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Natural allies against type 2 diabetes: the promises of probiotics and medicinal plants

Abstract

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder whose prevalence is steadily increasing worldwide. In light of the limitations of conventional pharmacological treatments, particularly their side effects and costs, interest in natural alternatives has grown, especially regarding medicinal plants and probiotics. Medicinal plants hold an important place in traditional medicine. Many plant species have demonstrated hypoglycemic and antioxidant effects, contributing to the reduction of fasting blood glucose and improvement of insulin sensitivity. The World Health Organization encourages the scientific evaluation of these plants to standardize their use and ensure their safety. Meanwhile, probiotics are gaining increasing interest due to their ability to modulate the gut microbiota, which is implicated in the pathophysiology of T2DM. Randomized clinical trials have shown that probiotic supplementation can improve insulin resistance, reduce glycated hemoglobin, and fasting blood glucose, although results remain heterogeneous depending on strains, doses, and duration of intervention. This review thoroughly examines current studies on medicinal plants and probiotics and their influence on metabolic functions associated with diabetes. The chapter concludes with the necessity of integrating these strategies into a comprehensive management plan, based on scientific evidence and appropriate patient education.

Keywords: type 2 diabetes, natural therapeutic alternatives, medicinal plants, probiotics, hypoglycemic activities

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Introduction

Current statistics and projections of diabetes

The diabetes epidemic has reached alarming levels, necessitating immediate attention and effective strategies for prevention and management. The International Diabetes Federation (IDF) reported that approximately 537 million adults were living with diabetes in 2021. This number is expected to reach 643 million by 2030 and 783 million by 2045. Such increases reflect not only the rising prevalence of the disease but also highlight a significant public health challenge on a global scale. Understanding these statistics is essential to grasp the broader implications of diabetes on individual and community health, as well as on health economics.[1–3]

Demographic changes significantly influence the rising incidence of diabetes. Urbanization, population aging, and lifestyle changes are key contributors to this trend. The World Health Organization (WHO) indicates that the prevalence of diabetes is particularly high in low- and middle-income countries, where rapid economic growth often leads to increased consumption of processed foods and reduced physical activity.[4]

The risk factors associated with diabetes are complex, involving genetic, environmental, and behavioral elements. Obesity, a major risk factor, is closely linked to the onset of Type 2 diabetes.[5] The WHO reports that global obesity rates have nearly tripled since 1975, with over 1.9 billion adults classified as overweight in 2021. This concerning trend is particularly evident among children and adolescents, who increasingly face unhealthy eating habits and sedentary lifestyles. The interaction of these risk factors creates a challenging landscape that demands targeted interventions to mitigate the impact of diabetes.[6]

Furthermore, disparities in diabetes prevalence across different regions and populations complicate the issue. The International Diabetes Federation (IDF) highlights that the highest prevalence of diabetes is found in the Middle East and North Africa, where approximately 12.2% of the adult population is affected. In contrast, while Sub-Saharan Africa has lower prevalence rates, it faces unique challenges related to access to healthcare and resources for diabetes management. These disparities underscore the need to tailor interventions to meet the specific needs of diverse populations, ensuring that prevention and management strategies are both effective and equitable.[1–3]

Economic burden of diabetes

The rising prevalence of diabetes is not only an urgent public health issue; it also represents a substantial economic challenge that impacts healthcare systems and economies worldwide. The financial implications of diabetes create a complex web of costs that require immediate attention and innovative solutions.[7] According to the IDF, the global economic cost of diabetes was estimated at USD 966 billion in 2021, with projections suggesting that this figure could reach USD 1.03 trillion by 2045.[2]

This staggering amount includes direct medical expenses such as hospitalizations, medications, and outpatient care, as well as indirect costs related to lost productivity, premature mortality, and decreased quality of life. For example, Zhang et al. found that individuals with diabetes incurred medical costs approximately 2.3 times higher than those without the condition. A 2023 report from the American Diabetes Association revealed that the average annual medical expenses for a person with diabetes were about USD 16,752, with nearly half of these costs attributed to hospitalizations.[8] These figures highlight the financial pressure on healthcare systems, particularly in low- and middle-income countries where resources are already scarce.[9,10]

Indirect costs, often overlooked, can be equally significant. Productivity losses due to diabetes-related complications and absenteeism can severely hinder economic growth. A systematic

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review published in Health Affairs in 2023 estimated that diabetes-related productivity losses in the United States exceeded USD 90 billion per year. Additionally, the emotional and psychological consequences of living with diabetes can lead to increased healthcare utilization and additional financial strain, creating a vicious cycle that intensifies the overall economic impact.[11]

Beyond direct and indirect costs, the broader implications of diabetes extend to public health resources. As the prevalence of diabetes continues to rise, healthcare systems face increasing pressure to allocate resources effectively. This challenge is exacerbated by the rising incidence of comorbidities associated with diabetes, such as cardiovascular diseases and renal failure, which further increase healthcare costs. Rosella et al. demonstrated that individuals with diabetes and comorbid conditions had healthcare costs 3.5 times higher than those without diabetes (Table 1).[12]

Table 1 Global prevalence of diabetes (all types)[1,2,13,14]

Metric	2021	Projection 2030	Projection 2045
Total cases	537 million adults (ages 20–79)	643 million	783 million
Prevalence rate	10.5% of adults	~11.4% (estimation)	~13.9% (estimation)
Undiagnosed cases	~50% of all cases	Unspecified data	Unspecified data
Healthcare expenditures	$966 billion	> $1 trillion (forecast)	Unspecified data

Understanding Type 2 diabetes mellitus (T2DM): pathophysiology, causes, diagnosis, and pharmacological treatments of diabetes

Commonly referred to as diabetes, diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia when treatment is not received. There are three main types of diabetes with distinct characteristics (Table 2). Type 1 diabetes mellitus (T1DM) is an autoimmune condition where the immune system destroys insulin-producing beta cells in the pancreas, resulting in little or no insulin production; it typically develops during childhood or early adulthood but can occur at any age. Type 2 diabetes mellitus (T2DM) results from insulin resistance, where the body fails to use insulin effectively, often linked to obesity, a sedentary lifestyle, and genetic factors; it is more common in adults but increasingly affects younger populations.[13,14] Monogenic DM is a rare form caused by mutations in a single gene, leading to atypical presentations of diabetes such as neonatal diabetes or maturity onset diabetes of the young (MODY); it differs significantly from type 1 and type 2 diabetes in its genetic basis and management.[15–17]

Table 2 Types and general characteristics of DM[16,17]

