Int. j. adv. multidisc. res. stud. 2025; 5(4):270-276

Received: 22-05-2025
Accepted: 02-07-2025

International Journal of Advanced Multidisciplinary Research and Studies

ISSN: 2583-049X

Review of Type 2 Diabetes Mellitus and Plant-Based Treatment for Type 2 Diabetes Mellitus

[1] Godwin Obadiah, [2] Geoffrey Chukwuanugo Okeke, [3] Uchechukwu Nzubechukwu Odionu, [4] Ellis Ehizojie Momoh, [5] Agu Ijeoma Thelma, [6] Sunday Faith Bakel, [7] Chimaobi Jude Nwiyi, [8] David Kennedy Nkweke, [9] Chika Louisa Uche, [10] Jonathan Boomni Oye, [11] Nnamdi Hyacinth Nnubia, [12] Uche Nkem Okeke, [13] Emmanuel Chidera Ngwu, [14] Ejiofor Johnson Chidiebere, [15] Isuajah Chukwuka Emmanuel, [16] Chibuike Solomon Igwe, [17] Olonade Oluwafemi, [18] Onuoha Paul Chukwuemeka, [19] Ugwuanyi Isaiah Ifechukwu, [20] Udeh ifunanya Joan, [21] Oku Victoria Chisom

[1] Department of Physiology Federal, University of Lafia, Nasarawa State, Nigeria
[2, 3, 19, 21] Department of Medical Laboratory Science, University of Nigeria, Enugu Campus, Enugu State, Nigeria
[4] Department of Medical Laboratory Science, Ambrose Alli University, Ekpoma, Edo State, Nigeria
[5] Department of Science Laboratory Technology (Microbiology Option), Institute of Management and Technology, Enugu State, Nigeria
[6] Department Science Education (Biology Option), Rivers State University, River State Nigeria
[7, 16] Department of Clinical Pharmacy and Pharmacy Management, University of Nigeria, Nsukka, Enugu State, Nigeria
[8] Department of Human Anatomy, University of Port Harcourt, Rivers State, Nigeria
[9] Department of Cell Biology and Genetics, University of Lagos, Akoka, Lagos State, Nigeria
[10] Public Health Care Epidemiology, IM Sechenov, First Moscow State Medical University, Moscow, Russia
[11] Department of Sciences, Immaculate Comprehensive Secondary School, Omoku, Rivers State, Nigeria
[12] Department of Public Health, First Moscow State Medical University, Sechenov, Russia
[13] Department of Biochemistry, University of Nigeria Nsukka, Enugu State, Nigeria
[14] Department of Nursing, Medical Faculty, People's Friendship University (RUDN), Moscow, Russia
[15] Department of Clinical Pathology, College of Medicine, Lead City University, Ibadan, Nigeria
[17] Department of Plant Science and Biotechnology, Adekunle Ajasin University Akungba Akoko, Ondo State, Nigeria
[18] Department of Medical Laboratory Science, University of Nigeria, Enugu Campus, Enugu State, Nigeria
[20] Department of Computer and Mathematics Education, Enugu State University of Science and Technology, Enugu State, Nigeria

Corresponding Author: **Godwin Obadiah**

Abstract
Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and impaired glucose metabolism, accounting for over 90% of all diabetes cases worldwide. The global prevalence of T2DM has been rising rapidly, driven largely by lifestyle factors such as poor diet, physical inactivity, and obesity. Conventional treatments primarily focus on pharmacological interventions to manage blood glucose levels and reduce the risk of complications. However, these medications often come with side effects and may not address the underlying causes of the disease. In recent years, increasing attention has been directed toward alternative and complementary therapies, particularly plant-based treatments, due to their potential to improve glycemic control and reduce dependence on synthetic drugs. This review explores the pathophysiology of T2DM, highlighting key mechanisms including insulin resistance, beta-cell dysfunction, and systemic inflammation. It also examines the therapeutic potential of various plant-derived compounds such as flavonoids, alkaloids, terpenoids, and polyphenols, which have demonstrated hypoglycemic, antioxidant, and anti-inflammatory properties in both preclinical and clinical studies. Notable examples include Gingerbread plum (*Neocarya macropylla*), bitter melon (*Momordica charantia*), and cinnamon (*Cinnamomum spp.*). The review further discusses the mechanisms by which these plant-based agents exert their effects, such as enhancing insulin sensitivity, promoting insulin secretion, and modulating glucose metabolism. Overall, while plant-based treatments offer promising complementary strategies for managing T2DM, further rigorous clinical trials are needed to validate their efficacy, safety, and long-term benefits in diverse populations. Integrating plant-based therapies with conventional care may provide a more holistic and sustainable approach to T2DM management.

