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Article

Histological Detection and Anti-oxidant Effect of Bee Venom on the Pancreas of Diabetic Mice

Rana A.H. Al-Sarray[1] and Sattar J. J. Al-Shaeli[2,]*
[1] *Department of Biological Science, College of Education for Pure Sciences, Wasit University, Wasit, Iraq; ranaalihameed2@gmail.com.*
[2] *Department of Medical Basic Sciences, College of Dentistry, Wasit University, Wasit, Iraq; salshaeli@uowasit.edu.iq.*
** Correspondence: salshaeli@uowasit.edu.iq;*
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ABSTRACT

Bee venom BV draws attention in the medical field to manage several diseases, including type 2 diabetes mellitus (T2DM). Due to limited research on this field in Iraq, the study aimed to detect BV's histological and anti-oxidant impact in diabetic mice. Fifteen male mice were randomly assigned into three groups. The first group is control (C), the second is diabetic, and the last group is BV. At the end of 30 days, the obtained serum was used to measure the level of glucose, insulin, superoxide dismutase (SOD), and malondialdehyde (MDA). Furthermore, the pancreas was histologically assessed using the Gomori stain. Alloxan showed significant elevation and reduction in the level of glucose and insulin compared to the control. These alterations were positively enhanced by BV. BV promoted significant elevation in the activity of SOD and suppressed MDA compared to diabetic mice. Histologically, diabetic mice pancreas displayed a reduction of capsular tissue, islets and beta cells vacuolization, beta cells initial degeneration, reduction in the shape and size of the islets and beta cells, and vascular hemorrhage. These changes were remarkably enhanced nearly to normal by BV. Therefore, BV could control the diabetic condition, which may be considered a potential anti-diabetic agent.

Keywords: Diabetes mellitus, SOD, MDA, pancreas, mice, BV

INTRODUCTION

Diabetes is a chronic metabolic disorder that occurs due to inhibition synthesis and production of insulin as progressive pancreatic cell dysfunction and/or failure of specific tissues to respond appropriately to insulin.[1] These defects can cause a disturbance in the normal glucose and lipid metabolism, which leads to hyperglycemia and hyperinsulinemia, which ultimately induces several pathologies.[2, 3] According to the International Diabetes Federation4, there were 537 million adults people diagnosed with diabetes mellitus worldwide. This number is predicted to

reach 643 million by 2030 and 783 million by 2045. Based on these estimates and predictive numbers of diabetes, the prevalence has dramatically increased and is considered a global health issue. Type 2 diabetes is a crucial form of metabolic dysfunction accounting for 90% of all diagnosed diabetes.[4] Although insulin resistance and beta cell failure are the main factors that participated in the development of T2DM, the modern lifestyle, including high-calorie food availability, intake behavior, lack of physical movement, aging, and urbanization, also involved in the development of T2DM.[4, 5, 6, 7] Therefore, the disease is considered multifactorial disorder which can be triggered through several pathways.

Honeybee venom is a naturally occurring animal toxin recently applied to manage several disorders, including diabetes.[8] The potential health benefits of BV are attributed to several bioactive compounds including apamin, melittin, adolapin, and mast cell degranulation phospholipase A2. [9, 10, 11] The potential therapeutic effect of BV included anti-diabetes and regulation of glucose and lipid metabolism,[12] anti-microbial,[13] anti-neoplastic[14], anti-oxidant,[15] anti-inflammation.[16]

Recently, a few types of research were conducted to identify the potential therapeutic impact of BV to manage the diabetic condition through the regulation of glucose and insulin levels concomitant with changes in the histological architecture of the pancreas in Iraq.[17, 18] Thus; the current study is performed to detect the potential anti-oxidant role of BV to improve nominated diabetic biomarkers and ameliorate the histological structure of the pancreas in diabetic mice.

MATERIALS AND METHODS

Study Ethic

This study was performed under the regulation of Ethical Committees/ College of Pure Sciences at Wasit University (Wasit, Iraq) and the work license was approved.

Animal housing and diabetes induction

Fifteen male mice weighing 26-27 g at two months old were obtained from the Ministry of Sciences and Technology, Iraq, the main animal house. The mice were placed in the animal house of Al Qadisiya Veterinary Medicine College. The animals were housed in plastic cages and left for one week with free food and water for acclimatization. The animals were housed in standard environments, including humidity, temperature, and 12:12 light and dark cycle. After one week, ten mice were fasting overnight and intraperitoneally injected with alloxan (Sigma-Aldrich, UK) at 95 mg/kg body weight. The glucose solution was provided for three days, and the blood glucose level was estimated at day 4 by collecting blood from the tail. The average circulating blood glucose level was recorded as more than 200 mg/dl. Therefore, diabetes in these animals was confirmed.