Characteristic	T1DM	T2DM	Monogenic diabetes
Main cause	Autoimmune destruction of β cells	Progressive dysfunction of β cells + insulin resistance	Genetic mutations affecting insulin production (e.g., MODY, neonatal diabetes)
Age of onset	Typically <30 years	Typically >30 years	Generally <25 years
Association with obesity	Uncommon	Very common	Variable (depends on subtype)
Risk of ketoacidosis	High (common at diagnosis)	Rare (usually stress-induced)	Rare
Insulin levels	Extremely low/undetectable	Variable (can be normal, high, or low)	Normal or high (depending on the mutation)
Autoantibodies	Present (e.g., GAD, IA-2)	Absent	Absent
Genetic factors	HLA-D antigen associations	Polygenic inheritance	Autosomal dominant inheritance
Treatment	Life-long insulin required	Lifestyle modifications, oral medications, or insulin	Insulin or oral sulfonylureas (e.g., neonatal diabetes)
Prevalence	~5–10% of diabetes cases	~90–95% of diabetes cases	Rare (<1% of diabetes cases)

T2DM pathophysiology

The T2DM results from a dual pathophysiological mechanism involving insulin resistance (IR) and β-cell dysfunction, with obesity, genetic predisposition, and environmental factors exacerbating these processes (Table 3). Insulin resistance, often associated with visceral adiposity, reduces glucose uptake in skeletal muscles and adipose tissue while increasing hepatic glucose production due to elevated free fatty acids (FFAs) and pro-inflammatory cytokines such as IL-1β and TNF-α.[18,19]

Table 3 Pathophysiology of Type 2 diabetes mellitus[18,19]

Mechanism	Key features	Consequences
Main pathways in type 2 diabetes mellitus		
Insulin resistance	Reduced glucose absorption in muscle/adipose tissues; increased hepatic glucose production	Hyperglycemia, compensatory hyperinsulinemia, dyslipidemia
β-cell dysfunction	Altered insulin synthesis/secretion; endoplasmic reticulum stress due to misfolded proinsulins/amyloid peptides	Inadequate insulin response to hyperglycemia; progressive β-cell failure
Secondary pathways and contributing factors		

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Table 3 Continued...

Inflammation	Adipose tissue infiltration of macrophages; pro-inflammatory cytokines (IL-1 β, TNF- α)	Altered insulin signaling via NF- κ B/ JNK pathways; oxidative stress
Mitochondrial dysfunction	Altered electron transport chain activity; overproduction of ROS	Apoptosis of β cells, altered ATP production, and insulin secretion
Lipotoxicity	Increased free fatty acids (FFA) disrupt β cell function; accumulation of ceramide in tissues	Insulin resistance, dedifferentiation of β cells, and apoptosis
Hyperglucagonemia	Increased glucagon secretion by α cells disrupts the insulin-glucagon balance, exacerbating hyperglycemia. Related to the paracrinopathy of islets.	- Loss of reciprocal regulation of β cells/ α cells - Increased hepatic glucose production
Epigenetic modifications	Persistent metabolic memory due to epigenetic modifications induced by hyperglycemia (e.g., DNA methylation, histone acetylation).	- Long-term activation of pro-inflammatory genes - Suppression of the AMPK pathway
Activation of NF- κ B	Triggered by hyperglycemia/inflammation; promotes pro-inflammatory genes	Chronic inflammation, insulin resistance, and β cell damage
Suppression of AMPK	Reduced adiponectin/LKB1 activity; AMPK degradation mediated by PP2A/C	Altered glucose/lipid metabolism; exacerbation of hyperglycemia

At the same time, pancreatic β cells fail to compensate for insulin resistance (IR) with adequate insulin secretion, partly due to glucolipotoxicity from chronic hyperglycemia and free fatty acids (FFAs), which disrupt glucose detection via GLUT2 and ATP-dependent potassium channels. This stress on β cells triggers endoplasmic reticulum (ER) dysfunction, oxidative stress via reactive oxygen species (ROS), and inflammation, accelerating apoptosis and amyloid deposition. Over time, the architecture of the islets deteriorates, altering paracrine signaling between α and β cells, leading to further hyperglycemia. Mitochondrial dysfunction in β cells and peripheral tissues, driven by FFA metabolism and ROS, exacerbates metabolic inefficiency. Chronic inflammation, intestinal dysbiosis, and epigenetic changes perpetuate IR and β cell failure, creating a self-reinforcing cycle that progresses to overt diabetes. Although IR often precedes the decline of β cells, their combined effects amplify hyperglycemia, with advanced disease potentially involving pancreatic atrophy and exocrine dysfunction.[18,19]

T2DM causes

T2DM risk factors can be classified into non-modifiable and modifiable factors, with lifestyle choices playing a significant role in reducing risk (Table 4). Non-modifiable factors include age (particularly beyond 35 to 45 years), family history of diabetes, race/ethnicity (higher risk among African Americans, Hispanics/ Latinos, Asian Americans, Native Americans, and Pacific Islander populations), and pregnancy-related conditions such as gestational diabetes or giving birth to a baby weighing over 9 pounds. Modifiable factors involve lifestyle and metabolic conditions: overweight (BMI ≥25 for most adults, ≥23 for Asian Americans) or obesity, physical inactivity, diets high in saturated fats and simple carbohydrates, hypertension (≥130/80 mmHg), dyslipidemia (low HDL cholesterol or high triglycerides), smoking, and prediabetes. Environmental influences such as sedentary environments and air pollution also contribute to modifiable risks. Although non-modifiable factors cannot be altered, it is possible to address modifiable factors through weight management, regular physical activity (e.g., 150 minutes/week of moderate exercise), dietary adjustments, blood pressure control, and smoking cessation, which can significantly reduce or delay the onset of Type 2 Diabetes Mellitus.[20,21]

Table 4 Key risk factors for Type 2 diabetes[20,21]

Risk factor	Description	Key details
Age	Increased risk with advanced age	The risk increases after 35-45 years, although cases among young individuals are on the rise
Obesity	Excess body weight or obesity	BMI ≥25 (≥23 for Asian Americans); waist circumference >40" (men), >35" (women)
Family history	First-degree relative with Type 2 diabetes	Parent or sibling with diabetes
Ethnicity	Higher risk in certain populations	African American, Hispanic, Asian American, Native American, Pacific Islander
Prediabetes	Glucose intolerance or impaired fasting glucose	IGF or IGT
Hypertension/ Dyslipidemia	High blood pressure or abnormal lipid profiles	BP ≥130/80 mmHg or HDL <40 mg/dL/triglycerides >150 mg/dL
Gestational diabetes	History of diabetes during pregnancy	Previous gestational diabetes or delivery of a baby >9 lbs
Polycystic ovary syndrome	Hormonal disorder related to insulin resistance	PCOS increases the risk
Sedentary lifestyle	Physical inactivity	Low activity levels or prolonged sitting
Low birth weight	Reduction in fetal growth	Associated with subsequent insulin resistance
Obstructive sleep apnea	Sleep disorders related to insulin resistance	Independent risk factor, particularly in obese adults

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Table 4 Continued...