Keywords: Type 2 Diabetes Mellitus, Plant-Based Treatments, *Neocarya Macropylla*, Insulin Resistance, T2DM Management

Introduction

Diabetes mellitus (DM) is a group of metabolic disorders characterized by chronic hyperglycemia resulting from defects in insulin secretion, action, or both with an increased risk of microvascular and macrovascular complications [1, 2]. Hematological changes in diabetes are directly related to endothelial dysfunction and inflammation [3]. Hyperglycemia and its metabolic syndrome may be associated with changes in the various hematological parameters, including the morphology, size, and

physiological function of red blood cells (RBCs), white blood cells (WBCs), and platelets [4].

Diabetes comprises many disorders that are characterized by hyperglycemia. The current classification divides the disorder into two main categories: Type 1 Diabetes (T1DM) and Type 2 Diabetes (T2DM) [5]. Historically, the distinction between these two types has been based on several factors, such as the onset age, the extent to which β cell function has been impaired, the level of resistance to insulin, the presence of auto-antibodies associated with diabetes, and the need for insulin treatment to survive [6]. However, these factors alone do not provide a definitive answer to the question of which type of diabetes is best suited to a particular condition, nor do they cover the entire range of diabetic phenotypes.

Type 1 Diabetes Mellitus (T1DM)

Type 1diabetes was previously known as insulin-dependent diabetes mellitus (IDDM), juvenile diabetes, or childhood-onset DM. It is a condition in which beta cells are destroyed due to an autoimmune process. This usually results in an absolute insulin deficiency [5]. Type 1 is typically characterized by the presence of anti–glutamic acid decarboxylase, islet cells, or insulin antibodies, which detect the autoimmune process that destroys beta cells [7]. Ultimately, all patients with type 1 diabetes will require insulin therapy to maintain normal blood glucose levels.

Type 2 Diabetes Mellitus (T2DM)

Type 2 Diabetes was formerly known as non-insulin-dependent-diabetes mellitus (NIDDM), type II, or adult-onset diabetes. It is much more common than type 1 diabetes and constitutes about 90–95% of all cases of diabetes [8]. This type of diabetes is characterized by two primary insulin-related disorders: insulin resistance and β-cell insufficiency [9,10, 11].

Prevalence of Diabetes

Diabetes is one of the fastest-growing global public health emergencies of the 21st century it is associated with metabolic, cellular, and blood disturbances. According to the International Diabetes Federation (IDF), 537 million people are living with diabetes. It is projected by 2045, 783 million people will have the disease worldwide. Diabetes has devastating effects on individuals, societies, and countries or territories and leads to over 4 million deaths a year. It affects all ages, communities, and continents [12]. Although its prevalence varies from region to region. In 2021, excluding the mortality risks related to the COVID-19 pandemic, the estimated number of adults between the ages of 20 and 79 who died from diabetes or its associated complications was estimated to be 6.7 million. This equates to a 12.2% global mortality rate for all causes among adults aged 20 to 79. Approximately 32.6% of all diabetes-related deaths occurred among working-age individuals under the age of 60, which equates to an 11.8% global mortality rate among individuals aged under 60 [12].

In sub-Saharan Africa (SSA), the prevalence of diabetes Mellitus is noteworthy, with an estimated 527 million cases in 2021 and a concerning 416,000 deaths attributed to the disease and related conditions, predominantly affecting individuals between 20–79 years of age. The projected escalation of diabetes cases in SSA, attributed to demographic shifts and urbanization, is expected to bring the regional total to approximately 696 million cases by 2030 and 1.05 billion by 2045. The estimated People with diabetes in Nigeria, was approximately 50 million in 2000, 75 million in 2011, 96 million in 2021, with projections of 125 million in 2030, and 191 million in 2045. This rapid surge places SSA at the forefront of the diabetes burden globally [12]. The challenges faced by the sub-Saharan African region in combating diabetes are multifaceted. These include insufficient funding for non-communicable diseases, limited availability of population-specific studies and guidelines, medication scarcity, disparities between urban and rural patients, and healthcare inequities between the public and private sectors [13].

