Journal of Plant Biota

Original Research Article
ISSN: 3048-4863
Journal homepage: https://plant.researchfloor.org/

Effects of ethanol extract of *Ocimum sanctum* leave on glycemic, lipidemic, and platelet aggregation status in neonatal streptozotocin-induced type 2 diabetic rats

J. M. A. Hannan[1*], Asma Ahammed[1] and P. R. Flatt[2]

[1] *Department of Pharmacy, School of Pharmacy and Public Health, Independent University, Bangladesh (IUB), Dhaka, Bangladesh*
[2] *Diabetes Research Centre, School of Biomedical Sciences, University of Ulster, Coleraine, Northern Ireland BT52 1SA, UK*

Abstract

Ocimum sanctum leaf extracts have been reported to augment insulin secretion in perfused pancreas, isolated islets, and BRIN-BD11 cells, as well as to decrease postprandial blood glucose levels in diabetic rats by retardation of carbohydrate digestion and absorption. In this study, the glycaemic, lipidemic, and platelet aggregation effects of the ethanol extract of the O sanctum leaves were evaluated in streptozotocin-induced type 2 diabetic rats. O sanctum significantly decreased serum glucose (p<0.01) and fructosamine (p<0.01) by 25% and 14%, respectively in 28 days of oral administration, the extract lowered serum cholesterol (p<0.01) and triglyceride (p<0.01) levels by 29% and 26%, respectively, and increased HDL cholesterol by 18% (p<0.05). O sanctum significantly reduced NEFA level by 50% (p<0.01), and platelet aggregation was decreased by 21% (p<0.05). Body weights were unchanged, and, over a 24-hour study period, there were no variations in food intake, water consumption, urination, or defecation. In conclusion, beyond its blood glucose-lowering effects, ethanol extract of O sanctum leaves lowers atherogenic lipids and decreases platelet aggregation. O sanctum is, therefore, a useful addition in controlling diabetes and its complications.

Keywords: *Ocimum Sanctum, Diabetes Mellitus, Serum Glucose, Cholesterol, Triglyceride, HDL, NEFA, Platelet Aggregation*

1. Introduction

Diabetes mellitus is recognized as a significant health concern worldwide and is a primary determinant of disability, morbidity, and mortality. Nevertheless, progress in knowledge and therapeutic approaches presents significant challenges in managing diabetes [1] [2]. Type 2 diabetes is a widespread and critical chronic condition arising from complex genetic-environment interactions, aggravated by additional risk factors such as obesity and a sedentary lifestyle [3]. There are several different classes of drugs, both oral and injectable, for the management of type 2 diabetes (T2DM) [4]. However, these nonprescription drugs are costly, not freely available to some populations, and often associated with significant drawbacks, let alone the inability to insure against complications of the disease [5].

The World Health Organization (WHO) has documented approximately 21,000 plant species globally that are frequently used for medicinal purposes. Of these, around 2,500 species are utilized in India, with nearly 150 species being commercially available on a large scale. India is recognized as the largest producer of medicinal herbs and is often referred to as the "botanical garden of the world" [6]. According to a WHO survey, traditional medicine systems account for approximately 80% of healthcare treatments in India, 85% in Myanmar (Burma), and 90% in Bangladesh [7]. Medicinal plants play a significant role in the traditional management of type 2 diabetes mellitus (T2DM) across various countries. Many of these plants have demonstrated notable antidiabetic activity, often with minimal or no side effects.

These plants are rich sources of bioactive compounds such as flavonoids, alkaloids, phenolics, and tannins, which are known to enhance pancreatic islet function, stimulate insulin secretion or improve insulin action, and reduce intestinal glucose absorption [8]. Due to these properties, herbal medicines have gained widespread popularity, especially in communities with limited access to conventional pharmaceuticals [5]. Such plant-based therapies are often preferred in economically disadvantaged populations due to their affordability, accessibility, and lower risk of drug-related adverse effects. Consequently, they are increasingly being used as alternatives or adjuncts to synthetic antidiabetic drugs to help manage and reduce the complications associated with diabetes [9].