Menstrual irregularities	Prolonged/irregular cycles or early menopause	Irregular cycles increase the risk by 32 to 66%; early menopause (before age 40) increases the risk
Alcohol/ Smoking	Substance consumption	Alcohol consumption and smoking are linked to metabolic dysfunction

T2DM diagnosis

The diagnosis of T2DM primarily relies on blood glucose tests and clinical evaluation (Table 5). The glycated hemoglobin (HbA1c) test is the most common method, measuring average blood sugar levels over two to three months: results below 5.7% are normal, 5.7% to 6.4% indicate prediabetes, and ≥6.5% on two separate tests confirm diabetes. When HbA1c is not available or unreliable, fasting plasma glucose (≥126 mg/dL on two tests) or random blood glucose (≥200 mg/dL with symptoms such as polyuria, polydipsia, or blurred vision) are used. The oral glucose tolerance test (OGTT) is less common for type 2 but may be employed in specific cases, with diabetes diagnosed if levels exceed 200 mg/dL after two hours. Screening is recommended for adults aged ≥35 years, those with obesity or risk factors (e.g., family history, gestational diabetes), and children with obesity and risk factors. After diagnosis, distinguishing type 2 from type 1 involves assessing insulin production and autoimmune markers, although some research proposes subtypes such as severely insulin-deficient diabetes or insulin-resistant diabetes based on metabolic profiles. Regular monitoring of HbA1c (every 2 to 6 months) and management through lifestyle modifications (diet, exercise, weight loss) or pharmacotherapy help prevent complications.[22,23]

Table 5 Diagnosis of T2DM[22,23]

Test	Normal	Prediabetes	Diabetes
HbA1c	<5.7% (<39 mmol/mol)	5.7–6.4% (39–47 mmol/mol)	≥6.5% (≥48 mmol/mol)
Fasting plasma glucose (FPG)	<100 mg/dL (<5.6 mmol/L)	100–125 mg/dL (5.6–6.9 mmol/L)	≥126 mg/
2-hour glucose tolerance test	<140 mg/dL (<7.8 mmol/L)	140–199 mg/	≥200 mg/
Random plasma glucose	N/A	N/A	≥200 mg/dL (≥11.1 mmol/L) with symptoms

T2DM management by lifestyle modifications

Lifestyle modifications play a crucial role in the management and prevention of diabetes, supported by extensive evidence. Table 6 presents a structured summary of the main lifestyle modifications for diabetes management, synthesized from clinical guidelines and recommendations. Dietary changes are fundamental, emphasizing the consumption of whole grains, fiber-rich foods, and non-starchy vegetables while reducing intake of added sugars, processed foods, and saturated fats. The Mediterranean diet, characterized by healthy fats, lean proteins, and plant-based foods, is particularly effective for diabetes management and prevention. Portion control strategies, such as the diabetic plate method, help regulate carbohydrate intake and stabilize blood sugar levels. Physical activity is equally vital; engaging in at least 150 minutes of moderate-intensity aerobic exercise per week improves insulin sensitivity, glucose regulation, and weight management. Resistance training and muscle-strengthening exercises further enhance glycemic control. The timing and composition of meals are also important; consuming proteins and vegetables before carbohydrates can moderate post-meal glucose spikes. Weight loss is a major factor in reducing the risk of T2DM, with studies showing that lifestyle interventions can reduce diabetes risk by up to 58% in individuals with impaired glucose tolerance (IGT). Behavioral counseling programs focused on diet and exercise are recommended to maintain long-term benefits. Evidence also suggests that lifestyle changes may mitigate genetic predispositions to diabetes. Together, these modifications offer a comprehensive approach to effectively manage diabetes while reducing complications such as cardiovascular diseases and renal failure.[24–27]

Table 6 Preventive strategies for T2DM

Strategy	Key components	Evidence and outcomes
Lifestyle interventions	- Weight Loss: Aim for a reduction of ≥7% in body weight. - Physical Activity: ≥150 min/week of moderate-intensity exercise (e.g., brisk walking). - Dietary patterns: Mediterranean, low-carb, plant-based, or DASH diets emphasizing whole grains, vegetables, and minimally processed foods	- 58% reduction in diabetes incidence (DPP trial). - Lasting benefits: 27% to 43% risk reduction 7 to 30 years post-intervention
Structured programs	- Diabetes Prevention Program (DPP): Weight loss and activity plans based on specific goals. - Technology-assisted programs: Digital tools for monitoring and support	- Cost-effective and scalable for population health. - Certified programs recommended for accessibility

T2DM pharmacological treatments

Pharmacological agents for T2DM include several classes with distinct mechanisms of action. Metformin, a biguanide, remains the first-line treatment by reducing hepatic glucose production and improving insulin sensitivity, although gastrointestinal side effects may occur. Sulfonylureas (e.g., glimepiride, glyburide) stimulate pancreatic insulin secretion but carry risks of hypoglycemia and weight gain, with evidence suggesting earlier insulin dependence compared to insulin itself. Meglitinides (e.g., repaglinide) act similarly but have shorter durations of action, requiring dosing at meal times. Thiazolidinediones (TZD) like pioglitazone improve insulin sensitivity via PPARγ activation but are limited by cardiovascular

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risks and fluid retention. DPP-4 inhibitors (e.g., sitagliptin) prolong the activity of incretin hormones without causing hypoglycemia, making them safer alternatives. SGLT2 inhibitors (e.g., empagliflozin) promote urinary glucose excretion, providing cardiovascular and renal benefits but increasing the risk of genital infections. GLP-1 agonists (e.g., liraglutide) enhance glucose-dependent insulin secretion and appetite suppression, often preferred over sulfonylureas in patients with cardiovascular comorbidities. Alpha-glucosidase inhibitors, such as acarbose, slow carbohydrate absorption in the intestine, thereby contributing to better post-meal blood glucose control (Table 7).[28,29]

Table 7 Medications for T2DM[28,29]

Drug class	Examples	Effectiveness	Key benefits	Common side effects
Biguanides	Metformin (Glucophage®)	First-line therapy; reduces hepatic glucose production	Weight neutral; reduces cardiovascular risk in overweight patients	Gastrointestinal discomfort (diarrhea, nausea), risk of lactic acidosis
Sulfonylureas	Glipizide (Glucotrol®), Glimepiride (Amaryl®)	Moderate efficacy; stimulates insulin release	Rapid glucose lowering	Hypoglycemia, weight gain
Meglitinides	Repaglinide	Rapid insulin secretion; short duration	Flexible dosing before meals	Hypoglycemia, weight gain
Thiazolidinediones	Pioglitazone (Actos®)	Moderate efficacy; improves insulin sensitivity	Neutral effect on weight	Weight gain, water retention, risk of bladder cancer (pioglitazone)
DPP-4 Inhibitors	Sitagliptin (Januvia®), Saxagliptin (Onglyza®)	Slight to moderate efficacy; enhances incretin effect	Neutral effect on weight; low risk of hypoglycemia	Risk of nasopharyngitis, pancreatitis
SGLT-2 Inhibitors	Canagliflozin (Invokana®), Empagliflozin (Jardiance®)	Moderate efficacy; promotes renal excretion of glucose	Cardiovascular protection (reduction of major cardiovascular events, heart failure); renal protection (slowing the progression of chronic kidney disease); weight loss (2-3 kg)	Genital fungal infections, risk of DKA, hypotension
GLP-1 receptor agonists	Liraglutide	High efficacy; slows gastric emptying, reduces glucagon	Weight loss (5-15% of body weight); cardiovascular benefits (reduction of strokes)	Nausea, vomiting, risk of pancreatitis
Alpha-glucosidase inhibitors	Acarbose	Moderate efficacy; delays carbohydrate absorption	Low risk of hypoglycemia	Flatulence, abdominal pain

The positive impact of probiotics on T2DM and health

Definition and diversity of probiotics

T2DM is associated with dysbiosis of the gut microbiota, characterized by imbalances in bacterial populations, such as altered Firmicutes/Bacteroidetes ratios and a reduction in beneficial species. Dysbiosis exacerbates insulin resistance through mechanisms including increased intestinal permeability, systemic inflammation mediated by cytokines such as TNF-α and IL-6, and altered glucose metabolism.[30,31] Probiotics are live microorganisms that confer health benefits when consumed in adequate amounts. Often referred to as "good" or "beneficial" bacteria, probiotics show therapeutic potential by restoring microbial balance, improving insulin sensitivity, and enhancing glycemic parameters such as HbA1c and fasting blood glucose.[32,33]

Microbial probiotics have been collected directly from the gastrointestinal tract (GIT) or other sources such as feces and milk. The most common probiotic strains are lactic acid bacteria (LAB), which are considered safe according to the Food and Drug Administration (FDA).[33] The most common and well-studied probiotic genera include *Lactobacillus* and *Bifidobacterium.*[32,34,35] Within the genus *Lactobacillus*, notable species include *L. acidophilus*, *L. casei*, *L. rhamnosus*, and *L. helveticus*, which have been associated with various health benefits.[36] Important species of *Bifidobacterium* include *B. animalis*, *B. breve*, *B. lactis*, and *B. longum*, each having distinct potential benefits such as immune system support and aiding digestion.[37]

Other significant probiotic genera include *Saccharomyces* (particularly *S. boulardii*), Escherichia (specifically *E. coli* Nissle 1917), *Streptococcus*, *Enterococcus*, and *Bacillus.*[32,34] These various probiotic species have been studied for their ability to modulate the gut microbiota, potentially influencing various aspects of human health, including immune function, digestive health, and even metabolic processes.[33] The efficacy of probiotics often depends on the specific strain used, as different strains within the same species can have distinct effects on the host. This diversity in probiotic species and strains allows for targeted approaches to address various health concerns and highlights the complexity of the human microbiome and its interaction with probiotic supplementation.[38,39]

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Mechanisms of action of antidiabetic probiotics

The mechanisms of action of probiotics are diverse and include competitive exclusion of pathogens by occupying adhesion sites in the intestine, strengthening the intestinal mucosal barrier, modulating immune responses, and synthesizing neurotransmitters such as serotonin and dopamine via the gut-brain axis. Probiotics improve the composition of the gut microbiota by increasing beneficial bacteria and producing antimicrobial substances such as short-chain fatty acids, organic acids, and bacteriocins, which suppress harmful microbes. They also regulate immune responses by stimulating dendritic cells, macrophages, and lymphocytes to produce anti-inflammatory cytokines while balancing the activity of helper T cells to mitigate allergic reactions. Beyond gut health, probiotics have systemic benefits such as improving nutrient absorption, alleviating lactose intolerance, detoxifying environmental pollutants, and synthesizing essential vitamins like riboflavin and folic acid. Their role in disease prevention is notable; they inhibit carcinogenesis through mechanisms such as binding to carcinogens, modulating cell proliferation pathways (e.g., NF-kappa B), and inducing apoptosis in cancer cells. Probiotics also support mental health by influencing mood and stress pathways via neurotransmitter production. With applications ranging from managing gastrointestinal disorders like irritable bowel syndrome to reducing eczema in children, probiotics are increasingly recognized as essential for overall health and well-being.[39–42] Some probiotics, often derived from fermented foods or isolated from natural sources, exhibit hypoglycemic effects by inhibiting enzymes such as α-glucosidase and dipeptidyl peptidase-IV (DPP-IV), which are critical in carbohydrate digestion and glucose regulation. For example, strains such as *Lactobacillus acidophilus* and *Lacticaseibacillus plantarum* have shown effectiveness in lowering fasting blood glucose levels, HbA1c, and insulin resistance in diabetic models while improving antioxidant enzyme activity and gut microbiota composition (Table 8).[43]

Table 8 Key pathways and health benefits of probiotics[39–42]

Mechanism of action	Key pathways	Health benefits
Competitive exclusion	Compete with pathogens for nutrients/receptor binding sites	Prevent colonization by pathogens, reduce infections
Antimicrobial production	SCFAs, organic acids, hydrogen peroxide, bacteriocins	Inhibit pathogenic bacteria, detoxify toxins
Strengthening the intestinal barrier	Production of mucin, tight junction proteins (occludin, claudin-1)	Prevent intestinal permeability, reduce inflammation
Immunomodulation	Activation of dendritic cells/macrophages, anti-inflammatory cytokines (IL-10, TGF-β)	Mitigate allergies, autoimmune diseases
Modulation of neurotransmitters	Serotonin, GABA, dopamine via the gut-brain axis	Improve mood, reduce stress-related disorders
Anticancer effects	Induction of apoptosis (TRAIL, Bax), inhibition of the NF-κB pathway	Suppress carcinogenesis, inhibit tumor growth
Cholesterol regulation	Deconjugation of bile acids, modulation of lipid metabolism	Reduction of LDL cholesterol, improvement of cardiovascular health
Nutrient metabolism	Lactase production, synthesis of vitamins (K, B12, folate)	Improvement of nutrient absorption, alleviation of lactose intolerance

Clinical evidence supporting the use of probiotics

Recent meta-analyses and systematic reviews of randomized controlled trials (RCTs) demonstrate that probiotic supplementation shows promise as an adjunct therapy for the management of T2DM. A 2023 meta-analysis involving 30 RCTs with 1,827 patients found significant reductions in fasting blood glucose (FBG), HbA1c, insulin levels, and insulin resistance (HOMA-IR) compared to placebo, with more pronounced effects observed in Caucasian populations, those with a BMI ≥30 kg/m², and when using *Bifidobacterium*-based probiotics or foods.[44] Another meta-analysis highlighted that multi-strain probiotics improved HbA1c, FBG, and HOMA-IR in both short-term (≤8 weeks) and long-term (≥12 weeks) interventions, although heterogeneity in study results was noted.[30,44] A 2024 RCT evaluating fermented beverages containing *Lactobacillus* confirmed these trends, with probiotics reducing HbA1c and FBG while improving insulin sensitivity markers.[45] Subgroup analyses revealed time-dependent effects: reductions in HbA1c became significant after 6 to 8 weeks, while improvements in insulin and HOMA-IR were evident at both 6-8 weeks and 12-24 weeks.[44] Although some studies reported inconsistent results, meta-analyses consistently show that probiotics lower blood glucose levels by approximately 11 mg/dL on average.[45,46] These results suggest that probiotics may improve glycemic control through mechanisms involving the modulation of the gut microbiota, although optimal strains, dosages, and durations require further standardization.[44,46] A randomized controlled trial conducted by Kobyliak et al. in Ukraine studied the effects of *Lactobacillus rhamnosus* GRI and *Lactobacillus reuteri* RC-14 on glycemic control in patients with T2DM.[47] The study revealed that participants consuming these probiotics experienced a notable reduction in fasting blood glucose levels and an improvement in HbA1c levels compared to those in the placebo group. Another significant study conducted by Vrieze et al. in the Netherlands examined the effects of a multi-strain probiotic formulation on insulin sensitivity in prediabetic individuals. The results indicated that participants receiving the probiotic intervention showed significant improvements in insulin sensitivity, measured by the Homeostasis Model Assessment of Insulin Resistance.[48] This study not only reinforces the potential of probiotics in managing blood glucose but also highlights their role in preventing the progression from prediabetes to Type 2 diabetes. A meta-analysis conducted by Khalesi et al. examined various studies on different strains of probiotics and their impact on inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6). The analysis concluded that probiotics significantly reduced these inflammatory markers, which are often elevated in diabetic individuals. By mitigating inflammation, probiotics can improve insulin sensitivity and overall metabolic health.[49]

In addition to their direct influence on glycemic control, probiotics also affect the composition of the gut microbiota, which is crucial for metabolic processes. A study conducted by Zhang et al. explored the gut microbiome of individuals with Type 2 diabetes before and after

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probiotic supplementation. The results indicated a significant increase in beneficial bacteria, such as *Bifidobacterium* and *Lactobacillus*, accompanied by a decrease in pathogenic bacteria. This change in the gut microbiota was linked to better metabolic outcomes, further supporting the idea that probiotics can beneficially improve gut health for diabetes management.[50]

Despite the encouraging evidence, it is important to recognize the variability of individual responses to probiotic supplementation. Factors such as diet, genetics, and the existing composition of the gut microbiota can significantly influence the effectiveness of probiotics. Therefore, personalized approaches to the use of probiotics may be essential to optimize their benefits in diabetes management. Future research should aim to identify specific strains that produce the most significant effects in different populations and deepen our understanding of the underlying mechanisms governing these responses.[51]

Reflecting on the clinical evidence presented, it is clear that probiotics are a valuable complement to standard diabetes treatments. Their ability to improve glycemic control, enhance insulin sensitivity, and reduce inflammation makes them an attractive option for individuals seeking to manage their diabetes more effectively. Furthermore, incorporating probiotics into daily routines is feasible through dietary sources such as yogurt, kefir, and fermented foods, making them accessible and convenient for many (Table 9).[52]

Table 9 Clinical trials investigating probiotics for the management of Type 2 diabetes

Author (Year)	Patients	Probiotic strain(s)	Duration (weeks)	Key results
[53]	150	NM (multi-strain probiotic)	12	Reduction of FBG, postprandial blood glucose, and HbA1c with metformin
[54]	156	*Bifidobacterium animalis subsp. lactis (BB-12)*	12	Improvement of glycemic control, reduction of HbA1c, and treatment adherence
[55]	150	*Bifidobacterium animalis dn-173 010*	16	Improvement of glycemic control, lipid profile, and inflammatory markers
[56]	50	*Lactobacillus paracasei HII01*	12	Reduction of hyperglycemia and inflammatory indicators through modulation of the gut microbiota
[57]	58	*B. animalis M8, B. animalis V9, L. casei Zhang, L. plantarum P-8, L. rhamnosus Probio-M9*	12	Increased hypoglycemic response when combined with metformin
[58]	76	*Clostridium butyricum, Akkermansia muciniphila, C. beijerinckii, A. hallii, B. infantis*	12	Reduction of postprandial blood glucose in patients treated with metformin
[59]	40	*Lactobacillus casei*	8	Modified levels of SIRT1 and fetuin-A, improving glycemic response
[60]	150	*Multi-strain (B. bifidum, L. brevis, L. acidophilus, L. salivarius, L. casei, Lactococcus lactis, B. lactis)*	24	HOMA-IR reduced in monotherapy
[61]	60	*Lactobacillus with Bifidobacterium*	12	Improvement in glycemic control and cardiometabolic risk factors

Functional foods and innovative health supplements based on probiotics

Probiotic strains with anti-diabetic properties, particularly those from the *Lactobacillus*, *Bifidobacterium*, and *Lacticaseibacillus* species, have demonstrated significant potential in both food and pharmaceutical applications due to their ability to regulate glucose metabolism, reduce oxidative stress, and improve insulin sensitivity. These properties make them suitable for incorporation into functional foods such as fermented beverages or as nutraceutical and pharmaceutical ingredients aimed at managing T2DM. Furthermore, their ability to modulate gut health by increasing short-chain fatty acids (SCFAs) and reducing inflammation further supports their therapeutic use. Clinical studies suggest that these probiotics can be developed into dietary supplements or medications with fewer side effects compared to conventional anti-diabetic drugs, offering a promising avenue for the prevention and treatment of diabetes. Probiotics can be consumed through various food sources, including fermented foods like yogurt, kefir, sauerkraut, and kimchi, as well as dietary supplements.[53–61] The effectiveness of probiotics largely depends on the strain, dosage, and individual health conditions. Indeed, Garcia et al.[62] have shown that not all probiotics are equal; some strains may be more effective for specific health outcomes, including glycemic control in diabetes (Table 10).

Table 10 Examples of antidiabetic probiotic strains and their applications[60,62]

Strain	Source	Key antidiabetic mechanisms	Applications
Lactiplantibacillus	Fermented foods/ humans	Inhibition of α-glucosidase/ α-amylase (>75% and >85% activity), antioxidant activity	Functional foods, dietary supplements, probiotic formulations
Lacticaseibacillus	Fermented foods/ humans	Enzymatic inhibition similar to L. plantarum, survival of probiotics in the gastrointestinal tract	Probiotic supplements, fermented dairy products
Lactobacillus	Fermented dairy products	Reduces fasting blood glucose, improves OGTT/ HbA1c, inhibition of DPP-IV	Probiotic yogurt, functional beverages

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Table 10 Continued...

Lactobacillus bulgaricus	Fermented dairy products	Synergistic control of blood glucose with L. acidophilus, modulation of carbohydrate metabolism	Combined probiotic formulations
Lactobacillus	Fermented dairy products	Improves insulin sensitivity, reduces HbA1c, antioxidant effects	Clinical supplements, therapeutic foods
Lactobacillus	Fermented vegetables	Inhibition of α-glucosidase (24.11%), antioxidant properties	Fermented vegetable products, probiotic capsules
Lactobacillus	Fermented foods	Inhibition of α-amylase (>34%), modulation of the gut microbiota	Functional foods, supplements for gut health

Secrets of medicinal plants to combat T2DM

Diversity of antidiabetic medicinal plants

The botanical diversity of antidiabetic medicinal plants is remarkably rich and varied, with a multitude of species used in different regions of the world. In Côte d'Ivoire, for example, studies have highlighted the use of plants such as *Ageratum conyzoides*, *Anthocleista djalonensis*, and *Bidens pilosa* for their traditional antidiabetic properties.[63] In other regions, such as Morocco, plants like *Trigonella foenum-graecum* (fenugreek), *Olea europaea* (olive), and *Nigella sativa* are commonly used to treat diabetes. In Mauritania, traditional medicine uses *Ziziphus mauritiana*, whose leaf and root extracts have shown a significant reduction in blood sugar levels in animal models, in addition to being rich in bioactive compounds such as polyphenols and flavonoids.[64] In Tunisia, plants such as *Trigonella foenum-graecum* (fenugreek), *Olea europaea* (olive), and *Nigella sativa* are commonly used for the treatment of diabetes, with traditional preparations based on seeds and leaves used as infusions or decoctions. Scientific studies have confirmed the antidiabetic potential of *Nigella sativa*, demonstrating its ability to improve glycemic control, enhance β-cell function, and reduce oxidative stress and inflammation associated with diabetes.[65–67] Clinical trials further support its efficacy in lowering fasting blood glucose, postprandial glucose, and HbA1c levels, making it a promising complementary treatment for type 2 diabetes management.[66,67] In Lebanon, about forty species have been identified, with particular attention given to plants associated with specific symptoms of Type 2 diabetes.[68] In Togo, a study listed 112 species belonging to 51 botanical families, with plants like *Allium sativum* and *Moringa oleifera* being widely used.[68]

The most represented families were *Caesalpiniaceae/Fabaceae* (9 species), followed by *Euphorbiaceae* and Composite (8 species each). The *Combretaceae* (7 species), *Fabaceae, Annonaceae*, and *Apocynaceae* (6 species each) were also well represented. This diversity reflects not only the richness of local medicinal traditions but also the potential of these plants to develop new antidiabetic treatments. These medicinal plants offer a valuable source of active principles that could contribute to improving T2DM management in the future.[63,68]

Bioactive plant principles with antidiabetic properties: from extraction to understanding mechanisms

The extraction of bioactive compounds from medicinal plants with antidiabetic properties involves various methods and solvents suitable for optimizing yield and efficiency. Common techniques include Soxhlet extraction (SE), cold maceration (CM), microwave-assisted extraction (MAE), liquid-liquid extraction, and supercritical fluid extraction. Each method impacts the yield and biological activity of phytochemicals such as flavonoids, alkaloids, saponins, and phenolics. For example, MAE is recognized for higher yields of phenolics and saponins, while SE excels in extracting alkaloids and CM in flavonoids. Solvents like methanol (often 80% aqueous) are widely used due to their ability to dissolve a wide range of bioactive compounds. The choice of method depends on the target compounds; for instance, MAE is faster and more efficient but may degrade sensitive compounds, while CM better preserves bioactivity but is time-consuming. Advanced analytical techniques such as high-resolution liquid chromatography-mass spectrometry (HRLC-MS) and nuclear magnetic resonance (NMR) are used for the identification and profiling of antidiabetic compounds. The efficacy of these extracts has been validated in preclinical and clinical studies, highlighting their promise as complementary therapies or leads for new antidiabetic drugs.[69]

Understanding the mechanisms by which these plants exert their effects is essential for their integration into diabetes management strategies. Scientific studies are beginning to clarify the biochemical pathways influenced by these natural remedies, providing a clearer understanding of how they can complement existing medical treatments. These plants represent a promising natural approach for managing T2DM through various mechanisms such as insulin secretion, improved glucose absorption, enzyme inhibition, and antioxidant activity. For example, the antioxidant properties of many medicinal plants can help mitigate oxidative stress, a common issue in diabetes that contributes to complications such as cardiovascular diseases and neuropathy. Several medicinal plants from various botanical families have demonstrated antidiabetic properties, particularly for managing T2DM. These include *Morus alba* (white mulberry) from the Moraceae family, which contains DNJ and morin compounds that inhibit α-amylase and α-glucosidase, reducing glucose absorption and oxidative stress. *Trigonella foenum-graecum* (fenugreek) from the Leguminosae family is rich in galactomannans and 4-hydroxyisoleucine, which lower blood glucose levels. *Cinnamomum zeylanicum* (Ceylon cinnamon) from the Lauraceae family contains cinnamaldehyde and eugenol, which elevate plasma insulin and stimulate glucose absorption. *Zingiber officinale* (ginger) from the Zingiberaceae family contains shogaol and gingerol compounds that increase insulin levels and reduce fasting glucose. *Phaseolus vulgaris* (common bean) from the Leguminosae family contains phaseolamine, which inhibits α-amylase activity. *Panax ginseng* from the Araliaceae family includes ginsenosides that enhance GLUT-4 expression and lower blood glucose levels. Other notable plants include *Momordica charantia* (bitter melon) from the Cucurbitaceae family, which mimics insulin action; *Aloe barbadensis* (aloe vera) from the Liliaceae family, which stimulates insulin synthesis; and *Opuntia ficus-indica* (prickly pear) from the Cactaceae family, which reduces postprandial glucose due to fiber-rich cladodes. Additionally, *Artemisia dracunculus* (tarragon) from the Asteraceae family promotes insulin release and protects β-cells through anti-inflammatory pathways.[50] In West Africa and the Sahel region, plants such as *Boscia senegalensis* (Capparaceae) have shown significant antidiabetic potential by improving insulin sensitivity and exhibiting strong antioxidant activity, attributed to their high polyphenol content.[70] *Combretum glutinosum* (Combretaceae), traditionally used in Mauritania and neighboring countries, contains flavonoids