Pathophysiology of Type 2 Diabetes

Type 2 diabetes mellitus is the most common type of metabolic disorder in the world. T2DM is caused by a complex combination of factors, including defective insulin secretion by pancreatic beta-cells and insulin resistance in insulin-sensitive tissues [14]. The disease is characterized by a disruption of the mechanisms of action between insulin and insulin secretion, resulting in elevated blood glucose levels [15]. In the event of β-cell dysfunction, the body's ability to maintain physiological glucose levels is impaired due to a decrease in insulin secretion. Conversely, Insulin resistance (IR) results in an increase in the production of glucose in the liver and a decrease in glucose uptake in muscle, liver, and fat tissue. Although both of these processes occur early in the pathogenesis process and contribute to the onset of the disease, the disease is typically more severe in β-cell dysfunction than in IR. However, in both cases, hyperglycemia is amplified resulting in the development of T2DM [16, 17].

Risk Factor of Type 2 Diabetes (T2DM)

The risk factors associated with (Type 2 Diabetes mellitus (T2DM) are a complex combination of genetics, metabolism, and environment, which interact with each other to contribute to its prevalence. While individual predisposition to T2DM is largely due to non-negligible risk factors (e.g., ethnicity, family history, and genetic predisposition) with a strong genetic basis, epidemiological studies suggest that a significant proportion of T2DM cases can be avoided by addressing the primary modifiable risk factors such as obesity, inadequate physical activity, and an unhealthy diet [18, 19].

Genetic factors have been found to play a significant role in the risk of T2DM [20, 21]. In particular, Dimas *et al* identified four genetic variants that were associated with insulin resistance, two with reduced insulin secretion when fasting high blood sugar was present, and nine with decreased insulin secretion when fasting glucose was normal. This study also identified one variant that was associated with insulin processing [22]. These findings suggest a polygenic genetic architecture for T2DM and further research is necessary to identify additional genetic factors associated with the condition [23]. Furthermore, interactions between genetic susceptibility loci, as well as environmental factors, may explain the persistence of T2DM heritability. This implies that the effects of a particular genetic variant may be affected by environmental factors and vice versa, as supported by both observational and clinical trials.

Ethnicity and Family History is another risk factor for type 2 diabetes. T2DM prevalence and incidence rates across the world vary significantly depending on ethnicity and

geographical region, with Japanese, Hispanic, and Native Americans being at the highest risk [24]. It has been demonstrated that Asian individuals are at a higher risk of developing T2DM compared to the White American population [25] and the White population in the United Kingdom [26], where the black population is at the highest risk [27]. Although no definitive causes have been identified, potential contributing factors include modern lifestyle factors (which contribute to obesity), socioeconomic factors, and direct genetic predisposition or gene-environmental interactions.

The risk of developing T2DM is highest in those with a body mass index (BMI) ≥30kg/m^2 [28] and is associated with metabolic abnormalities leading to IR. There is an inverse linear correlation between BMI and age at T2DM diagnosis [29]. The exact mechanism by which obesity leads to T2DM and is associated with IR is yet to be fully understood; however, several factors have been demonstrated to play a major role in this pathological pathway, which includes both cell-independent mechanisms and inter-organ communications.

Another risk factor is a sedentary lifestyle. Studies in women with a sedentary lifestyle showed a 34% and 56% reduction in developing T2DM, respectively, in participants who walked 2–3 hours a day or at least 40 minutes a week [30]. Physical activity has three primary benefits in delaying the onset of T2DM. First, it increases blood flow into the skeletal muscle, increasing glucose uptake from plasma. Second, it reduces intra-abdominal adipose tissue, which is a well-known risk factor for IR. Third, moderate-intensity exercise improves glucose uptake by 40%. Physical activity improves glucose uptake and insulin sensitivity, but it also improves or even reverses inflammation and oxidative stress, both of which are risk factors for T2DM [31].

Cellular Mechanism of T2DM

Insulin is produced by β-cells and is initially produced as pre-insulin. During the maturing process, pre-insulin undergoes conformational modification with the aid of several proteins in the Endoplasmic Reticulum (ER), resulting in the formation of proinsulin [32]. Proinsulin then translocate from the ER into the Golgi apparatus (GA), where it partitions into immature secreting vesicles and is broken down into C- peptide and insulin [33]. Once mature, insulin stores in granules until it is triggered by insulin release. Insulin release is primarily triggered by high glucose concentrations. However, some other factors (e.g., amino acids, fatty acids, and hormones) can also trigger insulin release [34]. When glucose levels rise in the blood, β-cells absorb glucose primarily via the glucose transporter 2 (GLUT2), a soluble carrier protein that also acts as a glucose sensor for β-cells. As glucose enters, glucose catabolism activates, increasing the intracellular ratio of ATP/ADP. This results in the closure of ATP-dependent potassium channels in the plasma membrane, causing membrane depolarization and opening of the voltage-dependent Ca2+ channels in which Ca2+ can enter the cell. The rise in the intracellular Ca2+ concentration triggers the priming and fusion of the secretory insulin-containing granules to the plasma membrane, resulting in insulin exocytosis [33].