Study design

After the confirmation of diabetes, the animals were divided as follows:

Control group: Five mice that received free food and water.

Diabetic group: Five mice that received 95 mg/kg alloxan and confirmed to have diabetes.

Bee Venom group: Five diabetic mice confirmed with diabetes and treated with 1 mg/kg body weight BV intraperitoneal for 30 days.

After 30 days, 0.3 mg/kg ketamine and 0.1 mg/kg lidocaine were used to anesthetize the mice. The blood was obtained from the heart and directly subjected to centrifuge for 15 minutes at 3000 cycles/minute to obtain serum. The serum was placed in tubes and maintained at -20°C until required. For the histological study,

the pancreas of all mice was removed and transferred into 10% formalin for 48 hours.

Serological examination

Specific ELISA kits were used to identify the level of glucose (Spinreact, Spain), insulin (Monobind, USA), superoxide dismutase (SOD) (Cohesion Sciences, USA) and malondialdehyde (MDA) (Cohesion Sciences, USA) in serum according to manufacturer instructions.

Histological detection

The fixed pancreas was moved to 70% graded ethanol alcohol after immersing in formalin. Then, the pancreas proceeded into the normal histological procedure. The resulting histological sections were stained with Gomori special stain for pancreatic islets. The Novel (China) light microscope with an optic (Italy) camera was used to investigate and image capture connective tissue stain. The histological process is performed in a proper, efficient way. However, some artifacts could appear as the mice's pancreas is inflated, small, and fragile.

Statistical analysis

All data were organized using Microsoft Office Excel version 2019 (Microsoft, USA). Then Way ANOVA, followed by Turkey's test for multiple comparisons, was applied computationally using GraphPad Prism version 6 (GraphPad Software Inc., USA) to analyze the data. The P values were stated as <0.05 (*), <0.01 (**), <0.001 (***) and <0.0001 (****) between groups. The presented data were expressed as Mean ± Standard Error of Mean.

RESULTS

BV enhanced the glucose and insulin concentration in diabetic mice

Alloxan-induced diabetic mice displayed massive increases in circulatory glucose concentration at 199% ± 3.24% compared to the control. This elevated glucose level was significantly reduced by 45.9% ± 5.8% in response to administration of 1 mg/ kg body weight BV for 30 days (Figure 1 A). Furthermore, the level of circulatory insulin was significantly decreased by 54.3% ± 10.24% in diabetic mice compared to control. Administration of BV positively improved this dropdown level of insulin and caused significant increases by 99.5% ± 9.3% compared to diabetic mice (Figure 1 B).

BV ameliorated the level of oxidant and anti-oxidant markers in diabetic mice

The lipid peroxidation marker malondialdehyde (MDA) was estimated in mice treated with alloxan. The displayed level was significantly increased by 94.4% ± 4% compared to control mice. Whereas injected BV for 30 days improved this high level of MDA and promoted a significant reduction by 29.4% ± 5% compared to diabetic mice (Figure 2 A). Furthermore, the anti-oxidant role of superoxide dismutase enzyme (SOD) was measured in diabetic mice, and the result showed a significant reduction in its activity by 58% ± 11.25% compared to control mice. However, BV significantly enhanced this alteration and caused marked increases in the level of SOD by 94.35% ± 4.24% compared to diabetics (Figure 2 B).