Several studies have demonstrated the antihyperglycemic benefits of medicinal plants in the management of type 2 diabetes mellitus (T2DM) [10]. One prominent example is *Ocimum sanctum* L. (syn. *Ocimum tenuiflorum* L.), commonly known as Holy Basil. This plant holds a distinguished place in traditional and folk medicine systems across Southeast Asia [11]. The leaves of *O. sanctum* have been widely used in Ayurvedic and Unani medicine for their therapeutic properties and have been traditionally applied in the treatment of various ailments, including diabetes, ulcers, and cancers. Additionally, the plant has been used to manage malaria, diarrhea, dysentery, skin diseases, arthritis, eye infections, insect bites, as well as bacterial and fungal infections [12].

Ocimum sanctum contains a complex profile of chemical constituents, including a variety of nutrients and bioactive compounds that contribute to its pharmacological properties [13].

26 February 2025: Received | 26 March 2025: Revised | 25 April 2025: Accepted | 26 May 2025: Available Online

Citation: J. M. A. Hannan, Asma Ahammed and P. R. Flatt (2025). Effects of ethanol extract of *Ocimum sanctum* leave on glycemic, lipidemic, and platelet aggregation status in neonatal streptozotocin-induced type 2 diabetic rats. *Journal of Plant Biota.* **117 to 122. DOI: https://doi.org/10.51470/JPB.2025.4.1.117**

J M A Hannan | jmahannan@iub.edu.bd

However, the concentrations and efficacy of these bioactive ingredients can vary significantly depending on cultivation practices, harvesting time, processing techniques, and storage conditions [14]. Various parts of the plant—including leaves, stems, flowers, roots, seeds, and even the whole plant—have been employed in traditional medicine for their therapeutic potential.

Ocimum sanctum leaves have been traditionally utilized in the management of diabetes mellitus for many years. A dietary supplement of fresh leaves at a dosage of 2 g/kg body weight administered to albino rabbits for 30 days resulted in a significant reduction in blood glucose levels [15]. Additionally, tulsi leaf powder has been reported to significantly decrease serum and tissue lipid profiles in both normal and diabetic rats [16]. Oral administration of the extract led to a marked reduction in blood glucose levels in glucose-fed hyperglycemic and streptozotocin-induced diabetic rats [17]. Ethanolic extracts of *O. sanctum* also significantly reduced glycosylated hemoglobin and urea levels in streptozotocin-induced diabetic rats, while concurrently increasing levels of glycogen, hemoglobin, and total protein. These changes were accompanied by an increase in insulin levels and improved glucose tolerance [18].

It is believed that several bioactive compounds present in *O. sanctum* leaf extracts exert stimulatory effects on insulin secretion, thereby contributing to its antidiabetic properties [19]. Supporting this, research by Chandra et al. [20] demonstrated that oral treatment with *O. sanctum* extract at a dose of 500 mg/kg body weight significantly reduced blood glucose levels in insulin-deficient, streptozotocin-induced diabetic rats. The extract also inhibited lipid peroxidation, reactivated key antioxidant enzymes, and helped restore glutathione (GSH) and antioxidant metal levels. Furthermore, it induced a notable increase in liver glycogen content in both normal and alloxan-induced diabetic rats.

To further understand the multiple actions of *Ocimum sanctum* in type 2 diabetes, the present study aimed to investigate the chronic effects of an ethanol leaf extract on the glycemic, lipidemic, and platelet aggregation status in type 2 diabetic rats.

2. Materials and Methods

2.1. Plant material and preparation of the extract

Dried *Ocimum sanctum* leaves were procured from Ramkrishna Mission, Kolkata, India, and botanically authenticated, with voucher specimens deposited at the National Herbarium, Bangladesh. The leaves were first washed thoroughly with water, and petioles and stems were removed. The cleaned leaves were then oven-dried at 40°C, ground into fine powder (200 mesh) using a Cyclotec grinding machine, and stored in an airtight plastic container.

