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UNDERSTANDING DIABETES MELLITUS AND ITS MANAGEMENT AND TREATMENT USING MEDICINAL PLANTS : A REVIEW

BY

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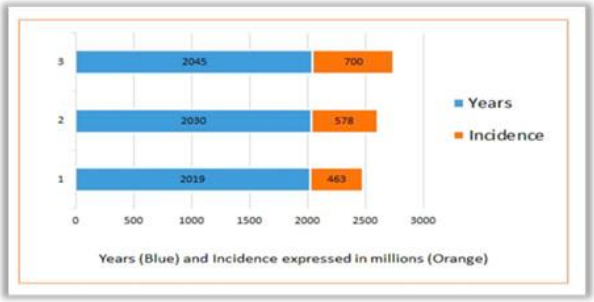
Abstract

Millions of people worldwide suffer from diabetes mellitus, a condition that is becoming a major global health concern. This paper provides a comprehensive overview of the disease's types, risk factors, pathophysiology, epidemiology, and consequences. The paper's second section, which focuses on medicinal plants' potential use in diabetes management, highlights the plants' efficacy, safety, and modes of action. We discuss the current state of affairs. Providing details on phytotherapeutic interventions and how they might be used to combat diabetes.

KEYWORDS: *Diabetes Mellitus, DM, Plants, Antidiabetic.*

INTRODUCTION

Hyperglycemia in the absence of therapy is a hallmark of a range of metabolic illnesses collectively referred to as diabetes. The diverse aetiopathology encompasses abnormalities in the metabolism of carbohydrates, fats, and proteins as well as deficiencies in the secretion, action, or both of insulin [1]. Chronic hyperglycemia is the primary symptom of a variety of metabolic diseases together referred to as diabetes mellitus. Either abnormal insulin secretion, different levels of insulin resistance, or typically both are the cause [2]. A metabolic condition known as chronic hyperglycemia is brought on by either insufficient insulin secretion, compromised insulin action, or both. Interestingly, insulin is a key anabolic hormone that influences how proteins, fats, and carbs are metabolized [3]. With around 60 million cases in India alone, diabetes is one of the top five serious health problems in developed countries [4].In just 34 years, the number of people with diabetes mellitus has quadrupled (from 108 million in 1980 to 422 million in 2014), while the global incidence of diabetes in individuals over the age of 18 has increased from 4.7% in 1980 to 8.5% in 2014. By 2030, diabetes is predicted by the WHO to rank as the seventh leading cause of death [5]. According to the International Diabetes Federation (IDF), there were about 463 million adults with diabetes in 2019, as shown in Figure 1. By 2030, that number is expected to rise to 578 million, and by 2045, it will reach 700 million [6].



(Fig.1): Projection of an increased incidence of diabetes patients worldwide[6].

Insulin and a variety of oral hypoglycemic medications, including glinides, biguanides, and sulfonylureas, are among the synthetic treatments for diabetes that are now on the market. Finding a safe and effective treatment is a crucial field of research because these methods have some very substantial side effects. Traditional medicine has shown promise in treating a wide range of illnesses, including diabetes. According to ethnobotanical data, about 800 plants may have anti-diabetic properties and have demonstrated advantages in the management or avoidance of issues associated with diabetes [7]. The majority of phytoconstituents derived from plants that have therapeutic

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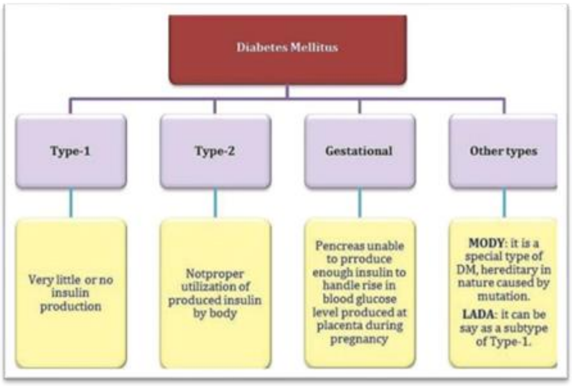
properties are described as secondary metabolites, which are produced by the primary metabolic pathways of the plant [8].The goal of the review is to compile the existing data on plants with antidiabetic activity in order to comprehend the significance of traditional herbs, as traditional medicines have shown a promising future in the treatment of diabetes [9].

