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Diabetes Mellitus: A Multisystem Disorder and the Therapeutic Potential of Herbal Interventions

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ABSTRACT

Chronic hyperglycemia brought on by insulin resistance or deficiency is a hallmark of diabetes mellitus, a chronic metabolic disease. Type 1, type 2, gestational, and monogenic forms are among the various forms of the condition, each with distinct pathophysiological characteristics. Diabetes has complications that impact the cardiovascular, renal, ocular, neurological, and immune systems, and it is a major cause of morbidity and mortality worldwide. According to recent research, diabetes is strongly correlated with the incidence of infectious diseases, psychological disorders, and cancer. The susceptibility of people with diabetes has been amplified by the COVID-19 pandemic. Although synthetic antidiabetic medications effectively control blood sugar levels, they are not recommended for long-term use and frequently have negative side effects. As a result, people are becoming increasingly invested in herbal remedies that provide multiple benefits, like *Gymnema sylvestre*, *Curcuma longa*, *Allium sativum*, and *Moringa oleifera*.

Keywords: Immune System, chronic hyperglycemia, Type 2 Diabetes

1. INTRODUCTION

A metabolic disease called diabetes mellitus (chronic hyperglycemia) is brought on by unusually high blood sugar levels [1]. This irregularity in blood glucose levels results from an imbalance between the amounts of insulin and glucagon produced by the pancreatic alpha and beta cells. Hyperglycemia is the result of wholly absent or ineffective insulin i.e, blood glucose levels above 180 mg/dl are considered to be hyperglycemic [2]. Due mostly to insulin resistance, aberrant insulin levels are linked to incorrect functioning of several tissues, including the liver, skeletal muscles, and adipose tissue [3]. It has emerged as one of the 21st century's most significant public health issues in recent decades [1,4] and according to the recent research on population studies it is found that there are over 537 million adults worldwide with diabetes and it is predicted that there will be a upsurge to 783 million worldwide by 2045 [5]. The economically and socially marginalized people are highly at risk in developing diabetes [6]. There are significant differences in the prevalence of diabetes and its complications by age and gender. For example, prevalence rates rise sharply after age 40, with older persons being disproportionately impacted. Given that women with diabetes are more likely than males to suffer from poor cardiovascular outcomes, gender-specific therapies are necessary [7]. Diet is another important factor for the risk of diabetes. Risk factors like obesity and restricted access to wholesome food are sometimes more common in underprivileged populations [5,8]. Research has also shown that ethnic backgrounds have a big impact on diabetes management and prevalence. Compared to Europeans, South Asians are reported to have lower body mass indices and a higher risk of type 2 diabetes at earlier ages [5]. Genetic factor also serves as a critical risk factor in the case of type 1 and type 2 diabetes. Polymorphism is shown to influence the risk for type 1 diabetes [2,9], however type 2 diabetes is shown to have complex relationship between genetics and lifestyle, this is because majority of the patients with diabetes are known to have at least one parent with T2DM [2,10]. India is the second largest country with highest number of diabetic patients [11]. According to the studies published on 2023, there are 10.1 crore people with diabetes in India (Pib.gov.in) and will continue to increase upto 124.9 million by 2045 [11].

Type 1, type 2, gestational diabetes, neonatal diabetes, maturity-onset diabetes of the young (MODY), and secondary causes resulting from endocrinopathies, steroid use, etc. are among the various types of diabetes mellitus. Children are typically affected by T1DM which results in destruction of beta cells in pancreas, while middle-aged and older individuals are affected by T2DM because of chronic hyperglycemia. T1DM is characterized by either no insulin or very little insulin, while T2DM is characterized by an imbalance between insulin sensitivity and insulin levels, which leads to a functional deficit. Gestational diabetes preferably occurs during pregnancy. The reason for its development is still unpredictable. Non-insulin-dependent diabetes that is diagnosed early (often before the age of 25) is a defining feature of MODY, a diverse illness. Unlike type 1 diabetes, it is transmitted autosomally dominantly and does not include autoantibodies [2].

Patients with diabetes are very much prone to various impaired functioning in their bodies. Insulin resistance leads to irregular or dysfunctional way of glucose transport and an increased fat breakdown [2]. Chronic hyperglycemia promotes nonenzymatic glycation of proteins and lipids that result in damage of blood vessels in retina, kidney and peripheral nerves. Such damages lead to severe complications such as blindness, dialysis, diabetic nephropathy etc [2,12]. The severity of the symptoms however depends upon the duration and the type of diabetes. Women with gestational diabetes are at a higher risk of complications during delivery and can also attain type 2 diabetes in the future (https://www.who.int/news-room/fact-sheets/detail/diabetes). Recent research indicates that among individuals with diabetes mellitus, cancer is the primary cause of death [1,13,14]. Additionally, there have been studies linking diabetes to a number of other conditions, sleep issues, and difficulties associated to infections [1,13].