A total of 2 kg of the powdered *O. sanctum* leaves was subjected to extraction with 80% ethanol (10 L) in a stainless steel extraction tank over four days at room temperature, with the solvent being replaced daily. The combined extracts were filtered and concentrated to dryness using a rotary evaporator. Residual solvent was removed using a membrane pump. The final extract (275 g) was freeze-dried using a Varian 801-model LY-3-TT freeze-dryer (USA) and stored in a reagent bottle at 4°C in a freezer until further use.

2.2. Animals

Adult male Long-Evans rats (180–220 g body weight) were used in all experiments.

The animals were housed under controlled environmental conditions at the animal facility of the Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Dhaka, Bangladesh. They were maintained on a 12-hour light/dark cycle at a temperature of 21 ± 2 °C. The standard laboratory diet provided consisted of 36.2% carbohydrate, 20.9% protein, 4.4% fat, and 38.5% fiber, with a metabolizable energy content of 1.18 MJ/100 g (282 kcal/100 g).

All experimental procedures involving animals were conducted in accordance with local institutional guidelines, the Animals (Scientific Procedures) Act 1986, and the EC Directive 86/609/EEC for animal experimentation.

Induction of type 2 diabetes: Type 2 diabetes was induced by a single intraperitoneal injection of STZ to 48-hour-old pups of adult Long-Evans [21]. The STZ solution was prepared fresh in 0.5M citrate buffer (pH 4.5) and was injected immediately following dissolution at a dose of 90 mg/kg body weight. Experiments were conducted in male rats 3 months after injection, when they had gained a weight of approximately 175 - 180 g. Prior to experiments, the diabetic status of the rats was checked by blood glucose estimation. It is understood that no animal model is identical to any human disease; none of the available animal models of Type 2 diabetes mellitus exactly replicate the human Type 2 diabetes mellitus. However, n-STZ rat models have several benefits over the other models and are the appropriate experimental animal models of Type 2 diabetes mellitus [22].

2.3. Chronic effects on glycemic, lipidemic, and body weight: Type 2 diabetic rats (n = 24) were randomly allocated into two groups (n = 12 per group). The treatment group received *Ocimum sanctum* extract at a dose of 1.25 g/kg body weight, dissolved in 10 mL water/kg body weight, administered orally via a metallic gavage tube twice daily for 28 days. The control group received an equivalent volume of distilled water (10 mL/kg body weight). The selected extract dose (1.25 g/kg bw) was based on prior studies demonstrating significant hypoglycemic activity without observable toxicity.

All animals were maintained under identical environmental conditions and were given free access to standard laboratory chow and water throughout the study. Body weights were recorded on day 0 and at 7-day intervals thereafter. Blood samples were collected at baseline (day 0) from the tail vein under light ether anesthesia and on day 28 via the abdominal aorta under pentobarbital anesthesia. Serum was separated by centrifugation and used for the analysis of glucose, fructosamine, insulin, total cholesterol, HDL-cholesterol, triglycerides, and non-esterified fatty acids (NEFA). All serum samples were immediately stored at −70 °C until further biochemical analysis.

2.4. Estimation of platelet aggregation: Platelet aggregation test was conducted by Chrono Log Lumi aggregometer (Chronolog Corp., Havertown, PA, USA) linked to a potentiometric recorder. Platelet-rich plasma (PRP) was prepared using anti-coagulated blood samples (with 3.8% sodium citrate), which were carefully centrifuged at 800 rpm for 15 min, and a portion of the supernatant was transferred into a polypropylene plastic tube. To generate platelet-poor plasma (PPP), the same supernatant was again centrifuged at 3000 rpm for 20 min.

This supernatant was then transferred into a polypropylene plastic tube. To estimate platelet aggregation, 500 µl of PRP and PPP were taken into cuvettes (P/N 312) and placed into the aggregometer. Which automatically sets the 100% (PRP) baseline. After 30 seconds, ADP (12 µl) was added to PRP using a micropipette, and the optical curve to run for 5 min. Platelet aggregation was presented as a percentage of the PPP transmission value.

