Biomedicine and Pharmacotherapy. 2018; 108, 634-645. DOI: 10.1016/j.biopha.2018.09.072