The medications currently used to treat this chronic condition are manufactured artificially and include a multitude of substances that can lead to diabetes as well as other side effects, overdose, and addiction. Even while the disease's therapy will be carefully designed to target specificity and is therefore highly efficient, the side effects are nevertheless quite severe [14]. This is where herbal medications, which have less well-known adverse effects and are reasonably priced and widely available to patients, come into play. The aim of this article is to review the harmful effects of this contagious disease which is leading to a huge economic loss worldwide and how the herbal drugs are better saviors in terms of their treatment.

2. MALICIOUS DIABETES

Globally, diabetes is increasingly the primary cause of rising death rates. The World Health Organization estimates that 830 million people worldwide have diabetes as of November 2024, with type 2 being the most common. Myocardial infarction is the leading cause of sudden cardiac deaths in the United States. The primary cause is impaired insulin sensitivity. Factors such as hypertension, hyperlipidemia, obesity etc which influence cardiovascular diseases are also found to be present in diabetic patients. Diabetes is also known to be the major cause of retinopathy, nephropathy and neuropathy. Among them, nephropathy due to the type 2 diabetes is known to cause majority of the cardiac conditions [15].

Nonetheless, the mortality rate from cardiovascular diseases has been observed to be decreasing [1], and cancer is currently the leading cause of death associated with diabetes in both T1DM and T2DM. [16,17]. Out of all the different types of cancer, gastrointestinal cancer was found to have the strongest connection with diabetes. In a case control study comprising 18 cohort studies with 3.5 million individuals, it was reported that the summary relative risk was 2.01 (95% confidence interval) in association with diabetes. Also, in the context of hepatitis C virus infection, diabetes mellitus independently raised the risk of hepatocellular carcinoma [1,18,19]. Pancreatic cancer was found to be at a higher risk in patients with T2DM. In this instance, diabetes is typically brought on by pancreatic cancer that was discovered after a patient's diabetes was identified. A study that included data from five nationwide registries reported that there is an higher risk of cancer in both male (HR 1.53, 95% CI 1.30–1.79) and female (HR 1.25, 95% CI 1.02–1.53) with T1DM [1,20]. In case of sex specific cancers, it was observed that females with diabetes are more prone to endometrial, breast and ovarian cancer. Breast cancer in females was found to vary in accordance with menopausal status which was observed in 11 studies that was conducted only with postmenopausal women was found to have SRR of 1.15. This mainly occurs because postmenopausal women are shown to have higher bioavailability of oestrogen associated with adiposity which is known to be a common cause in association with T2DM [1,21,22] . In case of male specific cancer, prostate cancer was more common and the rate of activity was associated with the ethnicity. A systemic review with more than 1.7 million men from South Korea, India, Taiwan and Japan showed that they were at higher of prostate cancer in association with diabetes. Also there it was also studied that there is an inverse association of diabetes and prostate cancer in white men with T2DM and confer higher rate of disease mortality [1,23].

The relationship between COVID-19 and diabetes is quite complex and has resulted in particularly poor outcomes for patients with diabetes mellitus. One significant issue is the direct effect of COVID-19, which can raise blood glucose levels and increase the levels of cytokines and inflammatory mediators. This escalation leads to insulin resistance and hyperglycemia. Consequently, hyperglycosylation of the ACE2 receptor occurs, which promotes viral proliferation. In addition, abnormal immune responses can contribute to heightened thrombotic and ischemic complications, potentially resulting in multi-organ failure and elevated mortality rates. Type 2 diabetes is recognized as a risk factor for worse COVID-19 prognosis. Patients with T2DM are known to develop severe forms of diseases and also have a high increase in the inflammatory markers compared to the non-diabetic patients. It is also studied that the genetic inheritance of T2DM also plays a part in the increased risk of this infection. Healthy individuals which have a family history of T2DM are also known to be prone to early endothelial dysfunction which is known to be a critical factor in the pathophysiology of COVID-19. In patients with COVID-19 the prevalence of T1DM is between 0.15% - 28.98%. According to the studies conducted in the United States, patients with these two diseases are highly obese with an population of 34% and some are also prone to hypertension and cardiovascular diseases (12.1%). A population based study with respect to age, gender and ethnicity was also conducted which showed among patients with T1DM, older age and male population are likely more associated to higher mortality rate due to COVID-19. The mortality was also found to be higher in case of black and Asian communities. Thus, the COVID-19 has caused a dramatic change in the world of diabetes and is likely to be more hazardous.