Classifications Of Diabetes Mellitus: According to World Health Organization, Diabetes Mellitus(DM) is classified as shown in figure 2.



(**Fig.2**): Classification of Diabetes Mellitus according to WHO [10].

1. Type 1 Diabetes Mellitus:

Between 5 and 10% of all instances of diabetes are type 1 diabetes mellitus (T1DM), often referred to as juvenile-onset diabetes, insulin-dependent diabetes mellitus (IDDM), or type 1A DM. T-cell-mediated death of pancreatic β-cells is a hallmark of this autoimmune disease, leading to insulin insufficiency and, eventually, hyperglycemia [11].The condition is characterized by immune-mediated beta cell death, with hyperglycemia only developing when 90% of beta cells are gone.[12].

2. Type 2 Diabetes Mellitus:

According to the old nomenclature, T2DM, sometimes referred to as adult-onset diabetes or non-insulin-dependent diabetes mellitus (NIDDM), accounts for 90–95% of all cases of diabetes. Insulin resistance and β-cell dysfunction are the two primary insulin-related abnormalities that define this type of diabetes [11].A consistently high blood glucose level or an increase in blood glucose following a carbohydrate-containing meal are characteristics of type 2 diabetes mellitus (T2DM) (Table 2.1) [13].

Table (2.1): Range of Blood glucose level before and after meal.

Diagnosis	HgbA1c	Fasting Glucose (mm/dL)	OGTT[a] (mg/dL)	Insulin (ulU/L)	Glucose in Blood[b] Grams
Normal	<5.7%	<100 (5.6)	<140 (7.8)	<10 (60)	<5.0
Pre-diabetes	5.7-6.4%	100–125 (5.6–6.9)	140–199 (7.8–11)	>10 (60)	5.0–6.25
Type-2 diabetes	≥6.5%	>125 (6.9)	≥200 (11.1)	>10 (60)	>6.25

[a]OGGT, oral glucose tolerance test. At 2 h after drinking 75 grams of glucose. [b]Assuming 5L of blood.

The following symptoms are typically present in type 2 diabetes mellitus (although they may not be present): frequent urination, particularly at night (nocturia); polyuria, polydipsia, polyphagia, and intense hunger; weight loss; weakness or fatigue; lack of interest or focus; nausea and stomach pain; blurred vision; common infections and inflammation; slow-healing wounds; and tingling in the extremities [14].

2.1 Complications of Type 2 Diabetes Mellitus:

People with type 2 diabetes are more likely to experience a number of short-term and long-term problems.Cancer is one of the complications.Microvascular conditions including retinopathy, nephropathy, and neuropathy, as well as macrovascular conditions like hypertension, hyperlipidemia, heart attacks, coronary artery disease, strokes, cerebral vascular disease, peripheral vascular disease, and cancer, are additional consequences [15].

2.2 Etiology of Type 2 Diabetes Mellitus:

Type 2 diabetes has a broad and complex etiology that includes genetic, behavioral, and environmental variables (see Table 2.2.1).

Table (2.2.1): Risk factors of Type 2 DM [16].

Modifiable	Non-modifiable
-Obesity -Diet -Physical inactivity -Smoking -Environment	-Age -Ethnicity -Family history -Gastational diabetes -Intrauterine environment/birth weight

3. Gastational Diabetes:

A prevalent antepartum illness affecting around 9–25% of births worldwide, GDM is defined as glucose intolerance with onset or first recognition during pregnancy. Rates vary based on study populations and diagnostic criteria. Impaired glucose tolerance due to maternal pancreatic β-cell malfunction, which results in insufficient insulin to maintain glucose homeostasis throughout pregnancy, is a hallmark of gestational diabetes mellitus [17].

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Table (3.1): Risk Factors For Gastational Diabetes [17]:

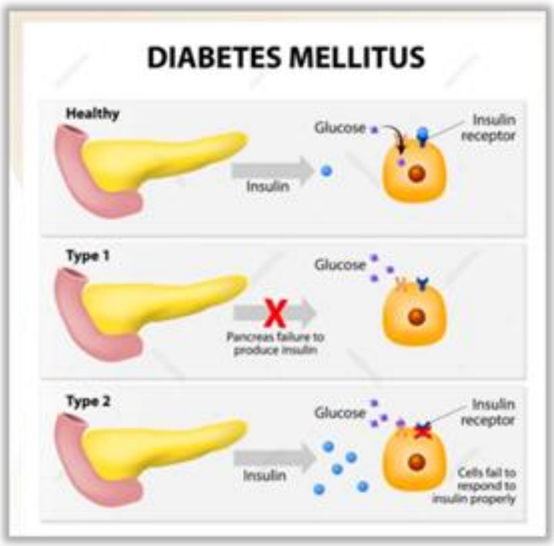
Modifiable	Non-modifiable
-Overweight -Obesity -Pre-Pregnancy Body Mass Index (BMI)	-Maternal Age -Ethnicity -Genetics and Family History of Hyperglycemia

4. General symptoms of Diabetes Mellitus include: [18]

- Increased hunger
- Increased thirst
- Weight loss
- Frequent urination
- Blurry vision
- Extreme fatigue
- Sores that don't heal

5. Pathophysiology:

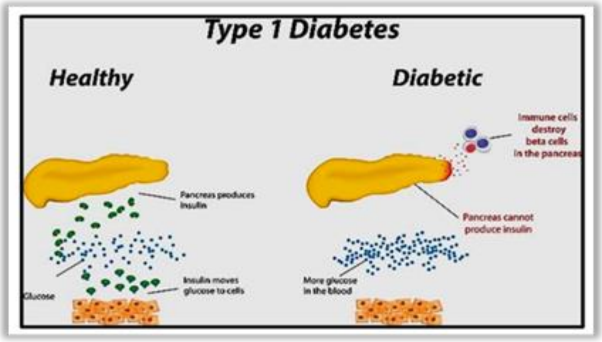
It depends on how much insulin the body uses and how much of it is present. Type 1 diabetes mellitus lacks insulin, whereas type 2 diabetes mellitus has peripheral tissues that resist the effects of insulin. When blood glucose levels rise, the pancreatic beta cells release insulin to support the brain, an organ that depends heavily on blood glucose levels for optimal operation. Medication that cure hyperglycemia include insulin and oral antihyperglycemics [19].



(Fig.3):General Pathophysiology of Diabetes Mellitus[20].

5.1 Pathophysiology of Type 1 Diabetes Mellitus:

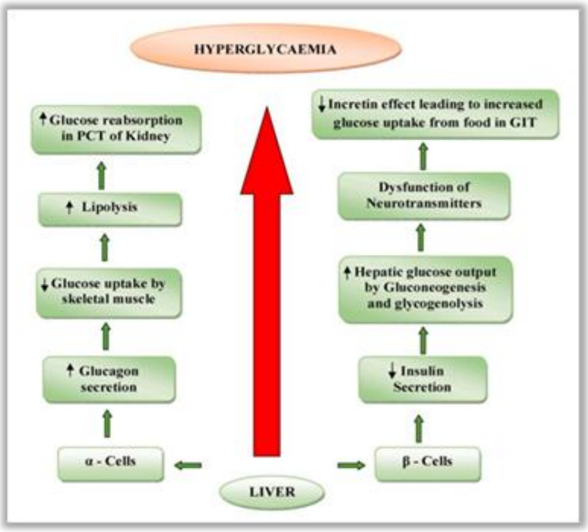
The pathophysiology of Type 1 diabetes appears to be significantly more complex than previously thought. Recent research suggests a complex interaction of genetic, epigenetic, and environmental variables [21].



(Fig.4): Pathophysiology of Type 1 DM [22].

5.2 Pathophysiology of Type 2 Diabetes Mellitus:

B-cell malfunction leads to diminished insulin release, restricting the body's ability to maintain normal glucose levels. On the other hand, Insulin Resistance increases glucose synthesis in the liver while decreasing glucose absorption in the muscle, liver, and adipose tissue[23].Insulin Resistance is the principal pathophysiological mechanism causing disruption in metabolic function. In this circumstance, mitochondria play a key role in the metabolism of energy in cells and homeostasis [24].



(Fig.5): Pathophysiology of Type 2 DM [25].

5.3 Pathophysiology of Gastational Diabetes Mellitus:

Insulin resistance and β-cell dysfunction contribute to the development of gestational diabetes mellitus. Abnormalities in the body prior to conception are a significant risk factor for the development of gestational diabetes mellitus and Type 2 diabetes. After delivery [26].

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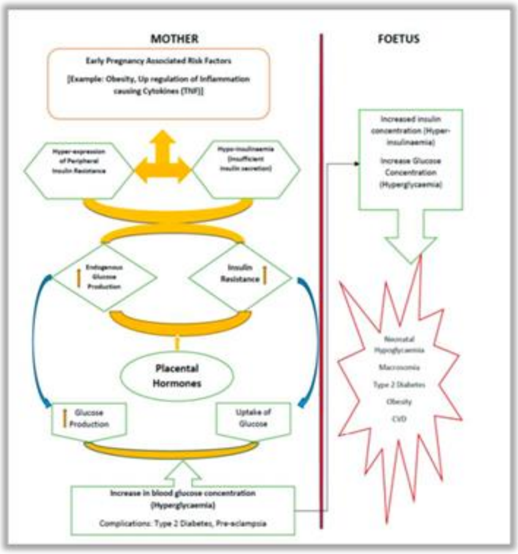
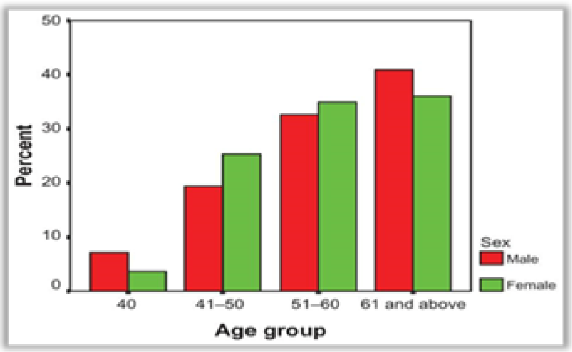


(Fig.6): Pathophysiology of Gastational Diabetes Mellitus [27].

6. Epidemiology:

6.1. Global burden of Diabetes Mellitus:

According to estimates, 463 million people worldwide—or 9.3% of the adult population aged 20 to 79—have diabetes in 2019. It is anticipated that this figure will rise to 700 million (10.9%) in 2045 and 578 million (10.2%) in 2030.According to Figure 8.8, the anticipated prevalence of diabetes in 2019 is 9.0% for women and 9.6% for men, broken down by age group **(Fig.7)**.The prevalence of diabetes rises with age, reaching 19.9% (111.2 million) among those 65 to 79 years of age [28].

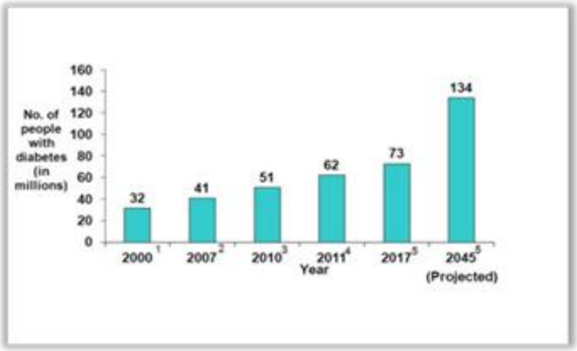


(Fig.7): Diabetes prevalence by age and sex [29].

6.2 Burden of Diabetes in India:

Diabetes prevalence in India has consistently increased since 1990, and has accelerated since 2000.Diabetes prevalence in India has increased from 7.1% in 2009 to 8.9% in 2019 [30].

(Fig.8): Diabetes prevalence in India [31].



7. Allopathic Medications

(Table 7.1): Classification of oral hypoglycemic drugs in treatment of Diabetes:[32,33,34]

Types	Available drugs	Their Actions
Biguanides	Metformin	It has insulin-sensitizing characteristics, lowering both basal and postprandial plasma glucose levels and increasing glucose absorption by the peripheral tissues.
Sulfonylureas	Gliclazide,glimepiride,glipizide,glibencla	Increases insulin release by pancreatic β-cells, lowering blood glucose levels and decreasing baseline hepatic glucose output.
α-glucosidase inhibitors	Miglitol and acarbose	Inhibits α-glucosidase enzyme in the small intestine, slowing digestion and absorption of carbohydrates and reducing blood glucose levels after meals.
Thiazolidinediones	Rosiglitazone and pioglitazone	Targets insulin resistance and improves insulin sensitivity in muscle tissues by activating intracellular receptors.

8. Plants used in management and treatment of Diabetes:

- **Fenugreek (Trigonella foenum-graecum):**

Trigonella foenum-graecum, commonly referred to as fenugreek, is a member of the Fabaceae family and is used extensively worldwide, especially in China, India, Egypt, and the Middle East, for both cooking and the management of

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type 2 diabetes [35]. It has long been used to treat a number of illnesses, including obesity and diabetes. It has galactagogic, antibacterial, antifungal, anti-inflammatory, antioxidant, and antihyperlipidemic qualities [36]. Numerous research have demonstrated the antidiabetic benefits of fenugreek in vitro, in animal experiments, and in trials including humans with diabetes and obesity [37].

(Fig.9): Fenugreek seeds.

- **Garlic (Allium sativum L.) :**

The herb Allium sativum L., generally referred to as garlic, is a member of the Liliaceae family and is found in Asia, Africa, and Europe. Originating in Asia, garlic is currently being used extensively as a condiment and spice, particularly in Asian cooking [38]. Chemical Constituents: Allicin, dially disulfide, dially trisulfide, and other sulfur-containing chemicals make up the 0.1–0.36% volatile oil found in garlic. The majority of garlic's pharmacological effects are believed to be caused by these volatile oils. The enzyme allinase is triggered when garlic is diced or crushed, converting alliin—which is found in whole garlic—into allicin. Additional significant substances found in garlic homogenate include ally methy thiosulfonate, 1-propenyl ally thiosulfonate, Garlic contains vitamins, minerals like selenium and germanium, and enzymes like myrosinase, peroxidase, and allinase. Garlic contains allicin, which has a strong hypoglycemic impact. This is assumed to be due to enhanced hepatic metabolism, insulin release, and insulin-sparing effect [39,40].

(Fig.10): Garlic.

- **Onion (Allium cepa L.):**

Allium cepa (commonly known as onion) is a perennial herb with its stem located in an underground bulb. Onions belong to the Liliaceae family [41]. The ethanolic extract of dried onion peel (Alium cepa L) has shown promising anti-diabetic activities by suppressing alpha-amylase activity. This inhibition reduces blood glucose levels and increases insulin production [42].

(Fig.11): Onion.

- **Ginseng**

Ginseng (Panax ginseng C. A. Meyer) from the Panax genus of Araliaceae is a well-known herbal medication used to treat type 2 diabetes [43]. The basic antidiabetic mechanism is to lower blood glucose levels, limit glucose absorption, reduce obesity, and raise the expression of GLUT-1 and GLUT-4 [44]. Ginseng and neutral ginsenosides have been shown to lower blood glucose, improve insulin sensitivity, control lipid metabolism, and lower body weight [45].

(Fig.12): Ginseng.

- **Aloe vera (L) Burm. (Asphodelaceae) :**

Aloe vera (L.) Burm. F., also known as Aloe barbadensis Mill., is an ancient herb of medicinal value from the Asphodelaceae family. Aloe vera comes in over 400 different types that are found in various locations. In India, it primarily grows in Rajasthan, Gujarat, Tamil Nadu, Andhra Pradesh, and Maharashtra [46]. Aloe vera has been shown to lower fasting plasma glucose levels, boost insulin levels, and repair pancreatic cells, both subjectively and quantitatively. Another study found that Aloe vera can increase insulin secretion by reducing oxidative stress and inflammation indicators [47].

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(Fig.13): Aloe vera plant.

- **Cassia auriculata L (Tanner's Cassia) :**

One such herb that is known to be beneficial for a variety of ailments is Cassia auriculata. It is an evergreen shrub with beautiful yellow flowers. This plant grows well in various parts of Asia, especially India [48]. In Indian traditional medicine, Cassia auriculata, also referred to as "Tanner's cassia," is frequently used to treat diabetes mellitus [49]. The aqueous extract of buds and flowers decreased blood sugar levels, the ethanolic extract of leaves and flowers controlled the diabetes condition by functioning as an insulin secretagogue agent, and the ethanolic extract of buds and flowers shown antidiabetic qualities both in vitro and in vivo [50].

(Fig.14): Plant of Cassia auriculata.

- **Cuminum cyminum L (Cumin):**

Cuminum cyminum, often known as 'zeera', is a popular spice used in cuisine due to its unique scent. It belongs to the Apiaceae family. It is the most primitively grown herb in Europe, Asia, and Africa [51]. This plant contains active components such as cumin aldehyde (49.4%), α-terpinen-7-al (6.8%), β-pinene (6.3%), g-terpinene (6.1%), γ-terpinene (6.1%), p-cymen-7-ol (4.6%), and thymol (2.8%). Cumin aldehyde, also referred to as 4-isopropyl benzaldehyde, is the most active of these components. It inhibits carbohydrate metabolism enzymes, including glycosidase and aldose reductase. The existence of these enzyme inhibitors could explain cumin's anti-diabetic benefits [52].

(Fig.15): Cumin.

- **Ocimum sanctum (L) (Tulsi):**

The genus Ocimum, which belongs to the Lamiaceae family, is highly valued for its therapeutic potential. Ocimum sanctum (Linn) (Tulsi) is referred to as "The Queen of Herbs," "The Incomparable One," or "The Mother Medicine of Nature" [53]. The Tetracyclic triterpenoid isolated from the aerial section of Ocimum sanctum possesses strong anti-diabetic properties [54].Oral administration of OS extract significantly reduced blood sugar levels in normal glucose-fed hyperglycemic and streptozotocin-induced diabetic rats [55].

(Fig.16): Plant of Tulsi.

- **Syzigium cumini (L) (Jamun):**

Syzygium cumini L., a native plant of the Myrtaceae family from Indonesia and India, is underutilized despite its significant occurrence in varied agroclimatic settings across South Asia [56].S. cumini's primary phenolic constituents, catechin, and gallic acid, have antioxidant and anti-diabetic qualities. They block intestinal α-glucosidases, promoting glucose transport via GLUT4 and glucose absorption properties [57,58].

(Fig.17): Fruit of Syzigium cumini.

- **Ficus bengalensis L. (Banyan tree):**

The British gave F. benghalensis (family Moraceae) its popular name after observing a particular colony known as the “Baniya” that used to rest in its shade. India’s national tree, the banyan, is revered and seen as a representation of spiritual wisdom. It is indigenous to several Asian countries, including China, India, Myanmar, Thailand, Malaysia, and Southeast Asia [59]. Banyan has significant therapeutic applications, including antidiabetic properties. Different aerial regions of FB were compared for their blood glucose-lowering activity. Fruits reduced blood glucose levels more effectively than root or bark. Aqueous extract of aerial roots of FB has antidiabetic properties due to high concentrations of certain glycemic components (calcium and magnesium) [60]. Stem bark extracts and chemicals have been shown to have antidiabetic properties in animal models [61].

(Fig.18): Tree of Ficus bengalensis.

- **Momordica charantia (Bitter melon):**

Momordica charantia (M. charantia), commonly known as bitter melon, karela, bitter gourd, or balsam pear, is a medicinal plant from the Cucurbitaceae family that is primarily grown in Africa, Asia, and South America [62].M. charantia contains a variety of hypoglycemic substances, such as insulin-like peptides, vicine, polypeptide-P, alkaloids, charantin, sterol glycosides, mcIRBP, triterpenoids, cucurbutanoid chemicals, flavonoids, and phenols [63].M. charantia contains a variety of bioactive chemicals with hypoglycemic properties, including cucurbitane-type triterpene glycosides, charantin, and momordicin [64].

(Fig.19): Fruits of bitter melon.

- **Nigella sativa L (Black cumin):**

Nigella sativa L. (NS) seeds, commonly known as black seed (English) and kalonji in South Asia, are the black-colored, funnel-shaped seeds of the Nigella sativa plant from the Ranunculaceae family. The plant grows in Southern Europe, North Africa, the Middle Eastern Mediterranean, and southern Asia (Syria, Turkey, India, Pakistan, and Saudi Arabia)[65]. Inhibiting carbohydrate-digesting enzymes (α-amylase and α-glucosidase) is crucial for preventing abrupt spikes in blood glucose levels [66].

(Fig.20): Flower and Seeds of Nigella sativa Plant.

- **Cinnamomum zeylanicum L.(Cinnamon):**

Cinnamomum zeylanicum (Family Lauraceae), also known as Ceylon cinnamon or real cinnamon, is an indigenous plant from Sri Lanka. Cinnamon has been demonstrated to offer numerous health benefits, including anti-hypertensive, anti-inflammatory, and blood glucose management (antidiabetic) qualities [67]. Cinnamon lowers blood glucose levels by decreasing insulin resistance and boosting hepatic glycogenesis. Cinnamon’s phenolic acid may play a role in regulating insulin signaling. Cinnamaldehyde has shown antihyperglycemic and antihyperlipidemic effects in diabetic mice [68].

(Fig.21): Cinnamon sticks.

- **Helicteres isora L :**

Helicteres isora L., also known as “Marorphali,” “Avartani,” and “Indian screw tree,” is a small tree or big shrub in the Malvaceae family [69]. It possesses glucose uptake activity at 200 mg/mL and has been demonstrated to be as effective as metformin and insulin. Because of its hypolipidemic and

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insulin-sensitizing qualities, the ethanolic extract has the potential to cure type 2 diabetes[70].

(Fig.22): Flower of Helicteres isora Linn.

CONCLUSION

Diabetes Mellitus is a complex metabolic condition that requires several management options. This paper discusses medicinal plants' potential as supplementary therapy for diabetes care, providing a natural and sustainable alternative. Further research is needed to completely understand the mechanisms of action and effective use of these plants. However, available evidence suggests they can improve glycemic control and reduce diabetes-related complications.

REFERENCES

1. Classification of diabetes mellitus. Geneva: World Health Organization; 2019. Licence: CC BY-NC-SA 3.0 IGO.
2. Schleicher E, Gerdes C,Petersmann A, Dirk Müller-Wieland, Ulrich A. Müller,Freckmann G. Definition, Classification and Diagnosis of Diabetes Mellitus.German Diabetes Association: Clinical Practice Guidelines.2021; 16 (2):110-118.
3. Antar S.A., Ashour N.A., Sharaky M. "Diabetes mellitus: Classification, mediators, and complications; A gate to identify potential targets for the development of new effective Treatments".Biomedicine & Pharmacotherapy. 2023; Volume 168 ; 01-20.
4. Singh KK, Singh SS and Sharma CL: Antidiabetic and antioxidant properties of important traditional medicinal plants from Northeastern India. Int J Pharm Sci & Res 2024; 15(6): 1728-36.
5. Alam, S.; Hasan, M.K.; Neaz, S.; Hussain, N.; Hossain, M.F.; Rahman, T. Diabetes Mellitus: Insights from Epidemiology, