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Review Article

Diabetes: Exploring the Intersection of Metabolic Disorders, Lifestyle Factors and Herbal Remedies: A Review

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ABSTRACT

A chronic metabolic disorder, Diabetes mellitus significantly poses a health challenge globally. The escalating prevalence of diabetes, coupled with concerns regarding the side effects of conventional antidiabetic drugs, has spurred increased interest in exploring alternative therapeutic approaches. Herbal medicines, deeply rooted in traditional healing practices, have emerged as promising candidates for managing diabetes. The objective of this review is to optimise the current scientific literature on herbal medicines employed as antidiabetic agents. The review encompasses an in-depth analysis of diverse medicinal plants which have potential for management of T2DM. The potential of these herbal remedies in improving insulin sensitivity, modulating glucose metabolism and mitigating diabetes-related complications are established. Furthermore, the review critically examines clinical studies evaluating the potency and safe usage of herbal medicines in diabetic populations. Emphasis is placed on highlighting the need for further research and addressing challenges associated with standardization and quality check of herbal preparation. The integration of herbal medicines into mainstream diabetes care is explored, considering the potential for synergistic use with conventional therapies. In nutshell; this review consolidates existing knowledge, sheds light on promising avenues for future research and emphasizes the significance of herbal medicines in the quest for effective, safe and sustainable antidiabetic interventions. The wealth of traditional wisdom encapsulated in these natural remedies presents a valuable resource in the pursuit of novel therapeutic strategies for diabetes management.

Keywords: Antidiabetic activity, Diabetes, Herbal Plants, Metabolic Disorder, T2DM.

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INTRODUCTION

A metabolic disorder and widely seen endocrine disorder Diabetes, results in increased glucose level is a result of the alteration in hormone underactive production by the gland. This secretion and resistance by pancreatic gland. These may be associated with overactive or imbalance linked with metabolic disorder which progressively leads to cardiovascular, neuropathy, nephropathy, retinopathy and some other pathologic changes in body. The urge towards junk food and unhealthy eating practice, sedentary lifestyle is also associated with the increase in diabetes cases day by day. There lie mainly two types where Type I Diabetes is an autoimmune disorder where cells of pancreas are damaged by which insulin production is hampered. Type II Diabetes arises by malfunctioning of pancreatic cells for the manufacturing of insulin.[1]

Epidemiology

Globally, 530 million people (84%) are estimated to be affected by the disease among which 10.5% are ranged from the age 20-79,[2] out of that ratio of disease prevalence in India is 10.1 crore (16%) as per study published in 2023 by Indian Council of Medical Research-India Diabetes (ICMR INDIAB) (Figure 1).[3] Prominent increase in data may reach more than 1.31 billion by 2050 said by a report published in Lancet.[4]

The etiological risk factors contributing to disease are obesity, age, physical inactivity and genealogy. Dietary habits like inclusion of high fat diet, processed meat, sugary drinks, some dairy products, less intake of fruits and vegetables and lifestyle modifications affecting chronological cycle are emerging contributors to the disease.

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Insulin Biosynthesis

The prominent role of insulin is to decrease glucose limits in blood. However, the equilibrium of maintained in body by 2 hormones: Glucagon and Insulin. Insulin is the secretion of β cells of pancreas secrets insulin while α cell produces Glucagon. Both antagonise each other's working. Insulin gets released to lower blood glucose level whereas glucagon is released when concentration of glucose in blood is low. This antagonising maintains homeostasis.

Insulin action is governed by either

Liver decreased function of Glycogenolysis and Gluconeogenesis resulting in decreased blood glucose level.

Muscle, fatty tissues and liver deposit more glucose by absorption.

Glucagon action is shown off as antagonising the reaction of glycogenolysis and gluconeogenesis in liver. Other than glucagon, catecholamine and cortisol release also results in increased glucose level. With these amylin and incretin are also contributors of glucose management. Amylin gets secreted along with insulin primarily functions to decrease gastric emptying time hence enhance glucose absorption after meal. Incretin are peptides derived from gut facilitating synthesis and production of insulin by β cells mainly through GLP (Glucagon like Peptide) and GIP (Glucose dependent Insulinotropic Polypeptide).[5]

Causes of Disease

Causes for different types of diabetes remains differential. Type I DM where genes play major role and is auto immune whereas Type II D M is the additive result of lifestyle and genetics. Being obese and overweight contributes to increase the risk of occurrence of disease.

i) Pancreatic Langerhans' β cells decrease production of insulin.

ii) α cells of pancreatic Langerhans islets release more glucagon.

iii) The liver's increased synthesis of glucose.

iv) Resistance of insulin in brain resulting neurotransmitter dysfunction.

v) Increased lipid breakdown.

vi) Reabsorption of glucose by increased kidney function.

vii) Incretin diminished action by small intestine.

viii) Peripheral tissues impaired or diminished action (Figure 2).[6]

Just as single-gene mutations produce monogenic diabetes, genetic mutations can also result in diabetes mellitus. MODY (Maturity Onset Diabetes of the Young) and neonatal diabetes are the most prevalent variants of monogenic diabetes.[7] Cystic fibrosis thick mucus production impairs secretion of adequate insulin, which results in multiple scars on the skin.[8] Hemochromatosis disorder visibility in which extra iron builds up in the body to harmful levels not only harm pancreas but other organs as well.[9]

Insulin resistance developed by other hormonal imbalance in body can occasionally lead to diabetes. Gestational diabetes results due to variation in hormones during pregnancy. Hormones produced by the placenta reduce cellular sensitivity to the effects of insulin.[10,11] Cushing's syndrome due to excessive amounts of cortisol (The stress hormone) develops.[12] Acromegaly is a condition in which the body overproduces Growth hormone.[13] The overproduction of thyroid hormone by the thyroid gland results in hyperthyroidism.[14]

Damage to β cells or reduction in capacity to produce insulin due to pancreatitis, trauma or pancreatic cancer may lead to removal/ destruction of pancreases develops diabetes as a result of the loss of β cells if the injured pancreas is removed.[15-17] Drug associated Diabetes which damage β cells and impair their ability for lowering blood glucose levels. Some medications such as niacin, anti-seizure drugs, diuretics, psychiatric meds and prescription pharmaceuticals, pentamide, glucocorticoids, anti-rejection medications and statins even for the treatment of HIV.[18]

When a child or teen has type 1 diabetes, their likelihood of disease prevalence rises if a parent or sibling also has the disease.[19] factors contributing to the risk of T2DM includes being obesity, eating pattern, middle age generally 45 and above, genetics, less physical work, pre-diabetes or gestational diabetes, hyperlipidaemia.[20-23] Being overweight and age above 25 gestational diabetes risk rises. Gestational diabetes during pregnancy where child born weigh more than nine pounds, PCOS (Polycystic Ovarian Syndrome), past family history.[24]

Few literated medicinal plants from the plethora of herbs

Wood Apple

Wood apples contribute to a variety of phytoconstituent's with significant medicinal properties. These include alkaloids, flavonoids, tannins, phenolic compounds, vitamins and minerals. Among these, polyphenols, particularly flavonoids, are of particular interest in the context of diabetes management. Flavonoids possess antioxidant and anti-inflammatory properties, which are beneficial in mitigating the oxidative stress and chronic inflammation associated with diabetes. Studies have shown that wood apple extracts stimulate insulin secretion both *in vitro* and in animal models, suggesting its potential as a natural insulin secretagogue. Furthermore, wood apple exhibits insulin-like activity, whereby it enhances glucose uptake in peripheral tissues such as muscle and adipose tissue.[25-30]

Garlic

Garlic, known scientifically as *Allium sativum*, has been in use form decades for its therapeutic properties not only as a culinary

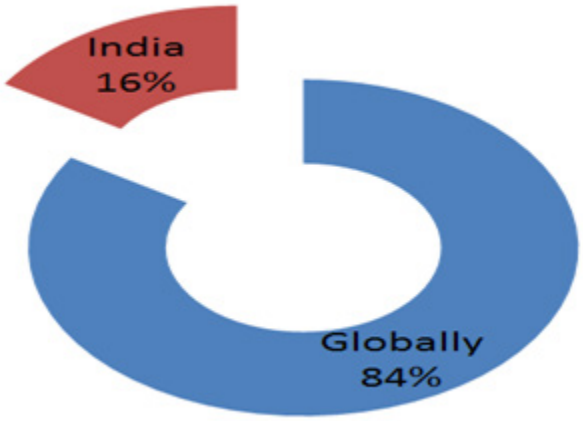

Figure 1: Demographic Representation.[2,3]

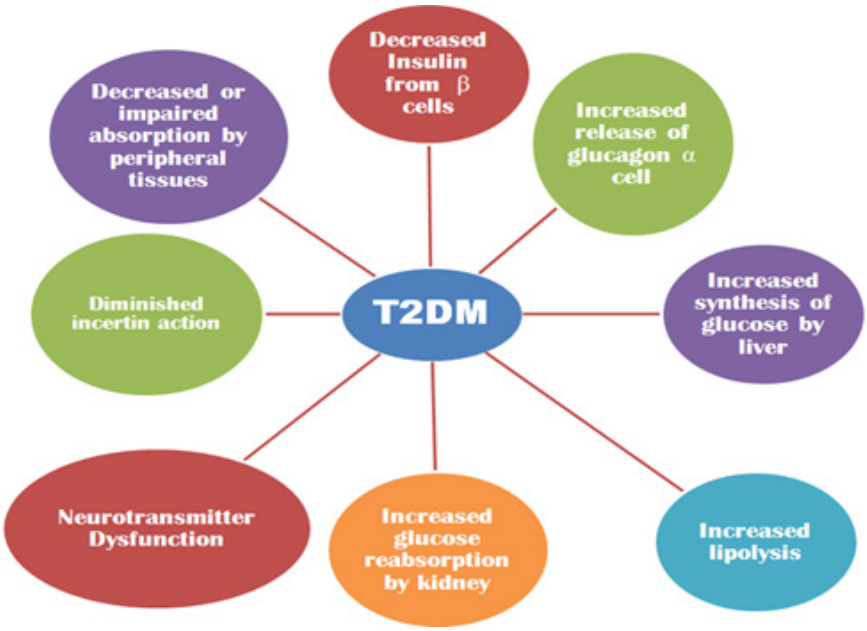

Figure 2: Causes of T2DM: Disease leading to T2DM.

ingredient. From various health benefits, it has gained attention for its significant antidiabetic activity due to the presence of phenolic acids. Allicin, a sulphur-containing compound found in garlic, primarily contributes to its therapeutic effects and for its characteristic aroma. Diallyl disulfide and diallyl trisulfide the other sulphur compounds present in garlic also contributes to its biological activity. Garlic helps attenuate the rapid rise in blood sugar following carbohydrate-rich meals, thus contributing to improved glycaemic control.[31-35]

Bitter gourd

Bitter gourd contains a diverse array of bioactive compounds, including cucurbitane-type triterpenoids, flavonoids, phenolic acids and lectins, which contribute to its medicinal properties. Among these, charantin, polypeptide-p and vicine are some of the key constituents responsible for bitter gourd's antidiabetic effects. Studies have shown that bitter gourd extracts stimulate insulin secretion both *in vitro* and in animal models, suggesting its potential as a natural insulin secretagogue. Empirical evidence supporting the antidiabetic activity of bitter gourd is accumulating, although clinical studies necessitate further validating safety and efficacy in human beings. Animal studies demonstrated its ability to decrease blood glucose levels, improving insulin sensitivity and preserving pancreatic beta cell function. Additionally, epidemiological studies reported a contrarily amid bitter gourd consumption and risk of development of type 2 diabetes.[36-40]

China Rose

Hibiscus shows promise as a natural adjunctive therapy for diabetes management, owing to its potential antidiabetic, antioxidant and anti-inflammatory properties. Preclinical and clinical evidence suggests that hibiscus supplementation may

help improve glycaemic control, insulin sensitivity and lipid profile in individuals with diabetes. Hibiscus has a variety of phytoconstituents such as anthocyanins, polyphenols, flavonoids and organic acids, contributing for pharmacological properties. Hibiscus may add great value to the armamentarium of antidiabetic agents, presenting a safe and natural alternative for improving metabolic health.[41-46]

Ginger

Ginger (*Zingiber officinale*), with wide use as a spice and therapeutic herb, attracted attention for its potential antidiabetic properties. It contains chemical compounds like gingerol, paradol, shogaol which contribute to its pharmacological effects. Animal and cell culture experiments have demonstrated the efficacy of ginger extracts or isolated compounds in reducing blood sugar, improving sensitivity to insulin and ameliorating diabetic complications such as neuropathy and nephropathy. These effects have been attributed to various mechanisms, including enhanced insulin signalling, inhibition of gluconeogenesis and modulation of lipid metabolism. Ginger when consumed as culinary ingredient or as dietary supplement has attained safety window. However, ginger may showcase gastrointestinal adverse effects such as heartburn and bloating in some individuals if used in larger doses. Additionally, ginger may interact with certain medications, including anticoagulants and antidiabetic drugs, potentially altering their effects.[47-51]

Fenugreek

fenugreek (*Trigonella foenum-graecum*) being one of the most widely studied. Fenugreek, a member of the Fabaceae family, has been used since antient times for its medicinal properties. Fenugreek contains bioactive compounds such as trigonelline, galactomannan and saponins, contributing to its pharmacological effects. Fenugreek shows promising effects as a natural and complementary therapy for diabetes management, offering multiple mechanisms of action and extensive clinical evidence supporting its efficacy. Through its effects on insulin sensitivity, insulin secretion, carbohydrate metabolism and inflammation, fenugreek helps improve glycaemic control and mitigate diabetic complications.[52-55]

Neem

Neem (*Azadirachta indica*), a all-rounder and a tree with Indian origin, used since centuries in Ayurveda for various health ailments. Neem contains a diverse array of flavonoids, triterpenoids and polysaccharides, which contribute to pharmacological effects. Neem is safe for consumption when used in small amounts or as a dietary supplement. However, high doses may result in adverse GI effects such as nausea and vomiting in some individuals. Additionally, neem may interact with certain medications, including antidiabetic drugs and immuno suppressants, potentially altering their effects.[56-62]

Jamun

Jamun (*Syzygium cumini*), also known as Java plum or Indian blackberry, is one such plant with historic evident for its potential health benefits and usage in traditional medicine. A common practice followed traditionally to cure diabetes using *Syzygium cumini* (Myrtaceae) by homemade decoction, extract with water and alcohol, lyophilized powder prevails. Jamun containing potential bioactive compounds ranges from polyphenols, flavonoids, and anthocyanins, which contribute toward pharmacological effects. Jamun is safe for consumption when used in culinary amounts or as a dietary supplement. However, jamun may cause gastrointestinal side effects such as diarrhoea and abdominal discomfort in some individuals high doses. Additionally, jamun may interact with certain medications, including antidiabetic drugs and anticoagulants, potentially altering their effects.[63-68]

Papaya

Papaya (*Carica papaya*), a tropical fruit known for its sweet flavor and nutritional benefits, has gained attention for its potential antidiabetic properties. Papaya contains various bioactive compounds, including phenolic compounds, flavonoids and enzymes such as papain, which contribute to its pharmacological effects. Papaya, when consumed in moderate amounts as part of a balanced diet, is generally considered safe. However, individuals with latex allergy may experience allergic reactions to papaya. Additionally, high doses of papaya or papaya supplements may cause gastrointestinal side effects such as diarrhoea and abdominal discomfort in some individuals.[69-74]

Mango

Mango (*Mangifera indica*), a popular tropical fruit cherished for its sweet taste and rich nutritional profile, has garnered attention for its potential antidiabetic properties. Mango has a variety of bioactive compounds such as polyphenols, flavonoids and vitamins, who contribute to its pharmacological effects: Mango has been shown to improve glucose metabolism by enhancing insulin sensitivity and glucose uptake in peripheral tissues. Studies suggest that bioactive compounds present in mango, such as mangiferin and quercetin, stimulate the translocation of Glucose Transporter proteins (GLUT4) to the cell membrane, facilitating glucose uptake and utilization.[75-78]

Barriers in consumption of herbal Plants

While herbal plants offer a natural and potentially effective alternative for managing diabetes, there are several challenges that patients face in consuming herbal drugs. Lack of standardized dosage and their quality check is among the main challenges. Unlike pharmaceutical drugs, herbal plants vary in their chemical composition, making it difficult to establish consistent dosage guidelines. This can lead to inconsistent results and potential side effects. Another challenge is the limited

scientific evidence supporting the efficacy and safety of herbal plants. While there have been numerous studies exploring their antidiabetic properties, more research is needed to validate their effectiveness and establish optimal dosage regimens. Additionally, interactions between herbal plants and other medications are not well understood, which can pose a risk to patients who are on multiple medications. Furthermore, the challenge is to access, identify and making herbal plants available. In many parts of the world, certain herbal plants may be difficult to find or may not be affordable for everyone. This can limit their potential benefits to a select few. In conclusion, herbal plants have proved out to be as a favourable avenue for natural antidiabetic drugs. Their diverse chemical constituents and mechanisms of action offer potential alternatives for managing diabetes. However, challenges such as standardization, limited scientific evidence and accessibility need to be addressed to fully harness the benefits of herbal plants in diabetes management.

CONCLUSION

The growing evidence body supports the usage of herbal medicine in the cure of diabetes underscores potential of natural remedies to complement conventional approaches. Herbal remedies have demonstrated their efficacy in managing blood sugar levels, improving insulin sensitivity and addressing various complications associated with diabetes. The integration of herbal medicine into diabetes care not only offers a holistic and personalized approach but also opens avenues for exploring sustainable, nature-derived solutions. The rich history of herbal medicine across cultures further emphasizes its time-tested reliability in promoting overall well-being. Harnessing the power of plant-based compounds, herbal remedies not only target the symptoms but also address the root causes of diabetes. This holistic approach aligns with the growing trend towards personalized and patient-centred healthcare. Moreover, the relatively lower risk of side effects associated with many herbal treatments presents a compelling case for their inclusion in diabetes management plans. As we strive for more sustainable and natural healthcare solutions, herbal medicine stands out as a promising avenue for diabetic individuals seeking effective, safe and long-term strategies for their well-being. However, it is crucial to note that individual responses to herbal remedies may vary and consultation with healthcare professionals remains essential. Further research is required to integrate herbal medicine into mainstream diabetes care, collaboration of modern and traditional medicine and on-going exploration of the vast potential that nature offers in the fight against diabetes. In embracing the wisdom of traditional healing practices and combining it with modern scientific knowledge, we pave the way for a comprehensive and integrated approach to diabetes management. The continued exploration and utilization of herbal medicine mark a significant step towards a future where individuals with diabetes can access a diverse array of treatment options that prioritize both their health and the sustainability of our healthcare systems.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

T2DM: Type 2 Diabetes Mellitus; **GLP:** Glucagon like peptide; **GIP:** Glucose dependent insulinotropic polypeptide; **Type I DM:** Type One Diabetes Mellitus; **Type II DM:** Type two Diabetes Mellitus.

SUMMARY

Diabetes is the most prevalent metabolic disorder and endocrine disorder known by increased blood sugar levels due to either reduced secretion of insulin or reduced responsiveness of tissues to insulin. Diabetes is also associated with severe ramifications like cardiovascular disease, neural disorders, nephropathy and diabetic retinopathy. The increase cases of diabetes is partly attributed to poor diet and increased processed food consumption along with sedentary lifestyles. While there is a clear genetic predisposition for Type I, Type II often includes both genetic influences and lifestyle aspects. Pancreatic β cells lose their capacity to secrete insulin, meanwhile, α cells release excessive glucagon which induces the process of glucose generation in the kidneys. Factors that may also contribute to Type II diabetes include insulin resistance among others, which include the breakdown of lipids and renal re-absorption of glucose. Other health conditions are also known to contribute a predisposition toward diabetes (cystic fibrosis, haemochromatosis, Cushing's syndrome and acromegaly), they clinically follow a mechanism that involves either redesigned impaired insulin secretion or increased insulin resistance. There are pharmacological methods introduced to induce diabetes, including glucocorticoids amongst the more commonly prescribed anti-inflammatories, in addition to psychotropic medications. Notable plants with anti-diabetic action include wood apple, garlic, bitter gourd and fenugreek. Active ingredients within these plants that are bioactive include flavonoids, triterpenoids, polyphenols, etc., which safely ameliorate insulin sensitivity, stimulate insulin secretion and therefore improve glycaemic control. However, many of these products have only limited amounts of research undertaken to demonstrate their efforts and most have potential harmful interactions with pharmaceuticals at present and face challenges implementing a standardized dosage. Herbal medicine provides an important natural option with complementary

actions to manage diabetes, however there will still be a lot of academic research required to implement it within health care. A partnership between modern medicine and traditional medicine will result in a more integrated answer to diabetes care.

REFERENCES

1. Shaikh AA, Kolhatkar MK, Sopane DR, Thorve AN. Review on: diabetes mellitus is a disease. Int J Res Pharm Sci. 2022;13(1):102-9. doi: 10.26452/ijrps.v13i1.27.
2. Robertson PR. Type 2 diabetes mellitus: prevalence and risk factors [Internet]. UpToDate [cited Feb 1 2024]. Available from: https://www.uptodate.com/contents/type-2-diabetes-mellitus-prevalence-and-risk-factors.
3. Ministry of Health and Family Welfare. Update on treatment of Diabetes [press release] [cited Aug 1 2023]. Available from: https://pib.gov.in/PressReleasePage.aspx?PRID=1944600.
4. The Lancet. Diabetes: a defining disease of the 21st century. Lancet. 2023;401(10394):2087. doi: 10.1016/S0140-6736(23)01296-5, PMID 37355279.
5. Padhi S, Nayak AK, Behera A. Type II diabetes mellitus: a review on recent drug-based therapeutics. Biomed Pharmacother. 2020;131:110708. doi: 10.1016/j.biopha.2020.110708, PMID 32927252.
6. DeFronzo RA. Banting Lecture. From the triumvirate to the ominous octet: A new paradigm for the treatment of type 2 diabetes mellitus. Diabetes. 2009;58(4):773-95. doi: 10.2337/db09-9028, PMID 19336687.
7. Sun X, Yu W, Hu C. Genetics of type 2 diabetes: insights into the pathogenesis and its clinical application. BioMed Res Int. 2014; 2014:926713. doi: 10.1155/2014/926713, PMID 24864266.
8. Kayani K, Mohammed R, Mohiaddin H. Cystic fibrosis-related diabetes. Front Endocrinol. 2018;9(20):20. doi: 10.3389/fendo.2018.00020, PMID 29515516.
9. Barton JC, Acton RT. Diabetes in HFE hemochromatosis. J Diabetes Res. 2017; 2017:9826930. doi: 10.1155/2017/9826930, PMID 28331855.
10. Akhalya K, Sreelatha S, Rajeshwari SK. A review article-gestational diabetes mellitus. Endocrinol Metab Int J. 2019;7(1):26-39.
11. McIntyre HD, Catalano P, Zhang C, Desoye G, Mathiesen ER, Damm P. Gestational diabetes mellitus. Nat Rev Dis Primers. 2019;5(1):47. doi: 10.1038/s41572-019-0098-8, PMID 31296866.
12. Barbot M, Ceccato F, Scaroni C. Diabetes mellitus Secondary to Cushing's disease. Front Endocrinol. 2018;9(284):284. doi: 10.3389/fendo.2018.00284, PMID 29915558.
13. Ferraù F, Albani A, Ciresi A, Giordano C, Cannavò S. Diabetes secondary to acromegaly: physiopathology, clinical features and effects of treatment. Front Endocrinol. 2018;9(358):358. doi: 10.3389/fendo.2018.00358, PMID 30034367.
14. Wang C. The relationship between type 2 diabetes mellitus and related thyroid diseases. J Diabetes Res. 2013; 2013:390534. doi: 10.1155/2013/390534, PMID 23671867.
15. Kahn SE, Cooper ME, Del Prato SD. Pathophysiology and treatment of type 2 diabetes: perspectives on the past, present and future. Lancet. 2014;383(9922):1068-83. doi: 10.1016/S0140-6736(13)62154-6, PMID 24315620.
16. Ewald N, Hardt PD. Diagnosis and treatment of diabetes mellitus in chronic pancreatitis. World J Gastroenterol. 2013;19(42):7276-81. doi: 10.3748/wjg.v19.i42.7276, PMID 24259958.
17. De Souza A, Irfan K, Masud F, Saif MW. Diabetes Type 2 and pancreatic cancer: A history unfolding. JOP. 2016;17(2):144-8. PMID 29568247.
18. Corticosteroids are used to reduce harmful inflammation but can lead to diabetes-often referred to as steroid diabetes [Internet]; 2020. Diabetes [cited Jan 20 2024]. Available from: https://www.diabetes.co.uk/drug-induced-diabetes.html.
19. Streisand R, Monaghan M. Young children with type 1 diabetes: challenges, research and future directions. Curr Diabetes Rep. 2014;14(9):520. doi: 10.1007/s11892-014-0520-2, PMID 25009119.
20. Olokoba AB, Obateru OA, Olokoba LB. Type 2 diabetes mellitus: a review of current trends. Oman Med J. 2012;27(4):269-73. doi: 10.5001/omj.2012.68, PMID 23071876.
21. Khazrai YM, Defeudis G, Pozzilli P. Effect of diet on type 2 diabetes mellitus: a review. Diabetes Metab Res Rev. 2014; 30(1); Suppl 1: 24-33. doi: 10.1002/dmrr.2515, PMID 24352832.
22. Eckel RH, Kahn SE, Ferrannini E, Goldfine AB, Nathan DM, Schwartz MW, *et al.* Obesity and type 2 diabetes: what can be unified and what needs to be individualized? Diabetes Care. 2011;34(6):1424-30. doi: 10.2337/dc11-0447, PMID 21602431.
23. Boles A, Kandimalla R, Reddy PH. Dynamics of diabetes and obesity: epidemiological perspective. Biochim Biophys Acta Mol Basis Dis. 2017;1863(5):1026-36. doi: 10.1016/j.bbadis.2017.01.016, PMID 28130199.
24. Gambineri A, Patton L, Altieri P, Pagotto U, Pizzi C, Manzoli L, *et al.* Polycystic ovary syndrome is a risk factor for type 2 diabetes: results from a long-term perspective study. Diabetes. 2012;61(9):2369-74. doi: 10.2337/db11-1360, PMID 22698921.
25. Pandian P, Madhukar A, Kumar S. Evaluation of antidiabetic activity of isolated fractions of *Aegle marmelos*. J Pharm Negat Results. 2022;13(10):6589-97.
26. Murthy HN, Dalawai D. Bioactive compounds of wood apple (*Limonia acidissima* L.). In: Bioactive compounds in underutilized fruits and nuts; 2020. p. 543-69. doi: 10.1007/978-3-030-30182-8_39.
27. Shivanna A, Dandin G, Hiremath U, Hulamani S, Ripnar C. Perception of wood apple among diabetic subjects. 2016;22:S371-8.
28. Parvez GM, Sarker RK. Pharmacological potential of wood apple (*Limonia acidissima*): a review. IJMFM&AP. 2021;7(2):40-7. doi: 10.53552/ijmfmap.2021.v07ii02.003.
29. Thakur N, Chugh V, Dwivedi S. Wood apple: an underutilized miracle fruit of India. J Pharm Innov J. 2020;9:198-202.
30. Jatav S, Dwivedi P, Singh M, Sehra N, Mishra BB. Properties and important molecules of medicinal interest in wood apple (*Aegle marmelos*). In: Synthesis of medicinal agents from plants. Elsevier; 2018. p. 127-50.
31. Mahi FE, Hasib A, Boulli A, Boussadda L, Abidi O, Aabdousse J, et al. *In vitro* and *in vivo* antidiabetic effect of the aqueous extract of garlic (*Allium sativum* L.) compared to glibenclamide on biochemical parameters in alloxan-induced diabetic mice. Int J Pharm Sci Rev Res. 2023;80(1):106-13. doi: 10.47583/ijpsrr.2023.v80i01.015.
32. Eidi A, Eidi M, Esmaeili E. Antidiabetic effect of garlic (*Allium sativum* L.) in normal and streptozotocin-induced diabetic rats. Phytomedicine. 2006;13(9-10):624-9. doi: 10.1016/j.phymed.2005.09.010, PMID 17085291.
33. Saikat AS, Hossain R, Mina FB, Das S, Khan IN, Mubarak MS, *et al.* Antidiabetic effect of garlic. Rev Bras Farmacogn. 2021;31:1.
34. Kook S, Kim GH, Choi K. The antidiabetic effect of onion and garlic in experimental diabetic rats: meta-analysis. J Med Food. 2009;12(3):552-60. doi: 10.1089/jmf.2008.1071, PMID 19627203.
35. Phil RA, Khan RA, Ashraf I. Effects of garlic on blood glucose levels and HbA1c in patients with type 2 diabetes mellitus. J Med Plants Res. 2011;5(13):2922-8.
36. Mahmoud MF, El Ashry FE, El Maraghy NN, Fahmy A. Studies on the antidiabetic activities of *Momordica charantia* fruit juice in streptozotocin-induced diabetic rats. Pharm Biol. 2017;55(1):758-65. doi: 10.1080/13880209.2016.1275026, PMID 28064559.
37. Banerjee J, Chanda R, Samadder A. Antidiabetic activity of *Momordica charantia* or bitter melon: a review. Acta Sci Pharm Sci. 2019;3:24-30.