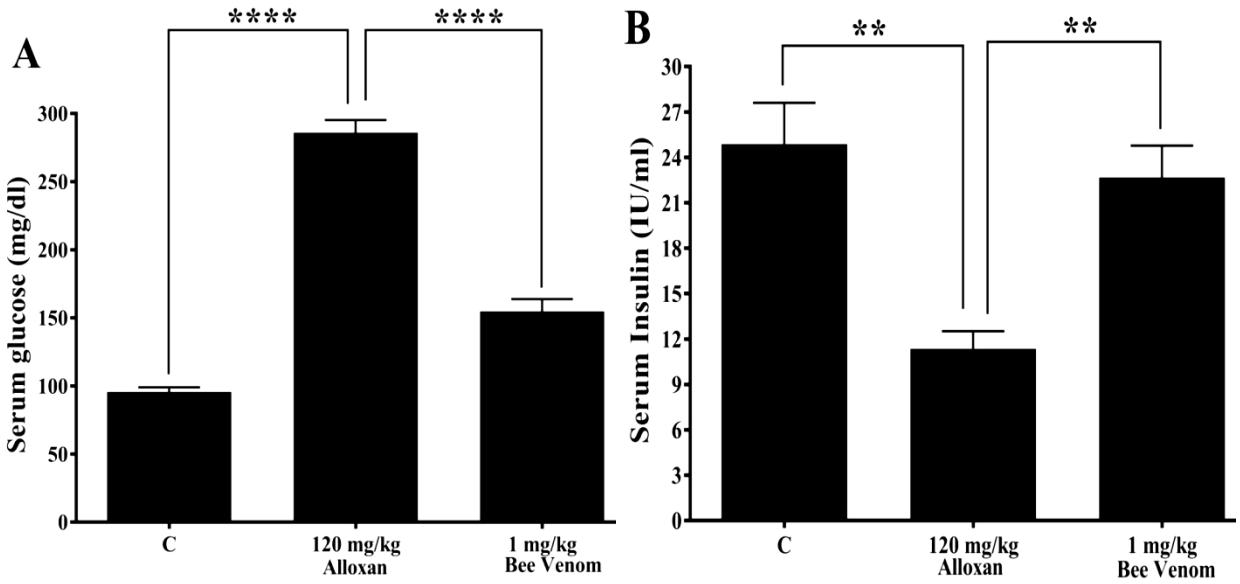

Figure 1. The effect of BV on glucose and insulin levels in diabetic mice. The **BV significantly reduced the level of (A) glucose and significantly increased the level of (B) insulin compared to diabetic mice.**

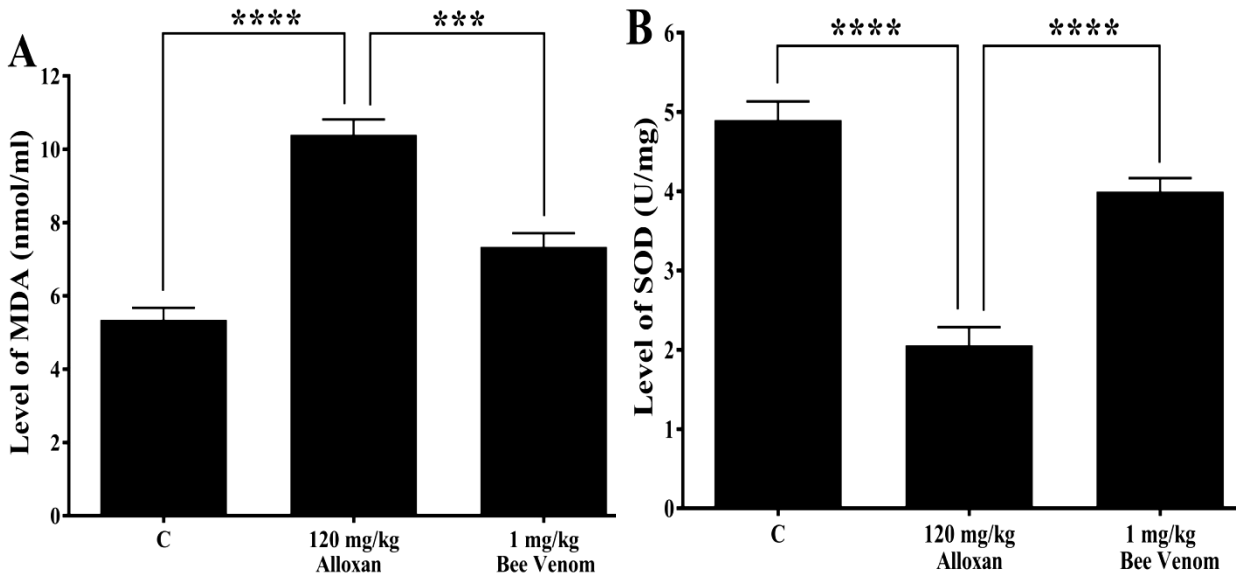

Figure 2. The role of BV on oxidant and anti-oxidant markers in diabetic mice. The BV significantly reduced the level of (A) MDA and significantly increased the level of (B) SOD compared to diabetic mice.

BV enhanced histological structure of the pancreas in diabetic mice

The histological architecture of the pancreas was determined using a special Gomori stain. The pancreas of the control group appeared to have an obvious distribution of acinar cells in the ordinary exocrine part. The acinar cells have dark, obvious rounded nuclei with neutral cytoplasmic stains. The oval clear islet of Langerhans was seen embedded into the exocrine part, which was delineated by distinct thin connective tissue that exhibited blood supply. Normal shape and size with clear arrangement of the cells were displayed. Abundant beta cells appeared normal, polygonal, and blue-stained, with obvious nuclei distributed throughout

the islet parenchyma. Furthermore, the alpha cells appeared round to oval in shape and stained nearly red with clear nuclei. (Figures 3 and 4 A).