Traditionally, the cause of β-cell dysfunction is thought to be the death of the β-cell [35]. However, recent evidence suggests that the dysfunction of β-cells in T2DM might be due to a more complex network of interactions between the environment and different molecular pathways implicated in cell biology. In an over-nourishment state, such as that associated with obesity, there is often hyperglycemia and hyperlipidemia are often present, favoring IR and chronic inflammation. In these conditions, the β-cells (because of their genetic susceptibility) are exposed to toxic pressures such as inflammation, inflammatory stress, ER stress, metabolic/oxidative stress, and amyloid stress, which may ultimately result in loss of islet integrity [35].

Insulin Resistance refers to the reduced metabolic response of insulin-sensitive cells to insulin or, at the systemic level, the impaired/lower response to circulating insulin by blood glucose levels [36]. There are three main types of IR or insulin deficiency: (1) diminished insulin secretion by β-cells; (2) plasma insulin antagonists, due to counter-regulatory hormones or non-hormonal bodies that impair insulin receptors or signaling; and (3) impaired insulin response in target tissues [37]. Insulin activity is influenced by the interaction of additional molecules, including growth hormone and IGF-1, in the fed state. During fasting, the insulin response is attenuated by glucagon, glucocorticoids, and catecholamines to prevent insulin-induced hypoglycemia. The insulin/glucagon plays a key role in this regulation, as it determines the relative degree of phosphorylation of enzymes downstream of the regulatory signaling pathway. While catecholamines promote lipolysis and glycogenolysis, glucocorticoids promote muscle catabolism, gluconeogenesis, and lipolysis. Therefore, excessive secretion of this hormone may be the cause of IR [38].

Hematological Complication of T2DM

Blood is made up of red blood cells, white blood cells (WBCs), and platelets, all of which perform vital functions such as tissue oxygenation by the red blood cells, infection control by white blood cells, and hemostasis by platelets. Hematopoietic processes in mammals can be affected by a variety of factors, including exposure to conventional drugs [39], plant extracts environmental pollutants, malignancies, and acute/chronic diseases.

Hematological parameters are regularly evaluated in diabetic patients. Some of these, such as white blood cell (WBC) count and hematocrit (HCT) level, have been linked to insulin resistance and incident T2DM [40]. Numerous studies examined the connections between hematological parameters and the existence of degenerative complications in type 2 diabetes. Hematological tests in animal diabetes studies are critical to understanding the systemic impact of diabetes on the hematopoietic system [41]. These tests provide valuable insights into physiological changes and aid in determining the overall health.

Hematological changes in diabetes are directly related to endothelial dysfunction and inflammation [3]. Hyperglycemia and its metabolic syndrome may be associated with changes in the various hematological parameters, including the morphology, size, and physiological function of red blood cells (RBCs), white blood cells (WBCs), and platelets [4]. Prolonged hyperglycemia may cause an increase in reactive oxygen species production (ROS), and the production of Advanced

Glycation End Products (AGEs), which are directly related to endothelial dysfunction and hematological alterations. The excessive release of oxidative stress due to the excessive production of ROS may result in tissue damage and hematologic alterations such as impaired red blood cell function (RBC), increased platelet hyperactivation, and impaired endothelial function. Insulin resistance is also linked to endothelial dysfunction; increased plasma levels of inflammatory markers; increased white blood cell count; and increased platelet hyperactivity, which may trigger and precipitate vascular complications in patients with type two diabetes (T2DM) [42]. Furthermore, oxidative stress leads to the dysfunction of red blood cells, the destruction of platelets, and tissue injury, which in turn may affect blood cell function and the hemostatic parameters, potentially leading to complications. Accelerated atherosclerosis plays a significant role in the development of diabetes. Platelet activation plays a major role in inflammation. Atherothrombotic processes contribute to the development of cardiovascular disease (CVD) in a T2DM patient. Mean platelet volume measures changes in either platelet stimulation or platelet production rate and increases in MPV have been observed in patients with diabetes with coronary heart disease (CHD), nephropathy, and retinopathy [43].

In general, hematological alterations have been reported in patients with T2DM. However, current guidelines for diabetes management do not suggest regular monitoring of hematological parameters. Studies conducted in various fields of study have yielded a variety of conflicting results. For example, some studies indicated that there was no clinically meaningful difference between diabetic and healthy subjects in terms of RBCs Indexes (RBCs), WBC Count, and Platelet Count, while another study indicated that the RBCs, WBCs, and PLT Indexes in diabetic patients were significantly higher than in healthy subjects [44]. Other studies indicated significantly lower RBC indices (RBCs excluding RDW) and WBCs and PLT Indices in diabetic versus control groups.