Individuals with diabetes face a 2 to 4-fold increased risk of infections compared to those without the condition. This heightened susceptibility arises from several factors, including neuropathy, which reduces sensation in extremities, altered skin conditions that hinder healing, and vascular insufficiency, which impairs blood flow and the body's ability to fight infections.

Common infection sites for diabetic patients include the kidneys (leading to urinary tract infections), feet (susceptible to ulcers and osteomyelitis), lungs (where pneumonia can occur), and skin (including influenza-related infections) [24]. Infections can disrupt glucose homeostasis by affecting insulin secretion and increasing insulin resistance. The production of counter-regulatory hormones and inflammatory cytokines during infections leads to reduced insulin effectiveness, resulting in impaired glucose uptake and exacerbated hyperglycemia. Understanding these interactions is vital for optimizing diabetes management and minimizing the risk of infections [24,25]. Viral infections, particularly hepatitis C virus (HCV), are significantly associated with type 2 diabetes as they increase insulin resistance by down regulating insulin receptor substrate 1[24, 26]. Bacterial infections like gingivitis and periodontitis can trigger local and systemic inflammation, negatively impacting blood sugar control. Pneumonia poses a major risk for individuals with diabetes, often exacerbated by poor glycemic management [24,27,28,29]. The primary pathogens causing lower respiratory infections in diabetics are gram-negative bacteria, notably *Klebsiella pneumoniae*, while *Staphylococcus aureus* is frequently found in the nasal passages of these patients. Additionally, diabetes is a key risk factor for thoracic empyema, which can arise from infections with *Klebsiella* and *Streptococci*, including *Staphylococcus aureus*. This highlights the importance of effective glycemic management to minimize the risk of serious complications [24,30,31]. Patients with diabetes are significantly more susceptible to developing tuberculosis compared to individuals without this condition [24,32]. In India, diabetes contributes to approximately 15% of all pulmonary tuberculosis cases and 20% of smear-positive tuberculosis cases, with the latter being particularly prevalent in densely populated urban areas [24,33]. This heightened risk is alarming, as diabetic patients not only face challenges in treatment adherence but are also more likely to experience treatment failures or, in severe instances, mortality during their healthcare journey [24,33]. Furthermore, diabetic foot ulcers pose a serious complication for individuals living with diabetes. Infections associated with these ulcers can exacerbate the situation, leading to chronic or recurrent wounds that are difficult to heal. The diagnosis of foot ulcers is typically based on the identification of classic signs of inflammation, including redness, warmth, swelling, and pain. Remarkably, the incidence of foot ulcers has decreased significantly in recent years, particularly in younger populations and among minority or indigenous ethnic communities, highlighting the need for continued awareness and prevention strategies in these vulnerable groups [24,35,36].

The psychological impact on diabetic patients is significant and highlights the need for targeted support. Research shows that approximately 14% of individuals with diabetes experience anxiety disorders, compared to 3-4% in the general population[1,37]. Additionally, around 28% of those with Type 2 Diabetes Mellitus (T2DM) face depression, emphasizing the importance of mental health care [1,38]. Anxiety symptoms are also prevalent, with 40% of diabetic patients affected. Furthermore, about 7% of individuals with Type 1 Diabetes Mellitus (T1DM) struggle with eating disorders [1,39]. Addressing these psychological challenges can enhance overall well-being and quality of life for those with diabetes.

3. CLASSIFICATION OF DIABETES

There are different classifications of diabetes currently as it is now impacting almost every age groups:

3.1. **TYPE 1**

Type 1 diabetes mellitus (T1DM) is an autoimmune disorder that leads to the destruction of pancreatic beta cells. The progression of T1DM can be divided into two stages. In Stage 1, individuals show the presence of two or more autoantibodies while maintaining normal blood glucose levels (normoglycemia). There is a 44% risk of developing symptomatic T1DM within five years; however, this risk varies based on the types, quantities, and titers of autoantibodies present, as well as genetic predisposition [41]. Stage 2 involves individuals with multiple islet autoantibodies and dysglycemia. In this stage, the risk of developing symptomatic T1DM increases to 60% within two years and 75% within five years [42]. The rate of beta-cell destruction can vary significantly—some individuals, particularly infants and children, may experience rapid destruction, while in others, especially adults, the process may be slower [43,44]. The incidence of diabetic ketoacidosis (DKA) as the initial presentation of the disease in children and adolescents is rising. Conversely, some individuals may experience mild fasting hyperglycemia, which can progress to severe DKA during infections or other stressors. Adults with T1DM may retain some beta-cell function but often become insulin-dependent for life due to remission or decreased insulin needs, making them susceptible to DKA [45,46]. Type 1 diabetes is more commonly diagnosed in children and adolescents but can occur at any age. The autoimmune destruction of beta cells is believed to arise from a combination of genetic and environmental factors, though the exact causes are not well defined. Individuals with T1DM are also at a higher risk for other autoimmune disorders, including Hashimoto's thyroiditis, Graves' disease, celiac disease, Addison's disease, vitiligo, autoimmune hepatitis, myasthenia gravis, and pernicious anemia. Additionally, T1DM has been linked with several viruses, such as enteroviruses and coxsackievirus B. Notably, during the COVID-19 pandemic, there was an increase in cases of DKA and hyperglycemia, suggesting that the SARS-CoV-2 virus could significantly trigger T1DM. Viruses may damage beta cells through mechanisms such as direct viral-induced cell death, immune-mediated destruction, and damage from the infection of adjacent exocrine cells. The cytokine storm associated with COVID-19 is a highly inflammatory state that may also contribute to this deterioration [47].

3.2. TYPE 2

Type 2 diabetes mellitus (T2DM) is characterized by relative insulin deficiency and peripheral insulin resistance, accounting for 90% of diabetes cases worldwide. There are various forms of T2DM, but unlike other types, there is no autoimmune destruction of beta cells. Individuals with this type of diabetes often suffer from obesity, which gradually leads to insulin resistance. Even those who are not obese can have a significant amount of body fat concentrated in the abdominal area, including locations involved in nonalcoholic fatty liver disease. Diabetic ketoacidosis (DKA) can spontaneously occur in T2DM patients and is particularly prevalent among those treated with insulin, as well as those susceptible to infections like COVID-19 and conditions such as myocardial infarctions. This type of diabetes often goes undiagnosed for many years because the hyperglycemia is not severe enough to produce noticeable symptoms such as dehydration or unintentional weight loss [48,49].

In young and middle-aged populations, men show a higher prevalence of type 2 diabetes. However, postprandial hyperglycemia tends to increase in women as they age, leading to a higher prevalence of undiagnosed diabetes in women after the age of 60, and total diabetes cases increase after age 70. The lifetime risk of developing diabetes appears to be higher in men [50,51,52]. Obesity is significantly contributing to the rise of T2DM, which now affects approximately 10.5% of the world's population. According to the International Diabetes Federation (IDF), 90% of those who are undiagnosed live in lower-middle-income countries, with a significant portion in Africa, South-East Asia, and the Western Pacific [53,50]. The American Diabetes Association emphasizes the importance of individualizing patient therapy. There are various antihyperglycemic agents available for the treatment of T2DM, with metformin being the first-line therapy. However, it is unsuitable for patients with chronic renal insufficiency. Sulfonylureas are another option but are associated with weight gain, hypoglycemia, and an increased risk of mortality and cardiovascular disease [55-58]. The likelihood of developing T2DM increases with age, obesity, and physical

inactivity, and it is also more common among individuals with hypertension and certain racial and ethnic groups, including African Americans, Asian Americans, and Hispanics/Latinos [50].

3.3. GESTATIONAL DIABETES

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance that is first recognized during pregnancy [59]. It is categorized into early GDM, which is preferred for diagnosis before 20 weeks of gestation, and late GDM, which is identified between 24 and 28 weeks of gestation. However, there are limitations to this definition. Evidence suggests that GDM often represents pre-existing hyperglycemia, which can be detected through routine screening during pregnancy. With the rising rates of obesity and type 2 diabetes mellitus (T2DM) among individuals of reproductive age, more pregnant women are entering pregnancy with undiagnosed T2DM. Poor glucose metabolism can be identified in individuals at higher risk for adverse pregnancy and neonatal outcomes, particularly when fasting glucose levels reach 110 mg/dL or the A1C level is at 5.9%. These individuals often require insulin treatment [60,61].

According to the International Association of Diabetes and Pregnancy Study Groups (IADPSG), the global prevalence of GDM is approximately 14% [62]. Ethnic differences also play a crucial role in this condition, influenced by a combination of socioeconomic, cultural, and genetic factors. GDM is associated with an increased risk of pregnancy complications. For example, in studies where there was no maternal insulin treatment, GDM was linked to higher risks of cesarean delivery and preterm delivery. Additionally, GDM can have a psychological impact on women, leading to increased rates of depression, anxiety, and stress during pregnancy. It has also been observed that breastfeeding rates decline when GDM is diagnosed between 24 and 28 weeks of gestation. In terms of oral health, pregnant women with GDM are at a higher risk for periodontitis [63,64].

3.4. MONOGENIC DIABETES

Monogenic defects, such as neonatal diabetes and Maturity-Onset Diabetes of the Young (MODY), affect a small percentage of individuals with diabetes. Neonatal diabetes, also known as congenital diabetes, occurs in infants under 6 months of age, and approximately 80-85% of cases are attributed to monogenic causes. This condition can be either transient or permanent. Transient neonatal diabetes is caused by the overexpression of genes located on chromosome 6q24 and can be managed with medications other than insulin. In contrast, permanent neonatal diabetes arises from autosomal dominant mutations in genes that code for the Kir6.2 and SUR1 subunits of the beta-cell KATP channel. MODY is characterized by hyperglycemia that develops at an early age due to impaired insulin action. It follows an autosomal dominant inheritance pattern and involves abnormalities in at least 13 different genes located on various chromosomes. The most commonly identified types of MODY are GCK-MODY, HNF1A-MODY, and HNF4A-MODY. Individuals with GCK-MODY typically experience mild, stable fasting hyperglycemia, while those with HNF1A-MODY and HNF4A-MODY usually respond well to low doses of sulfonylureas. [50].

4. TREATMENT

4.1. SYNTHETIC VS HERBAL MEDICINES

Diabetes poses a significant challenge on a global scale, currently impacting around 830 million individuals (WHO). In lower- and middle-income countries, many face obstacles in accessing effective treatment. This issue is compounded by the presence of other health conditions that often accompany diabetes, thereby increasing mortality risks. It is essential to prioritize the development of better treatment options that are both effective and carry fewer side effects for long-term relief. Both synthetic and herbal medicines have shown considerable effectiveness, offering distinct pathways to health and wellness [65].

4.2. SYNTHETIC DRUGS

Synthetic drugs, commonly known as modern medicine, are the remarkable result of thorough research and innovative chemical synthesis. These expertly crafted substances are designed to target specific biological pathways with precision, delivering rapid and effective relief from a variety of symptoms. Each drug undergoes rigorous testing and meticulous regulatory processes, ensuring they meet the highest standards of potency, safety, and efficacy. Typically composed of a singular active ingredient or a carefully curated combination of ingredients, these drugs offer unparalleled consistency in their effects while minimizing variability. This level of precision not only enhances their effectiveness but also embodies the extraordinary advancements of contemporary medicinal science. The

mechanism of action reflects a targeted approach. The drug binds to a specific receptor to block signals or reduce inflammation, thus providing rapid relief. [65]. The journey began in the 1920s with the introduction of the first synthetic drug for type 2 diabetes mellitus (T2DM), which involved isolating insulin from animal pancreases. Today, patients have access to a wide range of orally administered and injectable medications to support their treatment. Some of the synthetic drugs that are currently in use for T2DM are [67-69]:

- Insulin sensitisers which decrease the insulin resistance such as biguanides and thiazolidinediones [67]. The major biguanide used is metformin which is derived from galegine 67,70-71). The metformin drug is involved in reducing the hepatic glucose production, increased insulin sensitivity and reduced insulin levels during fasting [67]. Thiazolidinediones which are also known as glitazones include pioglitazone and rosiglitazone. Application of this drug reduces the blood glucose levels, improvises the b-cell function and decreases insulin resistance [67,72-73].
- Insulin secretagogues support the first phase of insulin secretion. And stimulate shirt term insulin release. The second phase of insulin secretion is not permanent [67,74-75]. The drugs involved are sulphonylureas and meglitinides. Sulphonylureas are derivatives of sulphonamide and have an high affinity to pancreatic b-cell sulphonylurea receptor. They are involved in stimulating the insulin release through direct action on b-cells [67]. Meglitinides also known as glinides have fast but short duration of action, thus they are known as "short-acting type insulin secretagogues" [67]. They primarily control postprandial blood glucose levels by increasing the insulin secretion [67,77].