The architecture of the pancreas in diabetic mice showed a clear reduction in the capsular connective tissue that separated between the acinar and endocrine parts. The islet exhibited variable vocalization as well as some beta cells vacuolization. Furthermore, initial beta cell degeneration was seen to be associated with mild beta cell atrophy (Figures 3 and 4 B).

The histological architecture of mice pancreas injected with BV at 1 mg/ kg body weight for 30 days was examined. The histological result showed a clear enhancement of pancreas architecture compared to diabetic mice pancreas. The capsular connective tissue that delineated the islet of Langerhans was seen clearly. Furthermore, the islet and beta cell vocalizations were remarkably reduced, associated with improved islet shape, beta cell size and number. The beta and alpha cell arrangements were restored to the normal concomitant with the reduction or disappearance of the cellular initial degeneration (Figure 3 and 4 C).

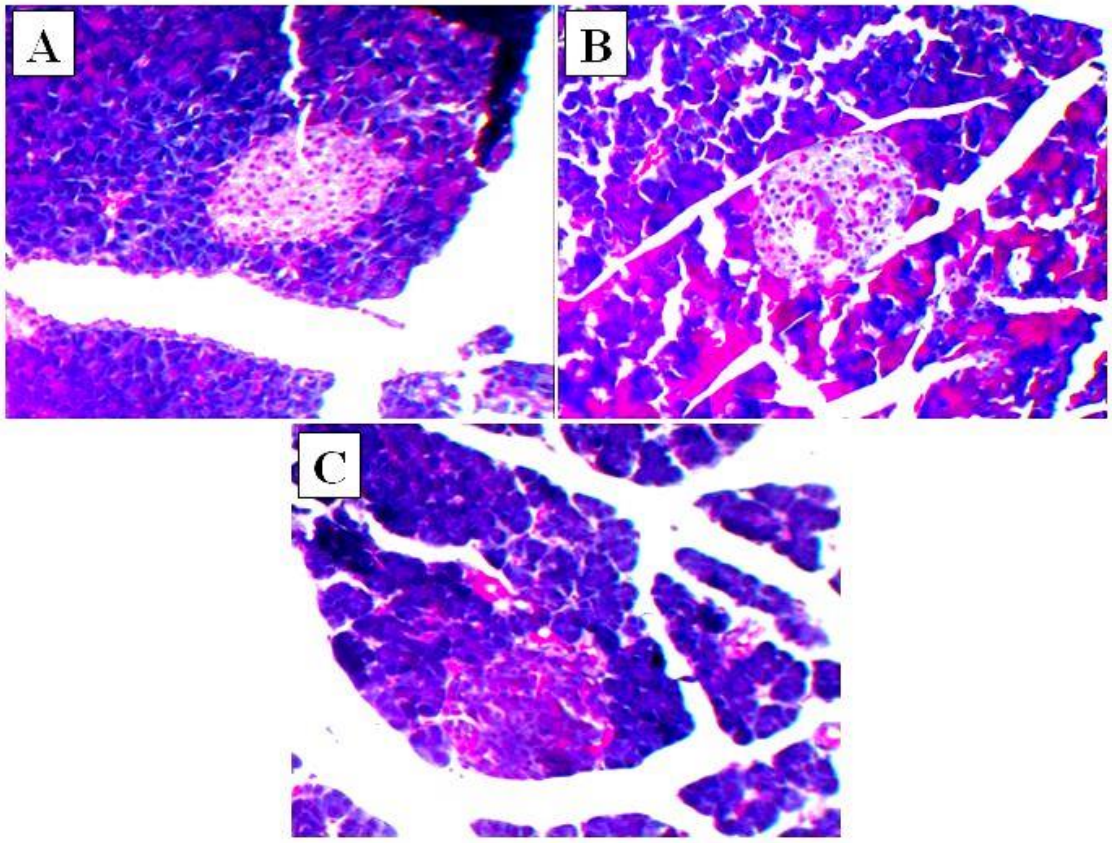

Figure 3. The effect of BV on the histological structure of the pancreas. The histological architecture of the pancreas in (A) control mice, (B) diabetic mice, and (C) diabetic treated with BV. Gomori special stain was used, and the images were captured at 10X.