Diagnosis and Treatment for T2DM

Since the discovery of diagnostic techniques such as urine glucose and blood glucose tests to determine DM among individuals, the diagnostic criteria for DM have been much debated. The emphasis has been on measuring blood glucose levels and responses to oral glucose challenges, but there has been disagreement about the appropriate cutoff point for correctly distinguishing diabetics from non-diabetics [45]. The World Health Organization (WHO) developed diagnostic criteria for diabetes using the oral glucose tolerance test (OGTT), in which the patient is given 75g of glucose orally and their blood glucose level is measured two hours later. If a patient's blood glucose level is higher than normal, the patient is said to have impaired glucose tolerance. A fasting plasma glucose (FPG) of >7.8 mmol/L or an OGTT two-hour blood glucose of 11.1 mmol/L was established as a diagnostic criterion for DM based on this test. The American Diabetes Association (ADA) updated and revised these guidelines in 2003, listing three guidelines: (1) FPG of 7.0 mmol/L with symptoms of hyperglycemia, (2) random blood glucose of 11.1 mmol/L, or (3) a post-two-hour OGTT value of 11.1 mmol/L. The diagnosis must be repeated on another day, and DM was confirmed based on any of the three criteria. Although the OGTT result is more sensitive and specific than FPG, it is less reproducible, so FPG is preferred for screening and diagnosing diabetes [1].

A comprehensive diagnostic criterion for diabetes has been a source of ongoing debate because each method of glucose measurement has its own set of drawbacks. Following extensive deliberation, the WHO implemented an updated guideline for diagnosing diabetes, as shown in Table 1. WHO's diagnostic criteria were based on HbA1c concentration, FPG level, and two-hour plasma glucose value following a 75-g oral glucose tolerance test (OGTT).

Table 1: Criteria to diagnose diabetes mellitus by World Health Organization

Diagnostic criteria	Diagnosed with diabetes if one or more of the following criteria are met	Diagnosed with Impaired Glucose Tolerance (IGT) if both criteria are met	Diagnosed with Impaired Fasting Glucose (IFG) if any of the following criteria are met
Fasting blood glucose	≥ 7.0 mmol/L (126 mg/dL)	< 7.0 mmol/L (126 mg/dL)	6.1 – 6.9 mmol/L (110 – 125 mg/dL)
Two-hour plasma glucose after 75g oral glucose load (OGTT)	≥ 11.1 mmol/L (200 mg/dL)	≥ 7.8 and < 11.1 mmol/L (140 - 200 mg/dL)	< 7.8 mmol/L (140 mg/dL)
HbA1C	≥ 48 mmol/mol (≥ 6.5%)		
Random blood glucose	> 11.1 mmol/L (200 mg/dL)		

Type 2 diabetes mellitus (T2DM) is a multi-faceted disease and risk factor, including genetic predisposition. Poor diet and sedentary lifestyles are contributing factors to T2DM. As we age and become more overweight and obese, our bodies become more resistant to insulin, which is what causes the pathogenesis of T2DM [1]. Healthy eating habits, such as eating a Mediterranean diet and engaging in more physical activity, are key to maintaining a healthy blood glucose level. According to Chan *et al*, lifestyle changes, such as ideal weight management, reducing saturated fat intake, increasing fiber intake, and increasing exercise, can reduce the incidence of diabetes-high-risk individuals [46]. When lifestyle changes are not sufficient to lower blood glucose levels, traditional or modern medication can be used to help manage blood glucose levels.

Pharmacological Treatment

The emergence of diabetes since time immemorial has prompted researchers from all over the world to investigate various treatments and medications for this disease. This investigation resulted in the discovery of numerous medications, both traditionally prepared herbal medications and pharmacological drugs. Thus far, there are numerous classes of diabetes drugs available in the market, such as biguanides, sulfonylureas, meglitinides, thiazolidinediones, dipeptidyl peptidase- IV (DPP-4) inhibitors, α-glucosidase

inhibitors, sodium-glucose transport protein 2, bile acid sequestrants, GLP-1 receptor agonist, amylin mimetics and insulin therapy [1]. It is known that each of these diabetes medication classes works by lowering blood glucose levels through a different, targeted mechanism of action.

Plant-Based Treatment for Type 2 Diabetes Mellitus

Traditionally, various types of medicinal plants have been used to treat diabetes and other ailments. There are over 400 different plant species that have been reported to have anti-diabetic properties, even though not all of them have been scientifically proven to have antidiabetic [47, 48]. In Nigeria, the use of many plant species has been documented to have powerful antidiabetic effects, thus making them of great importance in treating diabetes.

Ethnomedicine has reported almost 1200 plant species used to treat DM. The most commonly used plants to control blood glucose levels are *Persea Americana Mill, Mangifera indica L., Moringa oleifera Lam., Momordica charantia L. Aloe vera (L.) Burm.f, Cassia abbreviata Oliv, Allium sativum L., Vernonia amygdalina Delile, Trigonella foenum-graecum L., Rosmarinus officinalis L, Plantago ovate Cinnamomum verum J. Pres, Ocimum tenuiflorum L., Gymnema sylvestre (Retz.), Zingiber officinale Roscoe* to mention but a few. These medicinal plants are a rich source of phytochemicals such as flavonoids, terpenoids, saponins, carotenoids, alkaloids, and glycosides, which contribute to antidiabetic activities. In most of the medicinal plants and secondary metabolites used for the treatment of DM, the antidiabetic mechanisms of action involve regulation of insulin signaling pathways, translocation of GLUT-4 receptor, activation of PPARγ and inhibition of intestinal α-amylase and α-glucosidase.

Neocarya Macropylla

Neocarya macrophylla (Sabine) Prance (formerly) *Parinari macrophylla Sabine* is commonly known as Gingerbread plum or Neou oil trees. It belongs to the Chrysobalanaceae family which is composed of 17 genera and 525 species widely distributed along coastal savannahs from Senegal to Liberia, woody savannahs of Southern Mali, Niger, and Northern Nigeria [49, 48].

Taxonomic Classification of Neocarya Macrophylla

Kingdom	:	Plantae	
Phylum	:	Tracheophyta	
Class	:	Magnoliopsida	
Order	:	Malpighiales	
Genus	:	Neocarya	
Species	:	Macrophylla	[48]

Phytochemical Composition

Phytochemical tests on *Neocarya macrophylla* show that it contains a bunch of different compounds, like carbohydrates, alkalis, flavonoids, anthraquinone, saponin, tannin, glycoside, steroids, and triterpene [49, 48].

Traditional Use

Neocarya macrophylla has been widely used in the Northern part of Nigeria for the treatment of a variety of diseases, such as asthma, dysentery, inflammation, pulmonary issues, skin infection, and wounds [49, 48].

Aqueous stem bark extract of *Neocarya macrophylla* was found to possess antidiabetic properties [40]. Short term toxicological analysis of NM seed oil based diet in albino rats did not show any major significant changes in the hematological parameters in the experimental animals compared with the controls on their hematological parameters also a study conducted by on the Assessment of acute and sub-chronic toxicological effects of *Neocarya macrophylla* seed cake on wistar rats Shows no Significant Changes In the hematological Parameters [50].

Conclusion

Type 2 Diabetes Mellitus is a complex metabolic disorder with rising global prevalence, driven largely by lifestyle factors. Conventional treatments remain essential, yet growing evidence supports the potential of plant-based therapies as complementary approaches. These natural remedies, rich in bioactive compounds, may aid in glycemic control and reduce complications. Further research and clinical trials are needed to validate efficacy and safety, but plant-based treatments hold promise as sustainable, holistic options in diabetes management.

References

1. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care, Jan 1, 2014; 37(Supplement_1):S81-90.
2. Farooqui R, Afsar N, Afroze IA. Role and significance of hematological parameters in diabetes mellitus. Ann Pathol Lab Med. 2019; 6(3):A158-162.
3. Kaur R, Kaur M, Singh J. Endothelial dysfunction and platelet hyperactivity in type 2 diabetes mellitus: Molecular insights and therapeutic strategies. Cardiovascular diabetology, Dec 2018; 17:1-7.
4. Milosevic D, Panin VL. Relationship between hematological parameters and glycemic control in type 2 diabetes mellitus patients. Journal of Medical Biochemistry, Mar 3, 2019; 38(2):164.
5. Gloyn AL, Ibberson M, Marchetti P, Powers AC, Rorsman P, Sander M, *et al*. Every islet matters: Improving the impact of human islet research. Nature Metabolism, Aug 2022; 4(8):970-977.
6. Leslie RD, Palmer J, Schloot NC, Lernmark A. Diabetes at the crossroads: Relevance of Disease Classification to Pathophysiology and Treatment. Diabetologia, Jan 2016; 59:13-20.
7. Baynes HW. Classification, Pathophysiology, Diagnosis and Management of Diabetes Mellitus. J Diabetes Metab, May 1, 2015; 6(5):1-9.
8. Banday MZ, Sameer AS, Nissar S. Pathophysiology of Diabetes: An Overview. Avicenna Journal of Medicine, Oct 2020; 10(04):174-188.
9. DeFronzo RA. Pathogenesis of type 2 diabetes mellitus. Medical Clinics, Jul 1, 2004; 88(4):787-835.
10. Leahy JL. Pathogenesis of Type 2 Diabetes Mellitus. Archives of Medical Research, May 1, 2005; 36(3):197-209.
11. Muoio DM, Newgard CB. Molecular and Metabolic Mechanisms of Insulin Resistance and β-cell Failure in Type 2 Diabetes. Nature Reviews Molecular cell Biology, Mar 2008; 9(3):193-205.
12. Atlas ID. IDF diabetes atlas [Internet], 2021.
13. Pastakia SD, Pekny CR, Manyara SM, Fischer L.