Though the drugs provide immense efficacy and potency, there lies a limit to these synthetic drugs. They come with significant side effects because they target specific pathways with very high potency. Most of the synthetic drugs are used for short-term use, but if they are exposed for a longer time it can lead to toxicity and organ failure [65]. Thus there is a need for higher efficient drugs with fewer side effects which can provide safety for long term effects. At such situations, the natural medicines come in action.

4.3. NATURAL DRUGS

Natural medicines have been in use for over 1000 years and are now gaining popularity among developing and developed countries. Natural drugs involve natural treatments obtained from different parts of the plants which are known for their therapeutic property. Unlike synthetic drugs, natural drugs do not have drug-like actions or any adverse side effects. But, there can be certain toxic risks such as poisoning which are linked to misidentification of plants, improper identification etc. unlike synthetic drugs, these drugs contain a wide range of natural compounds that work together and this complex mechanism allows for multi targeted approach. Most of the medicinal plants are quite known for antioxidant properties which is an beneficial property required for diabetes. The mechanism of action of natural drugs is highly beneficial as they tend to act on multiple pathways and systems offering a holistic approach to treatment [65]. Some of the best herbs used for administration of T2DM are:

- ***Gymnema sylvestre, commonly known as 'gurmar' is a common antidiabetic plant which belongs to the family Asclepiadaceae. It is found in central and peninsular india. This plant contains gymnemic acid, gymnema and gymnemasides, where the gymnemic acid exhibit antidiabetic and antinflammatory property [78-80]. This bioactive compound activates the regeneration of pancreatic βcells and insulin secretion [78.81-82]. G. sylvestre also increased plasma insulin and C-peptide levels and decreased the glucose concentrations in T2DM [78,83].***
- *Curcuma longa* also known as turmeric belongs to the ginger family and is cultivated across asian countries. It is known to have antioxidant, antinflammatory, antiviral, antidiabetic, anticarcinogenic and cardioprotective properties [78,84] . C. longa contains erulic acid that stimulates the insulin secretion and free radical scavenging activity. The glucose metabolism is also known seen to be improved [78,85].
- *Allium sativum* also known as garlic, is a strong aromatic bulb found in many of the asian countries, USA [78,86]. It is famous for its anticancer, antidiabetic, antiatherosclerotic, antimicrobial, antioxidant and cardioprotective properties [78,87-88]. It is a plant which is rich in organic compound allylpropyl disulfide, that plays a major role in glycogen synthesis and insulin secretion. The different chemical constitutents responsible for its pharmacological properties are alliin, ajoene, arginine and diallyl disulfide [78,89]. The allicin, apigenin and alliin are also involved in targeting cholestrol and glycogen synthesis pathways [78,90-91].
- *Moringa oleifera* also known as the drumstick plant is an inhabitant plant in india [78.92]. The various plants of this plant act as antitumors, antidiabetic, antioxidant, antiulcer, antifungal, cholestrol lowering agents [78,93]. The aqueous extract of the leaves are shown to have antidiabetic property by inhibiting the action of

α-glucosidase and α-amylase, that improve the antioxidant activity and the rate of glucose uptake and tolerance [78,94].

Despite having lower side effects than synthetic drugs, there is potential for contamination with heavy metals, pesticides and various other harmful substances and can increase toxicity risks. But, herbal drugs can be used for long-term treatments as it focuses on balancing and supporting the body's natural process, it has a slow but steady relief treatment. Herbal drugs are known for particularly managing several chronic conditions and also boost immunity and improving the overall well-being [65-66].

5. CONCLUSION

Because of its increasing prevalence, multisystem complications, and related comorbidities like infections, cancer, mental illnesses, and cardiovascular disease, diabetes mellitus continues to pose a serious threat to global health. Even though synthetic antidiabetic drug development has advanced significantly, long-term use frequently leads to side effects, toxicity, and financial burden, particularly in low- and middle-income populations. Herbal medicine, which utilizes the therapeutic potential of naturally occurring bioactive compounds with fewer side effects and broader pharmacological actions, unveils a promising complementary or alternative approach in this regard. Medicinal plants with notable antidiabetic, anti-inflammatory, and antioxidant qualities include *Gymnema sylvestre*, *Curcuma longa*, *Allium sativum*, and *Moringa oleifera*. These plants may also be useful for glycemic control and the avoidance of complications from diabetes. Nevertheless, more investigation, standardization, and clinical testing.

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