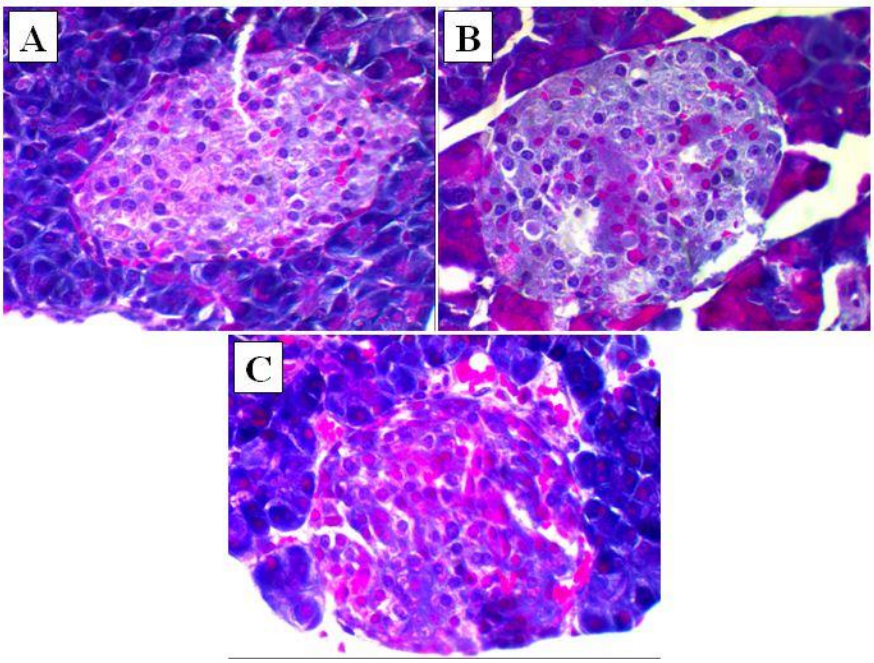

Figure 4. The effect of BV on the histological structure of the pancreas. The histological architecture of the pancreas in (A) control mice, (B) diabetic mice, and (C) diabetic treated with BV. Gomori special stain was used, and the images were captured at 40X.

DISCUSSION

The impairment of the balance between oxidant and anti-oxidant activity can tackle the oxidative stress condition, which could cause several cellular damages that lead to the development of many diseases, including diabetes.[19, 20, 21] The latter recognized by impairment of the normal glucose and lipid metabolism that causes elevated in the glucose concentration associated with reduction the insulin concentration. Thus, regulation of glucose and insulin levels is important to manage the diabetic condition. Recently, several complementary medicinal plants that possess active compounds were applied to manage diabetic conditions [22] Furthermore, the traditional use of specific animal toxins brought great attention as these toxins could trigger several pathologies, including diabetic.[17]

Several studies have investigated the effect of BV and its abundant active compounds, including phospholipase A2 and melittin, on diabetes.[23] The results showed the ability of the previous compounds to decrease the level of circulating glucose.[17, 23, 24, 25] Furthermore, these compounds improved the reduction level of insulin. They caused a rise in the secretion of insulin.[23, 25, 26, 27, 28] These results are similar to the current study result that showed significantly decreased glucose levels associated with significantly increased insulin levels in diabetic mice exposed to BV. The increased level of insulin could be due to the depolarization of the plasma membrane of beta cells, which opens the Ca^{+2}cannels that interred into the cells and trigger insulin secretion in response to BV.[23, 29] The high level of insulin triggered glucose uptake in the main insulin-sensitive cells which caused lowering blood glucose concentration.[1] This result suggested that the BV could participate in the management of diabetic conditions by maintaining the level of glucose

Fundamentally, the body maintains the balance between oxidant/anti-oxidant activities to perform the proper function. Oxidative stress is crucial in impairing the oxidant/anti-oxidant system and increased risk for pathogenesis development, like diabetes. Superoxide dismutase (SOD) is the anti-oxidant enzyme that scavenges

free radicals [30] and prevents cellular damage. [31] Oxidative stress can disrupt the anti-oxidant system, causing high levels of ROS, which is involved in cellular toxicity [32] and initiation of several diseases, including T2DM.[33] The present study displayed a marked reduction in the level of SOD associated with increased activity of MDA in diabetic mice. This result would be expected, as several other studies found.[34, 35, 36, 37] Furthermore, administration of BV to diabetic mice for 30 days caused a significant increase in the level of SOD and concomitant with a decreased level of MDA. This alteration in the oxidant/anti-oxidant system is attributed to the ability of BV to scavenge superoxide anion,[38] and reduced ROS formation through the increasing activity of anti-oxidant enzymes, including glutathione, SOD and catalase[39] and reduced activity of MDA.[27, 28] Thus, this result suggested that the administration of BV could exert oxidative stress and consequently control the diabetic condition.