Diabetes in sub-Saharan Africa–from Policy to Practice to progress: Targeting the existing gaps for future care for Diabetes. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, Jun 22, 2017, 247-263.
14. Roden M, Shulman GI. The Integrative Biology of type 2 diabetes. Nature, Dec 5, 2019; 576(7785):51-60.
15. Stumvoll M, Goldstein BJ, Van Haeften TW. Type 2 diabetes: Principles of Pathogenesis and Therapy. The Lancet, Apr 9, 2005; 365(9467):1333-1346.
16. Cerf ME. Beta cell dysfunction and insulin resistance. Frontiers in Endocrinology, Mar 27, 2013; 4:37.
17. Zheng Y, Ley SH, Hu FB. Global aetiology and Epidemiology of type 2 Diabetes Mellitus and its complications. Nature Reviews Endocrinology, Feb 2018; 14(2):88-98.
18. Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, *et al*. Diet, Lifestyle, and the risk of type 2 Diabetes Mellitus in women. New England Journal of Medicine, Sep 13, 2001; 345(11):790-797.
19. Schellenberg ES, Dryden DM, Vandermeer B, Ha C, Korownyk C. Lifestyle interventions for Patients with and at risk for type 2 Diabetes: A systematic Review and Meta-analysis. Annals of Internal Medicine, Oct 15, 2013; 159(8):543-551.
20. McCarthy MI. Genomics, Type 2 Diabetes, and Obesity. New England Journal of Medicine, Dec 9, 2010; 363(24):2339-2950.
21. Fuchsberger C, Flannick J, Teslovich TM, Mahajan A, Agarwala V, Gaulton KJ, *et al*. The genetic Architecture of type 2 Diabetes. Nature, Aug 4, 2016; 536(7614):41-47.
22. Dimas AS, Lagou V, Barker A, Knowles JW, Mägi R, Hivert MF, *et al*. Impact of type 2 Diabetes susceptibility variants on Quantitative Glycemic traits Reveals mechanistic heterogeneity. Diabetes, Jun 1, 2014; 63(6):2158-2171.
23. Flannick J, Florez JC. Type 2 Diabetes: Genetic data Sharing to Advance Complex Disease Research. Nature Reviews Genetics, Sep 2016; 17(9):535-549.
24. Chan JC, Cheung CK, Swaminathan R, Nicholls MG, Cockram CS. Obesity, Albuminuria and Hypertension among Hong Kong Chinese with non-insulin-dependent Diabetes Mellitus (NIDDM). Postgraduate Medical Journal, Mar 1993; 69(809):204-210.
25. Sattar N, Gill JM. Type 2 Diabetes in Migrant South Asians: Mechanisms, Mitigation, and Management. The lancet Diabetes & endocrinology, Dec 1, 2015; 3(12):1004-1016.
26. McKeigue PM, Shah B, Marmot MG. Relation of central obesity and insulin resistance with high diabetes prevalence and cardiovascular risk in South Asians. The Lancet, Feb 16, 1991; 337(8738):382-386.
27. Haines L, Wan KC, Lynn R, Barrett TG, Shield JP. Rising incidence of type 2 diabetes in children in the UK. Diabetes care, May 1, 2007; 30(5):1097-1101.
28. 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, Mar 20, 2018; 13(3):e0194127.
29. Hillier TA, Pedula KL. Complications in young adults with early-onset type 2 diabetes: Losing the relative protection of youth. Diabetes Care, Nov 1, 2003; 26(11):2999-3005.
30. Weinstein AR, Sesso HD, Lee IM, Cook NR, Manson JE, Buring JE, *et al*. Relationship of physical activity vs body mass index with type 2 diabetes in women. Jama, Sep 8, 2004; 292(10):1188-1194.
31. Venkatasamy VV, Pericherla S, Manthuruthil S, Mishra S, Hanno R. Effect of physical activity on insulin resistance, inflammation and oxidative stress in diabetes mellitus. Journal of Clinical and Diagnostic Research (JCDR), Jul 17, 2013; 7(8):1764.