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and tannins that inhibit α-glucosidase and α-amylase enzymes, thus reducing postprandial hyperglycemia.[71] The bitter fruit of *Citrullus colocynthis* (Cucurbitaceae) has been extensively studied for its hypoglycemic effects, acting through enhancement of peripheral glucose uptake and inhibition of gluconeogenesis.[72] *Balanites aegyptiaca* (Zygophyllaceae), commonly used in Saharan traditional medicine, demonstrates antidiabetic effects by stimulating insulin secretion and improving lipid profiles in diabetic models.[73] Lastly, *Ziziphus mauritiana* (Rhamnaceae), widely used in Mauritania and the Sahel, contains bioactive compounds such as flavonoids and saponins that exert antioxidant effects and improve pancreatic β-cell function, contributing to glycemic control.[64]

Clinical evidence supporting the use of medicinal plants

The Table 11 presents a summary of the main clinical and ethnobotanical studies conducted worldwide on antidiabetic medicinal plants, highlighting the diversity of species studied, methodologies, and geographical contexts. In North Africa, particularly in Algeria, Morocco, and Tunisia, ethnobotanical surveys and *in vivo* trials on diabetic rats have confirmed the frequent use of plants such as Artemisia herba-alba, Trigonella foenum-graecum, Olea europaea, Nigella sativa, and various Lamiaceae, with results reporting improved glycemic control in 75% of patients and hypoglycemic effects attributed to flavonoids and essential oils. In Senegal and Mali, ethnobotanical studies and some limited clinical trials on *Momordica charantia*, *Moringa oleifera*, and *Galega officinalis* have shown moderate reductions in blood glucose and increased well-being, although clinical trials remain rare. In Asia, randomized controlled trials in India, China, and Iran using *Momordica charantia*, berberine, and *Nigella sativa* have demonstrated significant reductions in HbA1c, a reduction in blood glucose comparable to metformin, and a reduction in LDL cholesterol. Studies conducted in Mexico, Brazil, and the USA using *Opuntia ficus-indica*, *Syzygium cumini*, and cinnamon have demonstrated a reduction in postprandial blood glucose, an improvement in insulin resistance, and a reduction in fasting blood glucose. Finally, trials in Nigeria and Germany using *Moringa oleifera* and *Gymnema sylvestre* have confirmed a significant reduction in blood glucose and an improvement in glycemic control. Overall, this research shows that many medicinal plants, derived from local traditions and validated by experimental trials, have interesting potential for the management of diabetes, although the methodological robustness and sample size vary among studies. Recently, a clinical trial conducted in India revealed that participants consuming *Gymnema extract* experienced a notable decrease in postprandial blood glucose levels compared to those in the placebo group.[74]

Table 11 Clinical and ethnobotanical studies on antidiabetic medicinal plants

Country / region	Studied plant(s)	Participants / population	Study duration / type	Experimental protocol / methodology	Observed effects in patients / animals	Reference
Algeria (Constantine)	*Artemisia herba-alba*, *Trigonella foenum-graecum*, *Olea europaea*	100 type 2 diabetic patients (48% use plants)	Observational ethnobotanical study	Surveys of patients and herbalists, collection of used plants	75% report improved glycemic control	[75]
Algeria (West)	*Ficus carica*, *Citrullus colocynthis*	470 diabetic patients	Ethnopharmacology + animal testing	Phytochemical analyses, in vivo tests on STZ-induced diabetic rats	Citrullus colocynthis hypoglycemic; variable effect of fig	[76]
Morocco	*Trigonella foenum-graecum*, *Olea europaea*, *Nigella sativa*, *Salvia officinalis*, *Artemisia absinthium*	Ethnobotanical and experimental studies	Surveys + in vivo tests on STZ diabetic rats	Combination of ethnobotanical survey and experimental validation	Decreased blood glucose, cholesterol; antioxidant activity	[77]
Tunisia	Lamiaceae family (*Origanum vulgare*, *Thymus* spp.)	Ethnobotanical and pharmacological studies	Literature review + *in vitro/in vivo* tests	Bibliographic review and experimental assays	Hypoglycemic effects linked to flavonoids and essential oils	[78]
Senegal	*Momordica charantia*, *Moringa oleifera*	Ethnobotanical studies, limited clinical trials	Surveys + small group trials	Ethnobotanical surveys and limited clinical testing	Moderate blood glucose reduction, improved well-being	[79]
Mali	*Galega officinalis*, other local plants	Bibliographic reviews and theses	Traditional use documentation	Literature data collection, traditional knowledge	Traditional use reported, few formal clinical trials	[80]
India	*Momordica charantia*	100 patients	12 weeks, randomized controlled trial (RCT) vs placebo	2 g capsules/day	HbA1c reduced by 1.5%	[81]

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Table 11 Continued...

China	Berberine	116 patients	3 months, comparison with metformin	500 mg three times daily	Blood glucose reduction comparable to metformin	[82]
Iran	*Nigella sativa*	94 patients	8 weeks, RCT vs placebo	2 g oil/day	LDL cholesterol and blood glucose decreased	[83]
Mexico	*Opuntia ficus-indica*	36 patients	6 weeks, crossover trial	300 g nopal/day	Postprandial blood glucose decreased	[84]
USA	Cinnamon (*Cinnamomum* spp.)	60 patients	12 weeks, RCT vs placebo	1 g extract/day	Fasting blood glucose decreased	[85]
Nigeria	*Moringa oleifera*	50 patients	4 weeks, open study	20 g powder/day	Blood glucose decreased by 28%	[86]
Brazil	*Syzygium cumini*	30 patients	8 weeks, non-randomized	10 mL extract/day	Insulin resistance decreased	[87]
Germany	*Gymnema sylvestre*	65 patients	6 months, RCT vs placebo	400 mg/day	Improved glycemic control (limited details)	[88]

The action of gymnemic acids is thought to involve modulation of taste receptors, potentially reducing sugar cravings and encouraging healthier food choices in individuals with diabetes.[75–88]

Applications of antidiabetic plants and their derivatives in food formulations

Antidiabetic plants and their derivatives have shown promising potential for multiple food applications. Powders from plants such as *Morus alba* (white mulberry), *Cinnamomum zeylanicum* (cinnamon), and *Trigonella foenum-graecum* (fenugreek) have been incorporated into various food products to lower blood glucose levels.[89] Plant extracts, such as those from *Momordica charantia* (bitter melon) and *Gymnema sylvestre*, are used to develop functional foods and beverages with hypoglycemic properties.[90] Bioactive compounds isolated from these plants, including galactomannans from fenugreek, cinnamaldehyde from cinnamon, and gymnemic acids from *Gymnema sylvestre*, are being explored for their potential as natural sweeteners, flavor enhancers, and functional ingredients in foods suitable for diabetics.[89,90] Moreover, nanoformulations of plant-derived antidiabetic compounds are emerging as a new approach to enhance bioavailability and efficacy in food applications.[91] These plant-based ingredients are integrated into a wide range of products, including baked goods, dairy alternatives, snacks, and dietary supplements, providing consumers with natural options for managing blood glucose through their daily diet.[92,93] Antidiabetic medicinal plants can be integrated into various food products to create health-beneficial formulations. For example, dietary supplements in the form of capsules or powders can be developed from these plants. Additionally, functional food products like cereals enriched with extracts of fenugreek or white wormwood could be developed. These products not only contribute to diabetes management but also offer additional nutritional benefits, such as fiber and antioxidants. Furthermore, incorporating these plants into sauces and condiments, such as rosemary (*Rosmarinus officinalis*) and oregano (*Origanum compactum*), can add flavors while providing health benefits (Table 12).[94]