Alteration of the pancreas architecture in response to oxidative stress is strongly linked to insulin resistance and T2DM. Therefore, induced diabetes caused variable degrees in the histological structure of the pancreas, including changes in the islet's shape, size, and number, islet vocalization, beta cell vocalization, hemorrhage, and initial degeneration of the pancreatic beta cells. All these changes were reversed with the variable degrees to the normal in response to BV.[40, 41] This ameliorative effect could be due to the ability of the BV and its active compounds to reduce the inflammatory status and stimulate anti-oxidant enzyme activity.[28, 40] Based on this histological improvement of the pancreas associated with all previously mentioned results, the study suggested the BV could be a potential agent that used to regulate glucose and lipid metabolism and consequently diabetic disorder.

CONCLUSIONS

Alloxan-induced diabetes caused alteration in the levels of circulatory glucose and insulin, which confirmed the onset of diabetes and are the comment characteristics of it. Limited research showed the potential health benefits of using animal toxins, including bee venom. Accordingly, the current study showed BV's ability to reduce the glucose level associated with rising insulin levels. Furthermore, the BV enhanced the alteration in the histological structure of the pancreas in diabetic mice. This anti-diabetic effect refers to increased anti-oxidant enzyme activity. Thus, the BV is a promising agent that could be used to prevent and control diabetes and its consequences. However, precise molecular studies are required quantitatively and qualitatively to accurately understand the mechanism of action and the effect pathway.

Author Contributions: The study design practical works (induction of diabetes, BV treatment and animal monitoring, samples collection and tests proceeding) were performed by Rana A.H. Al-Sarray and Sattar J. J. Al-Shaeli. Sattar J.J. Al-Shaeli performed the statistical analysis and histopathological reading. Writing the manuscript was performed by both authors, and the final manuscript version was read and approved by both authors.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki under the regulation of Ethical Committees/ College of Pure Sciences at Wasit University (Wasit, Iraq), and the work license (2021) was approved.

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Conflicts of Interest: The authors declare no conflict of interest

References

1. Sattar J. J. AL-Shaeli, Ali M. Ethaeb. Decaffeinated green tea extract regulates glucose metabolism in insulin-sensitive cell lines. Research J. Pharm. and Tech. 2019; 12(6): 2814-2823. doi: 10.5958/0974-360X.2019.00474.8
2. N. K. Jakovljevic et al., "Targeting mitochondria in diabetes," International Journal of Molecular Sciences, vol. 22, no. 12, 2021, doi: 10.3390/ijms22126642.
3. Roden, M., Shulman, G.I. The integrative biology of type 2 diabetes. Nature 576, 51–60 (2019). https://doi.org/10.1038/s41586-019-1797-8
4. P. Saeedi et al., "Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition," Diabetes Research and Clinical Practice, vol. 157, no. September 2019, p. 107843, 2019, doi: 10.1016/j.diabres.2019.107843.
5. Lean, M. E. J. et al. Durability of a primary care-led weight-management intervention for remission of type 2 diabetes: 2-year results of the DiRECT open-label, cluster-randomised trial. Lancet Diabetes Endocrinol. 7, 344–355 (2019).
6. Bellou, V., Belbasis, L., Tzoulaki, I. &Evangelou, E. Risk factors for type 2 diabetes mellitus: an exposure-wide umbrella review of meta-analyses. PLoS One 13, e0194127 (2018).
7. I. Hameed, S. R. Masoodi, S. A. Mir, M. Nabi, K. Ghazanfar, and B. A. Ganai, "Type 2 diabetes mellitus: From a metabolic disorder to an inflammatory condition," World Journal of Diabetes, vol. 6, no. 4, p. 598, 2015, doi: 10.4239/wjd.v6.i4.598.
8. Mousavi, S.M., Imani, S., Haghighi, S., Mousavi, S.E., and Karimi, A. (2012). Effect of Iranian honey bee (Apis mellifera) venom on blood glucose and insulin in diabetic rats. Journal of arthropod-borne diseases, 6 (2), 136-143.
9. Moreno, M.; Giralt, E. Three valuable peptides from bee and wasp venoms for therapeutic and biotechnological use: Melittin, apamin and mastoparan. Toxins 2015, 7, 1126–1150.
10. Wehbe, R.; Frangieh, J.; Rima, M.; El Obeid, D.; Sabatier, J.M.; Fajloun, Z. Bee Venom: Overview of Main Compounds and Bioactivities for Therapeutic interests. Molecules 2019, 24, 2997.
11. D. Scaccabarozzi et al., "Factors driving the compositional diversity of Apis mellifera bee venom from a Corymbia calophylla (marri) ecosystem, Southwestern Australia," PLoS ONE, vol. 16, no. 6 June, pp. 1–20, 2021, doi: 10.1371/journal.pone.0253838.
12. E. JJ Al-Shaeli, S., M. Ethaeb, A., & A. Al-Zaidi, "Serological and Histological Estimation of the Effect of Honeybee Venom on Pancreas and Liver in Diabetic Mice," Arch Razi Inst, 2022.
13. H. Zolfagharian, M. Mohajeri, and M. Babaie, "Bee venom (Apis mellifera) an effective potential alternative to gentamicin for specific bacteria strains-Bee venom an effective potential for bacteria," Journal of Pharmacopuncture, vol. 19, no. 3, pp. 225–230, 2016, doi: 10.3831/KPI.2016.19.023.
14. H. N. Lim, S. B. Baek, and H. J. Jung, "Bee venom and its peptide component melittin suppress growth and migration of melanoma cells via inhibition of PI3K/Akt/mTOR and MAPK pathways," Molecules, vol. 24, no. 5, 2019, doi: 10.3390/molecules24050929.
15. Ali, A. F., Mohammed, Th. T. & Al-Bandar, L. K. 2019. Effect of adding different levels of Optifeed®, Vêo® Premium and Oleobiotec® to the diets as appetite stimulants in the production and physiological performance of Male broiler under heat stress conditions. Plant Archives, 19(1): 1491-1498.
16. R. Wehbe, J. Frangieh, M. Rima, D. el Obeid, J. M. Sabatier, and Z. Fajloun, "Bee venom: Overview of main compounds and bioactivities for therapeutic interests," Molecules, vol. 24, no. 16. MDPI AG, Aug. 19, 2019. doi: 10.3390/molecules24162997.