32. Bunney PE, Zink AN, Holm AA, Billington CJ, Kotz CM. Orexin activation counteracts decreases in nonexercise activity thermogenesis (NEAT) caused by high-fat diet. Physiology & Behavior, Jul 1, 2017; 176:139-148.
33. Fu Z, R. Gilbert E, Liu D. Regulation of insulin synthesis and secretion and pancreatic Beta-cell dysfunction in diabetes. Current Diabetes Reviews, Jan 1, 2013; 9(1):25-53.
34. Boland BB, Rhodes CJ, Grimsby JS. The dynamic plasticity of insulin production in β-cells. Molecular metabolism, Sep 1, 2017; 6(9):958-973.
35. Christensen AA, Gannon M. The beta cell in type 2 diabetes. Current Diabetes Reports, Sep 2019; 19:1-8.
36. Czech MP. Insulin action and resistance in obesity and type 2 diabetes. Nature medicine, Jul 1, 2017; 23(7):804-814.
37. Pearson T, Wattis JA, King JR, MacDonald IA, Mazzatti DJ. The effects of insulin resistance on individual tissues: An Application of a Mathematical Model of Metabolism in Humans. Bulletin of Mathematical Biology, Jun 2016; 78:1189-1217.
38. Nussey SS, Whitehead SA. Endocrinology: An Integrated Approach.
39. Al Qahtani SA. Drug-induced megaloblastic, aplastic, and hemolytic anemias: Current Concepts of Pathophysiology and Treatment. Int J Clin Exp Med, Jan 1, 2018; 11(6):5501-5512.
40. Tamariz LJ, Young JH, Pankow JS, Yeh HC, Schmidt MI, Astor B, *et al*. Blood viscosity and hematocrit as risk factors for type 2 diabetes mellitus: The Atherosclerosis Risk in Communities (ARIC) Study. American Journal of Epidemiology, Nov 15, 2008; 168(10):1153-1160.
41. Kottaisamy CP, Raj DS, Prasanth Kumar V, Sankaran U. Experimental Animal Models for Diabetes and its Related Complications: A Review. Laboratory Animal Research, Aug 24, 2021; 37(1):23.
42. Lioy B, Webb RJ, Amirabdollahian F. The association between the atherogenic index of plasma and cardiometabolic risk factors: A review. In Healthcare, Mar 28, 2023; 11(7):p966.
43. Tavil Y, Sen N, Yazici H, Turfan M, Hizal F, Cengel A, *et al*. Coronary heart disease is associated with mean platelet volume in type 2 diabetic patients. Platelets, Aug 1, 2010; 21(5):368-372.
44. Jabeen F, Rizvi HA, Aziz F, Wasti AZ. Hyperglycemic induced variations in hematological indices in type 2 diabetics. IJAR. 2013; 1(8):322-334.
45. Kirchhof M, Popat N, Malowany J. A historical perspective of the diagnosis of diabetes. University of Western Ontario Medical Journal, Sep 1, 2008; 78(1):7-11.

46. Chen R, Ovbiagele B, Feng W. Diabetes and stroke: Epidemiology, pathophysiology, pharmaceuticals and outcomes. The American Journal of the Medical Sciences, Apr 1, 2016; 351(4):380-386.
47. Iweala EE, Oludare FD. Hypoglycemic effect, biochemical and histological changes of Spondias mombin Linn. And Parinari polyandra Benth. Seeds ethanolic extracts in alloxan-induced diabetic rats.
48. Yusuf AJ, Abdullahi MI, Muhammad AA, Ibrahim KG. Neocarya macrophylla (Sabine) Prance: Review on taxonomy, ethnobotany, phytochemistry and biological activities, Nov 1, 2021; 10. Preprints retrieved from: www. preprints. org
49. Halilu ME, Abah JO, Almustapha NL, Achor M. Phytochemical screening and mineral element analysis of the root bark of Parinari macrophylla Sabine (Chrysobalanaceae) and its effect on microorganisms.
50. Ajayi AI, Owolabi EO, Olajire OO. Alcohol use among Nigerian university students: Prevalence, correlates and frequency of use. BMC Public Health, Dec 2019; 19:1-11.