2.5. Acute metabolic studies

The non-diabetic mice housed in Nalgene Cages (USA) were administered with ethanol extract of *Ocimum Sanctum* (1.25g/kg bw). Food and water intake, as well as urination and defecation, were measured with an interval of one hour over 24 hours.

2.6. Biochemical analysis

Serum glucose was estimated by glucose oxidase (GOD-PAP) based enzymatic colorimetric method using kits from Boehringer Mannheim GmbH (Germany). Serum fructosamine was assessed by a colorimetric method using commercial kits from Boehringer Mannheim GmbH (Germany). Serum triglyceride was estimated by an enzymatic colorimetric method using commercial kits from SERA PAK, USA. Serum total cholesterol was determined by the enzymatic colorimetric (cholesterol oxidase/peroxidase) method using kits from SERA PAK, USA. HDL-cholesterol was determined by enzymatic colorimetric (cholesterol oxidase /peroxidase) method using kits from SERA PAK, USA. Serum NEFA was measured by an enzymatic colorimetric method using kits from SERA PAK, USA.

2.7. Statistical analysis

All statistical analyses were conducted using SPSS version 29 for Windows. Group comparisons were performed using the unpaired Student's *t*-test or the Mann–Whitney *U* test, depending on the normality of the data. For variables measured at multiple time points, repeated measures ANOVA was employed, with Bonferroni correction applied to maintain an overall Type I error rate of 5%. A *p*-value of less than 0.05 was considered statistically significant.

Results

2.8. Chronic effects on glycemic, lipidemic, and platelet aggregation status

After 28 days of feeding ethanol extract of *O sanctum* to type 2 diabetic rats, serum glucose ($p<0.01$) and fructosamine ($p<0.01$) levels were substantially reduced by 25% and 14%, respectively, compared to the control group (Fig. 1). In addition, the extract lowered the total cholesterol ($p<0.01$) and triglyceride ($p<0.01$) levels by 29% and 26%, respectively, and increased HDL levels by 18% ($p<0.05$, Fig 2). The extract substantially reduced the NEFA by 50% (Fig. 3a). Platelet aggregation was decreased by 21% compared to the control group ($p<0.05$, Fig. 3b).

3.2. *Effects on water intake, food intake, defecation and urination, and body weight*

During 24-hour studies, *O sanctum* induced no changes in water intake, food intake, defecation, water content of defecation, or urination compared to the control group (Fig. 4 & 5). Over the 28-day study period, administration of ethanol extract of *O sanctum* did not change body weights as compared to the control group.

The body weight increased in all the test groups from the initial to the final day (Fig. 6).

3. Discussion

Oral hypoglycemic agents remain the cornerstone of Type 2 diabetes mellitus (T2DM) treatment and are generally effective in managing hyperglycemia. However, they are often associated with significant side effects and typically fail to prevent or delay the progression of diabetes-related complications [23][24]. With the growing understanding of the heterogeneity of T2DM, there is an increasing need for more effective therapies that offer fewer adverse effects. Despite advances in modern pharmacotherapy—such as the development of insulin, biguanides, sulfonylureas, thiazolidinediones, DPP-IV inhibitors, GLP-1 receptor agonists, and SGLT2 inhibitors [25]—many of these treatments remain costly, are not universally accessible, and may still fall short in addressing long-term complications. Consequently, in many developing countries, traditional antidiabetic plants offer a promising and accessible alternative. However, with the exception of a few studies [26][27][28], the therapeutic potential of many of these medicinal plants has not been thoroughly investigated.

There are some scientific reports [29], [16],[30] regarding the antihyperglycemic action of *O sanctum,* but its metabolic effects and pointers towards effects on diabetes complications have not been evaluated. In this present study, we examined the effect of the ethanol extract of *O sanctum* on streptozotocin-induced type 2 diabetes rats in a chronic 28-day feeding experiment. As expected, we found that the extract significantly lowered serum glucose and fructosamine levels in the blood. Indeed, since serum fructosamine reflects the glycemic status over the preceding 2 to 3 weeks, this finding establishes, more conclusively, the anti-hyperglycemic properties of the ethanol extract of *O sanctum*.

Postprandial hyperglycemia is a well-recognized cardiovascular risk factor in patients with type 2 diabetes mellitus (T2DM) [31]. Studies have shown that elevated blood glucose levels after meals can double the risk of coronary heart disease and fatal cardiovascular events [32]. Furthermore, recent evidence suggests that tight glycemic control is closely linked to a reduced incidence and slower progression of microvascular complications. Similarly, effective management of hyperlipidemia significantly decreases both microvascular and macrovascular risks in individuals with T2DM [33][34].

Administration of ethanol extracts of *Ocimum sanctum* has been shown to reduce serum triglycerides and total cholesterol while concurrently increasing high-density lipoprotein (HDL) levels. These findings are consistent with previous studies [35][16][36]. Under normal physiological conditions, insulin activates the enzyme lipoprotein lipase, which plays a key role in hydrolyzing triglycerides [37]. However, in insulin-deficient states, this pathway is impaired, leading to hypertriglyceridemia. The ethanol extract of *O. sanctum* has been reported to enhance insulin secretion in streptozotocin (STZ)-induced hyperglycemic rats, which may help reduce triglyceride levels through the activation of lipoprotein lipase [19].

Patients with type 2 diabetes exhibit an elevated FFA level [38][39]. A high FFA can impair hepatic and peripheral insulin resistance and favour VLDL-triglyceride synthesis [40]. NEFA also influences platelet aggregation and vascular changes by accelerating the rate of prostacyclin in plasma [41][42]. In the present study, *O sanctum* leaf extract lowered NEFA levels.

In an earlier study, it was observed that *O sanctum* is effective as an analgesic, inflammatory, and antipyretic agent [43]. As *O sanctum* has anti-inflammatory action, it was assumed that it might have some antiplatelet activity. The extract lowered the platelet aggregation, which might be due to the reduction of NEFA. This reduction in the concentration of serum NEFA may contribute to the improvement in insulin action. A study reveals that metformin significantly decreases serum TG concentrations and NEFA levels in HHTg rats [41].

High levels of triglycerides and total cholesterol in blood are major coronary risk factors [44][45]. Several studies have shown that an increase in HDL cholesterol is associated with a decrease in coronary risk [46]. Hence, the extract not only helps to reduce hyperglycemia but also helps to prevent dyslipidemia and insulin resistance, both of which are important risk factors for the complications of diabetes.

In the 28-day chronic study, the *O sanctum*-administered group did not exhibit any significant changes in body weight compared with control rats. To check the possible effects of ethanol extract of O sanctum on the normal metabolic processes, food intake, defecation, water content in stool, water intake, and urination were observed during a 24-hour study. It was found that there was no change in any of these parameters in *O sanctum*-fed mice as compared to the control group. This finding recommends that the extract of *O sanctum* does not alter behaviour, suggesting also a lack of toxicity.

4. Conclusion

This research has exhibited that ethanol extract of *O sanctum* leaves lowers atherogenic lipids and NEFA in blood whilst also decreasing platelet aggregation. This indicates that *O sanctum* is beneficial as a source of invention of newer antidiabetic compounds and has promising benefits as an addition to the treatment of diabetes and its complications.

Ethical Approval

Principles of Laboratory Animal Care (NIH publication No. 85-23, revised 1985) were followed, as well as the UK Animals (Scientific Procedures Act 1986 and EU Directive 2010/63 EU) for all types of animal experiments and approved by the ethical committee.

Declaration of competing interests

The authors hereby declare that they have no conflicts of interest.

Acknowledgments

These studies were sponsored by the University of Ulster Research Strategy Funding and the Independent University, Bangladesh (IUB) URC Research Grant. All authors contributed to the idea and design of the experiment. J. M. A. Hannan and Asma Ahammed contributed to the experimental study, analysis, and preparation of the manuscript. Peter R. Flatt to the supervision of the study.

REFERENCES

1. Vuksan, V. et al., 2019. Efficacy and safety of American ginseng (Panax quinquefolius L.) extract on glycemic control and cardiovascular risk factors in individuals with type 2 diabetes: a double-blind, randomized, cross-over clinical trial. *European journal of nutrition,* 58(3), pp. 1237-1245.doi: 10.1007/s00394-018-1642-0.

2. Hossain MJ, Al-Mamun M, Islam MR. Diabetes mellitus, the fastest growing global public health concern: Early detection should be focused. Health Sci Rep. 2024 Mar 22;7(3):e2004. doi: 10.1002/hsr2.2004.

3. Wu, Y., Ding, Y., Tanaka, Y. & Zhang, W., 2014. Risk factors contributing to type 2 diabetes and recent advances in the treatment and prevention. *International journal of medical sciences,* 11(11), pp. 1185-1200.doi: 10.7150/ijms.10001.

4. Marín-Peñalver, J. J., Martín-Timón, I., Sevillano-Collantes, . C. & Cañizo-Gómez, F. J. d., 2016. Update on the treatment of type 2 diabetes mellitus. *World journal of Diabetes,* 7(17), p. 354–395.doi: 10.4239/wjd.v7.i17.354.

5. Jacob, B. & R.T, N., 2019. Role of medicinal plants in the management of diabetes mellitus: a review. *3 Biotech,* 9(1), p. 4.doi: 10.1007/s13205-018-1528-0.

6. Seth, S. D. & Sharma, B., 2004. Medicinal plants in India. *The indian journal of medical research,* 120(1), pp. 9-11.

7. Khan, M. R. I. et al., 2010. Antidiabetic Effects of the Different Fractions of Ethanolic Extracts of Ocimum sanctum in Normal and Alloxan Induced Diabetic Rats. *JOURNAL OF SCIENTIFIC RESEARCH* , 2(1), pp. 158-168.

8. Kooti, W. et al., 2016. The role of medicinal plants in the treatment of diabetes: a systematic review. *Electronic physician,* 8(1), pp. 1832-1842.doi: 10.19082/1832.

9. Modak, M. et al., 2007. Indian herbs and herbal drugs used for the treatment of diabetes. *Journal of clinical biochemistry and nutrition,* 40(3), pp. 163-173.doi: 10.3164/jcbn.40.163.

10. Malviya, N., Jain, S. & Malviya, S., 2010. Antidiabetic potential of medicinal plants. *Acta poloniae pharmaceutica,* 67(2), pp. 113-118.

11. Baliga, M. S. et al., 2013. Ocimum sanctum L (Holy Basil or Tulsi) and its phytochemicals in the prevention and treatment of cancer. *Nutrition and cancer,* 65(Suppl 1), pp. 26-35.doi: 10.1080/01635581.2013.785010.

12. Behera, P., Das, D., Panda, S. K. & Pattanayak, P., 2010. Ocimum sanctum Linn. A reservoir plant for therapeutic applications: An overview. *Pharmacognosy review,* 7(4), p. 95–105.

13. Siva, M., Shanmugam, K., Shanmugam, B. & Ravi, S., 2016. Ocimum sanctum: a review on the pharmacological properties. *International Journal of Basic & Clinical Pharmacology,* 5(3), pp. 558-565.

14. Pattanayak, P., Behera, P., Das, D. & Panda, S. K., 2010. Ocimum sanctum Linn. A reservoir plant for therapeutic applications: An overview. *Pharmacognosy Review,* 4(7), p. 95–105.doi: 10.4103/0973-7847.65323.

15. Sethi, J., Sood, S., Seth, S. & Talwar, . A., 2004. Evaluation of hypoglycemic and antioxidant effect ofOcimum sanctum. *Indian J Clin Biochem,* 19(2), p. 152–155.doi: 10.1007/BF02894276.