38. Panara JR. A short review on antidiabetic activity of bitter gourd. Int J Pharm Res Bio-Sci. 2013;2(4):333-6.
39. Ahmad Z, Zamhuri KF, Yaacob A, Siong CH, Selvarajah M, Ismail A, et al. *In vitro* anti-diabetic activities and chemical analysis of polypeptide-k and oil isolated from seeds of *Momordica charantia* (bitter gourd). Molecules. 2012;17(8):9631-40. doi: 10.3390/molecules17089631, PMID 22885359.
40. Leung L, Birtwhistle R, Kotecha J, Hannah S, Cuthbertson S. Anti-diabetic and hypoglycaemic effects of *Momordica charantia* (bitter melon): a mini review. Br J Nutr. 2009;102(12):1703-8. doi: 10.1017/S0007114509992054, PMID 19825210.
41. Amer SA, Al-Khalaifah HS, Gouda A, Osman A, Goda NI, Mohammed HA, *et al.* Potential effects of anthocyanin-rich Roselle (*Hibiscus sabdariffa* L.) extract on the growth, intestinal histomorphology, blood biochemical parameters and the immune status of broiler chickens. Antioxidants (Basel). 2022; 11(3). doi: 10.3390/antiox11030544, PMID 35326194.
42. Kumar TR, Kumar EU, Sekar M, Kumar MS. Antidiabetic activity of methanolic extract of *Hibiscus cannabinus* in streptozotocin-induced diabetic rats. Int J Pharm Biol Sci. 2011;2(1).
43. Bhaskar A, Vidhya VG. Hypoglycemic and hypolipidemic activity of *Hibiscus rosa-sinensis* Linn. on streptozotocin-induced diabetic rats. Int J Diabetes Dev Ctries. 2012;32(4):214-8. doi: 10.1007/s13410-012-0096-9.
44. Bule M, Albelbeisi AH, Nikfar S, Amini M, Abdollahi M. The antidiabetic and antilipidemic effects of *Hibiscus sabdariffa*: a systematic review and meta-analysis of randomized clinical trials. Food Res Int. 2020;130:108980. doi: 10.1016/j.foodres.2020.108980, PMID 32156406.
45. Sankaran M, Vadivel A. Antioxidant and antidiabetic effect of *Hibiscus rosa-sinensis* flower extract on streptozotocin-induced experimental rats: a dose-response study. Not Sci Biol. 2011;3(4):13-21. doi: 10.15835/nsb346348.
46. Sachdewa A, Nigam R, Khemani LD. Hypoglycemic effect of *Hibiscus rosa-sinensis* L. leaf extract in glucose and streptozotocin-induced hyperglycemic rats. Indian J Exp Biol. 2001 Mar;39(3):284-6. PMID 11495291.
47. Pakan P, Lidia K, Riwu M. Investigation of ginger (*Zingiber officinale*) aqueous extract as an anti-diabetic *in vitro*. IOP Conf Ser Earth Environ Sci. 4th International Conference on Bioscience and Biotechnology. 2021;913(1). doi: 10.1088/1755-1315/913/1/012108.
48. Noipha K, Ninla-Aesong P. Antidiabetic activity of *Zingiber officinale* Roscoe rhizome extract: an *in vitro* study. HAYATI J Biosci. 2018;25(4):160-4. doi: 10.4308/hjb.25.4.160.
49. Akhani SP, Vishwakarma SL, Goyal RK. Anti-diabetic activity of *Zingiber officinale* in streptozotocin-induced type I diabetic rats. J Pharm Pharmacol. 2004;56(1):101-5. doi: 10.1211/0022357022403, PMID 14980006.
50. Otunola G, Afolayan A. A review of the antidiabetic activities of ginger. Intech Open; 2020. doi: 10.5772/intechopen.88899.
51. Shidfar F, Rajab A, Rahideh T, Khandouzi N, Hosseini S, Shidfar S. The effect of ginger (*Zingiber officinale*) on glycemic markers in patients with type 2 diabetes. J Complement Integr Med. 2015;12(2):165-70. doi: 10.1515/jcim-2014-0021, PMID 25719344.
52. Khosla P, Gupta DD, Nagpal RK. Effect of *Trigonella foenum-graecum* (Fenugreek) on blood glucose in normal and diabetic rats. Indian J Physiol Pharmacol. 1995;39(2):173-4. PMID 7649611.