17. S. M. Mousavi, S. Imani, S. Haghighi, S. E. Mousavi, and A. Karimi, “Effect of Iranian honey bee (Apis mellifera) venom on blood glucose and insulin in diabetic rats,” Journal of Arthropod-Borne Diseases, vol. 6, no. 2, pp. 136–143, 2012.
18. J. Behroozi, A. Divsalar, and A. A. Saboury, “Honey bee venom decreases the complications of diabetes by preventing hemoglobin glycation,” Journal of Molecular Liquids, vol. 199, pp. 371–375, 2014, doi: 10.1016/j.molliq.2014.09.034.
19. S. Alam, Md. K. Hasan, S. Neaz, N. Hussain, Md. F. Hossain, and T. Rahman, “Diabetes Mellitus: Insights from Epidemiology, Biochemistry, Risk Factors, Diagnosis, Complications and Comprehensive Management,” Diabetology, vol. 2, no. 2, pp. 36–50, 2021, doi: 10.3390/diabetology2020004.
20. F. Noureen and A. S. Khan, "Analysis of Level of Anti-oxidants and Oxidative Stress in Diabetic Patients," Systematic Review Pharmacy, vol. 12, no. 5, pp. 361–363, 2021.
21. A. Singh, R. Kukreti, L. Saso, and S. Kukreti, “Mechanistic Insight into Oxidative Stress-Triggered Signaling Pathways and Type 2 Diabetes,” Molecules, vol. 27, pp. 950–969, 2022.
22. Choudhury, H., Pandey, M., Hua, C. K., Mun, C. S., Jing, J. K., Kong, L., Ern, L. Y., Ashraf, N. A., Kit, S. W., Yee, T. S., Pichika, M. R., Gorain, B., &Kesharwani, P. (2017). An update on natural compounds in the remedy of diabetes mellitus: A systematic review. Journal of traditional and complementary medicine, 8(3), 361–376. https://doi.org/10.1016/j.jtcme.2017.08.012 [7]
23. F. W. & S. A. Metz, “Phasic effects of glucose, phospholipase A2, and lysophospholipids on insulin secretion,” J Endocrinol, vol. 120, no. 5, p. 1750, 1987.
24. Noel G. Morgan & William Montague, “Stimulation of insulin secretion from isolated rat islets of Langerhans by melittin 1984,” vol. 4, pp. 665–671, 1984.
25. S. M. Hamdy, A. M. Shaaban, Z. A. El-khayaht, A. R. Farrag, and M. El-sayed, “Bee venom attenuates degenerative effects of diabetes associated with hyperlipidemia in Rats,” Biochemistry Letters, vol. 14, no. 4, pp. 49–63, 2019.
26. A. K. Hassan, D. A. El-kotby, M. M. Tawfik, R. E. Badr, and I. M. Bahgat, "Anti-diabetic effect of the Egyptian honey bee (Apis mellifera) venom in alloxan-induced diabetic rats,” The Journal of Basic and Applied Zoology, vol. 80, no. 1, Dec. 2019, doi: 10.1186/s41936-019-0127-x.
27. E. Simonsson, S. Karlsson, and B. Ahrén, "Islet phospholipase A2 activation is potentiated in insulin-resistant mice," Biochemical and Biophysical Research Communications, vol. 272, no. 2, pp. 539–543, 2000, doi: 10.1006/bbrc.2000.2820.
28. H. J. Park et al., “JNK pathway is involved in the inhibition of inflammatory target gene expression and NF-kappaB activation by melittin,” Journal of Inflammation, vol. 5, pp. 1–13, 2008, doi: 10.1186/1476-9255-5-7.
29. J. Y. Kim et al., “Effects of BCG, lymphotoxin and bee venom on insulitis and development of IDDM in non-obese diabetic mice,” Journal of Korean Medical Science, vol. 14, no. 6. pp. 648–652, 1999. doi: 10.3346/jkms.1999.14.6.648.
30. C. Mao et al., “Associations between superoxide dismutase, malondialdehyde and all-cause mortality in older adults: A community-based cohort study,” BMC Geriatrics, vol. 19, no. 1, pp. 1–9, 2019, doi: 10.1186/s12877-019-1109-z.
31. Y. MS, G. N, B. R, and K. IS, “Superoxide dismutase, glutathione peroxidase and catalase activities in patients with viral hepatitis C,” Integrative Molecular Medicine, vol. 7, no. 2, pp. 1–3, 2020, doi: 10.15761/imm.1000397.
32. G. N. Landis and J. Tower, “Superoxide dismutase evolution and life span regulation,” Mechanisms of Ageing and Development, vol. 126, no. 3, pp. 365–379, 2005, doi: 10.1016/j.mad.2004.08.012.
33. C. J. Tsai, C. J. Hsieh, S. C. Tung, M. C. Kuo, and F. C. Shen, “Acute blood glucose fluctuations can decrease blood glutathione and adiponectin levels in patients with type 2 diabetes,” Diabetes Research and Clinical Practice, vol. 98, no. 2, pp. 257–263, 2012, doi: 10.1016/j.diabres.2012.09.013.
34. K. N. Mistry, B. K. Dabhi, and B. B. Joshi, "Evaluation of oxidative stress biomarkers and inflammation in the pathogenesis of diabetes and diabetic nephropathy," Indian Journal of Biochemistry and Biophysics, vol. 57, no. 1, pp. 45–50, 2020.