16. Rai, V., Iyer, U. & Mani, U. V., 1997. Effect of Tulasi (Ocimum sanctum) leaf powder supplementation on blood sugar levels, serum lipids and tissue lipids in diabetic rats. *Plant Foods Hum Nutr,* 50(1), pp. 9-16.doi: 10.1007/BF02436038.

17. Chattopadhyay, R. R., 1993. Hypoglycemic effect of Ocimum sanctum leaf extract in normal and streptozotocin diabetic rats. *Indian journal of experimental biology,* 31(11), pp. 891-893.

18. Narendhirakannan, R. T., Subramanian, S. & Kandaswamy, S., 2006. Biochemical evaluation of antidiabetogenic properties of some commonly used Indian plants on streptozotocin-induced diabetes in experimental rats. *Clin Exp Pharmacol Physiol,* 33(12), pp. 1150-1157.doi: 10.1111/j.1440-1681.2006.04507.x.

19. Hannan, J. M. A. et al., 2006. Ocimum sanctum leaf extracts stimulate insulin secretion from perfused pancreas, isolated islets and clonal pancreatic beta-cells. *Journal of endocrinology,* 189(1), pp. 127-136.doi: 10.1677/joe.1.06615.

20. Bonner-Weir, S., DF, T. & RN, H., 1981. Responses of neonatal rat islets to streptozotocin: limited B-cell regeneration and hyperglycemia. *Diabetes,* Volume 30, pp. 64-69.doi: 10.2337/diab.30.1.64.

21. Arulmozhi, D. K.[*,**]; Veeranjaneyulu, A.[*]; Bodhankar, S. L.[**]. Neonatal streptozotocin-induced rat model of Type 2 diabetes mellitus: A glance. Indian Journal of Pharmacology 36(4):p 217-221, Jul–Aug 2004.

22. Ganesan K, Rana MBM, Sultan S. Oral Hypoglycemic Medications. [Updated 2023 May 1]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-.

23. Rang, H. P., Dale, M. M. & Ritter, J. M., 1991. The endocrine system pharmacology. *Pharmacology. Longman Group Ltd. UK,* p. 504–508.

24. Bailey, C. J. & Day, . C., 2018. Treatment of type 2 diabetes: future approaches. *British Medical Bulletin,* 126(1), pp. 123-137.doi: 10.1093/brimed/ldy013.

25. Grover, J. K., Vats, V. & Rathi, S. S., 2000. Anti-hyperglycemic effect of Eugenia jambolana and Tinospora cordifolia in experimental diabetes and their effects on key metabolic enzymes involved in carbohydrate metabolism. *Journal of ethnopharmacology,* 73(3), pp. 461-470.doi: 10.1016/s0378-8741(00)00319-6.

26. Srivastava, Y., Venkatakrishna-Bhatt, H. & Verma, Y., 1988. Effect of monordica charantia linn. Pomous aqueous extract on cataractogenesis in murrin alloxan diabetics. *Pharmacological Research and Communications,* 20(3), pp. 201-209. doi: 10.1016/s0031-6989(88)80041-9.

27. Karunanayake, E. H., Jeevathayaparan, S. & Tennekoon, K. H., 1990. Effect of Momordica charantia fruit juice on streptozotocin-induced diabetes in rats. *Journal of ethnopharmacology,* 30(2), pp. 199-204.doi: 10.1016/0378-8741(90)90008-h.

28. Chattopadhyay , R. R., 1999. A comparative evaluation of some blood sugar lowering agents of plant origin. *Journal of ethnopharmacology,* 67(3), pp. 367-372.doi: 10.1016/s0378-8741(99)00095-1.

29. Agrawal, P., Rai, V. & Singh, R. B., 1996. Randomized placebo-controlled, single blind trial of holy basil leaves in patients with noninsulin-dependent diabetes mellitus. *Int J Clin Pharmacol Ther,* 34(9), pp. 406-409.