53. Gad MZ, El-Sawalhi MM, Ismail MF, El-Tanbouly ND. Biochemical study of the anti-diabetic action of the Egyptian plants Fenugreek and Balanites. Mol Cell Biochem. 2006;281(1-2):173-83. doi: 10.1007/s11010-006-0996-4, PMID 16328970.
54. Mooventhan A, Nivethitha L. A narrative review on evidence-based antidiabetic effect of fenugreek (*Trigonella foenum-graecum*). Int J Nutr Pharmacol Neurol Dis. 2017;7(4):84-7. doi: 10.4103/ijnpnd.ijnpnd_36_17.
55. Bawadi HA, Maghaydah SN, Tayyem RF. The postprandial hypoglycemic activity of fenugreek seed and seeds' extract in type 2 diabetics: A pilot study. Pharmacogn Mag. 2009;5(18):134-8.
56. Gupta D, Raju J, Baquer NZ. Modulation of some gluconeogenic enzyme activities in diabetic rat liver and kidney: effect of antidiabetic compounds. Indian J Exp Biol. 1999;37(2):196-9. PMID 10641146.
57. Elavarasi S, Saravanan K, Renuka C. A systematic review on medicinal plants used to treat diabetes mellitus. Int J Pharm Chem Biol Sci. 2013;3(3):989-92.
58. Dholi SK, Raparla R, Mankala S, Nagappan K. *In vivo* antidiabetic evaluation of neem leaf extract in alloxan-induced rats. J Appl Pharm Sci. 2011;1(4):100-5.
59. Patil P, Patil S, Mane A, Verma S. Antidiabetic activity of alcoholic extract of neem (*Azadirachta indica*) root bark. Natl J Physiol Pharm Pharmacol. 2013;3(2):142-6. doi: 10.5455/njppp.2013.3.134-138.
60. G DN, K DJ, P Revankar DS. Evaluation of hypoglycemic activity of neem (*Azadirachta indica*) in albino rats. IOSR JDMS. 2014;13(9):4-11. doi: 10.9790/0853-13920411.
61. Dholi SK, Raparla R, Mankala S, Nagappan K. *In vivo* antidiabetic evaluation of neem leaf extract in alloxan-induced rats. J Appl Pharm Sci. 2011;1(4):100-5.
62. Patil SM, Shirahatti PS, Ramu R. Azadirachta indica A. Juss. (neem) against diabetes mellitus: A critical review on its phytochemistry, pharmacology and toxicology. J Pharm Pharmacol. 2022;74(5):681-710. doi: 10.1093/jpp/rgab098, PMID 34562010.
63. Kumar A, Ilavarasan R, Jayachandran T, Deecaraman M, Aravindan P, Padmanabhan N, *et al.* Antidiabetic activity of *Syzygium cumini* and its isolated compound against streptozotocin-induced diabetic rats. J Med Plants Res. 2008;2(9):246-9.
64. Rather GJ, Hamidudin M, Ikram M, Zaman R. Antidiabetic potential and related activity of Jamun (*Syzygium cumini* Linn.) and its utilization in Unani medicine: an overview. Int J Herb Med. 2019;7(5):7-11.
65. Gajera HP, Gevariya SN, Hirpara DG, Patel SV, Golakiya BA. Antidiabetic and antioxidant functionality associated with phenolic constituents from fruit parts of indigenous black jamun (*Syzygium cumini* L.) landraces. J Food Sci Technol. 2017;54(10):3180-91. doi: 10.1007/s13197-017-2756-8, PMID 28974803.
66. Baliga MS, Fernandes S, Thilakchand KR, D'Souza P, Rao S. Scientific validation of the antidiabetic effects of *Syzygium* jambolanum DC (black plum), a traditional medicinal plant of India. J Altern Complement Med. 2013;19(3):191-7. doi: 10.1089/acm.2011.0752, PMID 23030429.
67. Yadav D, Lalit A, Singh S, Galgut JM, Beg MA. Evaluation of antidiabetic and phytochemical activity of 50% methanolic extract of jamun seed (*Syzygium cumini*). Search Res. 2013;4(3):13-6.
68. Mulkalwar S, Kulkarni V, Deshpande T, Bhide H, Patel A, Tilak AV. Antihyperglycemic activity of *Syzygium cumini* (jamun) in diabetic rats. J Pharm Res Int. 2021;33:12-9. doi: 10.9734/jpri/2021/v33i35A31868.
69. Sobia K, Javaid MA, Ahmad MS, Rehmatullah Q, Hina G, Iram B, *et al.* Assessments of phytochemicals and hypoglycemic activity of leaves extracts of *Carica papaya* in diabetic mice. Int J Pharm Sci Res. 2016;7(9):3658-63.
70. Juárez-Rojop IE, Díaz-Zagoya JC, Ble-Castillo JL, Miranda-Osorio PH, Castell-Rodríguez AE, Tovilla-Zárate CA, *et al.* Hypoglycemic effect of *Carica papaya* leaves in streptozotocin-induced diabetic rats. BMC Complement Altern Med. 2012;12:236. doi: 10.1186/1472-6882-12-236, PMID 23190471.
71. Airaodion AI, Ogbuagu EO, Ekenjoku JA, Ogbuagu U, Okoroukwu VN. Antidiabetic effect of ethanolic extract of *Carica papaya* leaves in alloxan-induced diabetic rats. Am J Biomed Sci Res. 2019;5(3):227-34.
72. Agada R, Thagriki D, Esther Lydia DE, Khusro A, Alkahtani J, Al Shaqha MM, *et al.* Antioxidant and anti-diabetic activities of bioactive fractions of *Carica papaya* seeds extract. J King Saud Univ Sci. 2021;33(2):101342. doi: 10.1016/j.jksus.2021.101342.
73. Solikhah TI, Setiawan B, Ismukada DR. Antidiabetic activity of papaya leaf extract (*Carica papaya* L.) isolated with maceration method in alloxan-induced diabetic mice. Syst Rev Pharm. 2020;11(9):774-8.
74. Venkateshwarlu E, Dileep P, Sandhya P. Evaluation of antidiabetic activity of *Carica papaya* seeds on streptozotocin-induced type-II diabetic rats. J Adv Sci Res. 2013;4(2):38-41.
75. Mistry J, Biswas M, Sarkar S, Ghosh S. Antidiabetic activity of mango peel extract and mangiferin in alloxan-induced diabetic rats. Future J Pharm Sci. 2023;9(1):22. doi: 10.1186/s43094-023-00472-6.
76. Samanta S, Chanda R, Ganguli S, Reddy AG, Banerjee J. Antidiabetic activity of mango (*Mangifera indica*): a review. MOJ Bioequiv Availab. 2019;6(2):23-6.
77. Rodríguez-González S, Gutiérrez-Ruíz IM, Pérez-Ramírez IF, Mora O, Ramos-Gomez M, Reynoso-Camacho R. Mechanisms related to the anti-diabetic properties of mango (*Mangifera indica* L.) juice by-product. J Funct Foods. 2017;37:190-9. doi: 10.1016/j.jff.2017.07.058.
78. Gondi M, Prasada Rao UJ. Ethanol extract of mango (*Mangifera indica* L.) peel inhibits α-amylase and α-glucosidase activities and ameliorates diabetes related biochemical parameters in streptozotocin (STZ)-induced diabetic rats. J Food Sci Technol. 2015;52(12):7883-93. doi: 10.1007/s13197-015-1963-4, PMID 26604360.

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