Table 12 A structured overview of antidiabetic medicinal plants and their potential applications in food formulations, based on traditional uses and bioactive compounds

Scientific name (common name)	Main bioactive compounds	Antidiabetic mechanisms mechanism of action	Potential food applications applications in food formulations
Morus alba (White Mulberry)	1.5-dideoxy-1.5-imino D-sorbitol (DNJ), morine	Inhibition of α-amylase and α-glucosidase; antioxidant	Used in teas, functional beverages, and snacks for blood sugar control
Trigonella foenum-graecum (Fenugreek)	Galactomannans, 4-hydroxyisoleucine, saponins	Reduction of blood glucose concentration; hypocholesterolemic	Incorporated into bread, biscuits, and spice blends for glycemic management
Cinnamomum zeylanicum (Cinnamon)	Methylhydroxychalcone polymer, cinnamaldehyde	Stimulates glucose absorption; hypoglycemic	Added to desserts, beverages, and cereals to improve insulin sensitivity
Zingiber officinale (Ginger)	Shogaol	Increases insulin levels; decreases fasting glucose	Used in teas, smoothies, and spice blends for glycemic control

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Table 12 Continued...

Phaseolus vulgaris (Common bean)	Phaseolamine	Inhibits α-amylase activity; antioxidant	Incorporated into soups, salads, and flour blends to reduce postprandial glucose spikes
Panax ginseng (Ginseng)	Ginsenoside	Lowers blood sugar; increases GLUT-4 expression	Used in energy drinks and herbal supplements for diabetes management
Gymnema	Gymnemic acids	Regenerates islet cells; inhibits glucose absorption	Incorporated into capsules or herbal teas to reduce sugar cravings
Allium sativum (Garlic)	Sulfur-containing amino acids	Improves glycemic control; antioxidant	Added to condiments, spreads, and savory dishes for diabetes-friendly diets
Aegle	Limonene	Stabilizes the lipid profile; improves insulin sensitivity	Used in jams or beverages for its anti-diabetic properties
Allium	Allicin, S-allyl cysteine sulfoxide	Inhibition of α-amylase/ α-glucosidase, insulin secretion	Garlic-infused oils, spice blends, functional beverages, fermented foods (e.g., kimchi)
Artemisia	Absinthine, thujone derivatives	Hypoglycemic effects, weight management	Herbal teas, bitter flavor enhancers in beverages or baked goods
Aloe	Aloin, aloe-emodin	Hypoglycemic, inhibition of α-amylase	Functional juices, gel-based desserts, low-sugar jams
Cinnamomum	Cinnamaldehyde, cinnamic acid	Insulin sensitization, improvement of glucose absorption	Cinnamon-spiced cereals, sweeteners, baked goods
Gymnema	Gymnemic acids	Suppression of sweetness, insulin secretion	Sugar substitutes, low-calorie desserts, functional teas
Callistemon	Piceatannol	inhibition of α-amylase, control of postprandial blood glucose	Polyphenol-rich extracts for functional beverages or meal substitutes
Berberis	Berberine	activation of AMPK, modulation of glucose metabolism	Herbal supplements, fortified foods (e.g., energy bars)
Baccharis	Flavonoids, phenolic acids	hypoglycemic effects, regulation of lipid metabolism	Herbal infusions, functional snacks (e.g., roasted seeds)
Cynara	Chlorogenic acid, cynarin	Antioxidant, anti-glycation, vascular protection	Functional snacks based on artichoke, antioxidant-rich sauces
Boscia senegalensis (Hanza)	Polyphenols, flavonoids	Improves insulin sensitivity; antioxidant activity	Potential use in functional beverages and dietary supplements targeting oxidative stress
Combretum glutinosum	Flavonoids, tannins	Inhibition of α-glucosidase and α-amylase; reduces postprandial hyperglycemia	Extracts for incorporation in teas or nutraceutical formulations
Citrullus colocynthis (Bitter apple)	Cucurbitacins, flavonoids	Enhances peripheral glucose uptake; Gluconeogenesis inhibitors	Potential use in herbal teas and dietary supplements for glycemic control
Balanites aegyptiaca	Saponins, flavonoids	Stimulates insulin secretion; improves lipid profiles	Extracts for functional foods and supplements aimed at metabolic health
Ziziphus mauritiana (Jujube)	Flavonoids, saponins	Antioxidant effects; Improves Pancreatic β-cell function	Used in teas, jams, and functional food products for diabetes management

Conclusion and future perspectives

The relentless rise of the global diabetes epidemic calls for urgent, innovative, and multifaceted solutions. As highlighted throughout this review, natural therapies, particularly probiotics and medicinal plants, are gaining recognition as valuable complementary strategies in diabetes prevention and management. Recent research has brought to light novel probiotic strains and lesser-known medicinal plants with promising antidiabetic properties, underscoring the potential of integrating traditional wisdom with modern scientific advances. Nevertheless, the intricate and multifaceted character of diabetes, shaped by biological, environmental, and behavioral factors, requires comprehensive strategies beyond single, isolated interventions. It demands a collaborative, interdisciplinary framework that draws upon the strengths of nutrition science, pharmacology, and psychology. Nutrition remains foundational, with personalized dietary strategies such as the Mediterranean diet demonstrating

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significant improvements in glycemic control and overall metabolic health.[14] Pharmacological advances, including the use of probiotics to enhance medication efficacy, further illustrate the benefits of bridging disciplines and tailoring treatments to individual patient profiles.[95,96] Equally important is the psychological dimension of diabetes care. Addressing the emotional and mental health challenges faced by individuals living with diabetes is essential for improving adherence to treatment regimens and achieving better health outcomes. Integrating psychological support into diabetes management acknowledges the critical role of mental well-being in chronic disease care.[97–100] The convergence of these disciplines not only enhances care at the individual level but also informs broader public health strategies. Comprehensive community-based interventions that combine nutritional education, improved access to healthy foods, and psychological support have demonstrated success in reducing diabetes prevalence among high-risk groups.[101,102] Such collaborative efforts among healthcare providers, researchers, and community organizations are vital for developing innovative, effective solutions to combat diabetes on a global scale.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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