35. S. D. M. Bandeira et al., “Characterization of blood oxidative stress in type 2 diabetes mellitus patients: Increase in lipid peroxidation and SOD activity,” Oxidative Medicine and Cellular Longevity, vol. 2012, 2012, doi: 10.1155/2012/819310.
36. T. Adachi, M. Inoue, H. Hara, E. Maehata, and S. Suzuki, “Relationship of plasma extracellular-superoxide dismutase level with insulin resistance in type 2 diabetic patients,” Journal of Endocrinology, vol. 181, no. 3, pp. 413–417, 2004, doi: 10.1677/joe.0.1810413.
37. K. Prasad, “Oxidative stress as a mechanism of diabetes in diabetic BB prone rats: Effect of secoisolariciresinoldiglucoside (SDG),” Molecular and Cellular Biochemistry, vol. 209, no. 1–2, pp. 89–96, 2000, doi: 10.1023/a:1007079802459.
38. S. D. Somerfield, J. Stach, and E. Skamene, “BEE VENOM INHIBITS SUPEROXIDE PRODUCTION BY H U M A N N E U T R O P H I L S l Bee stings , or bee venom therapy (apitherapy), have been reported to be effective in the treatment of human rheumatic disease (1 , 2) and experimental animal models of chro,” vol. 8, no. 6431, 1984.
39. N. M. Meligi, S. A. Ismail, and N. S. Tawfik, “Protective effects of honey and bee venom against lipopolysaccharide and carbon tetrachloride-induced hepatoxicity and lipid peroxidation in rats,” Toxicology Research, vol. 9, no. April, pp. 693–705, 2021, doi: 10.1093/TOXRES/TFAA077.
40. Y. A. elSenosi, A. R. A. Zaid, A. D. A. Elmaged, and M. A. M. Ali, “Biochemical Study on the Regenerative Effect of Bee,” World Journal of Pharmacy and Pharmaceutical Sciences, vol. 7, no. 10, pp. 209–225, 2018, doi: 10.20959/wjpps201810-12445.
41. S. A. Gawad, H. Fikry, M. M. Amin, A. R. Elmahdi, and D. A. Elaziz, “Effect of Apitherapy on the Pancreas & Liver of Streptozotacin Induced Diabetic Rats . a Biochemical and Histological Study,” European Journal of Pharmaceutical and Medical Research, vol. 3, no. 7, pp. 555–565, 2016.

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