30. Paolisso, G. et al., 2003. Cardiovascular risk in type 2 diabetics and pharmacological regulation of mealtime glucose excursions. *Diabetes & metabolism,* 29(4 Pt 1), pp. 335-40.doi: 10.1016/s1262-3636(07)70044-7.

31. Aryangat, A. V. & Gerich, J. E., 2010. Type 2 diabetes: postprandial hyperglycemia and increased cardiovascular risk. *Vasc Health Risk Manag,* 6(1), p. 145–155.

32. UKPDS, 1998. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group. *BMJ,* 317(7160), pp. 703-713.

33. Pyörälä, K. et al., 1997. Cholesterol lowering with simvastatin improves prognosis of diabetic patients with coronary heart disease. A subgroup analysis of the Scandinavian Simvastatin Survival Study (4S). *Diabetes care,* 20(4), pp. 614-620.doi: 10.2337/diacare.20.4.614.

34. Janabi, G., Suganthi, B. & Meera, G., 1987. Effect of Tulasi (Ocimum sanctum) on Diabetes Mellitus. *The Indian Journal of Nutrition and Dietetics,* Volume 24, pp. 337-341.

35. Taskinen, M. R., 1987. Lipoprotein lipase in diabetes. *Diabetes Metab Rev,* 3(2), pp. 551-570.doi: 10.1002/dmr.5610030208.

36. Wu, M. S. et al., 1990. Effect of metformin on carbohydrate and lipoprotein metabolism in NIDDM patients. *Diabetes Care,* 13(1), pp. 1-8.doi: 10.2337/diacare.13.1.1.

37. Hollenbeck, C. B. et al., 1991. Effects of metformin on glucose, insulin and lipid metabolism in patients with mild hypertriglyceridaemia and non-insulin dependent diabetes by glucose tolerance test criteria. *Diabete & Metabolism,* 17(5), pp. 483-489.

38. Boden, G. & Shulman, G. I., 2002. Free fatty acids in obesity and type 2 diabetes: defining their role in the development of insulin resistance and beta-cell dysfunction. *Eur J Clin Invest,* 32(Suppl 3), pp. 14-23. doi: 10.1046/j.1365-2362.32.s3.3.x.

39. Reinilä, A., 1981. Long-term effects of untreated diabetes on the arterial wall in rat. An ultrastructural study. *Diabetologia,* 20(3), pp. 205-212.doi: 10.1007/BF00252629.

40. Gjesdal, K. et al., 1976. Effects of fasting on plasma and platelet-free fatty acids and platelet function in healthy males. *Thromb Haemost,* 36(2), pp. 325-333.

41. Godhwani, S., Godhwani, J. L. & Vyas, D. S., 1987. Ocimum sanctum: an experimental study evaluating its anti-inflammatory, analgesic and antipyretic activity in animals. *J Ethnopharmacol,* 21(2), pp. 153-163.doi: 10.1016/0378-8741(87)90125-5.

42. Miklankova D, Markova I, Hüttl M, Zapletalova I, Poruba M, Malinska H. Metformin Affects Cardiac Arachidonic Acid Metabolism and Cardiac Lipid Metabolite Storage in a Prediabetic Rat Model. Int J Mol Sci. 2021 Jul 19;22(14):7680. doi: 10.3390/ijms22147680.

43. Bainton, D. et al., 1992. Plasma triglyceride and high density lipoprotein cholesterol as predictors of ischaemic heart disease in British men. The Caerphilly and Speedwell Collaborative Heart Disease Studies. *British Heart Journal,* 68(1), pp. 60-66.doi: 10.1136/hrt.68.7.60.

44. National Cholesterol Education Program, 1994. National Cholesterol Education Program. Second Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel II). *Circulation,* 89(3), pp. 1333-1445.

45. Wilson, P. W., 1990. High-density lipoprotein, low-density lipoprotein and coronary artery disease. *American Journal of Cardiology,* 66(6), pp. 7A-10A.doi: 10.1016/0002-9149(90)90562-f.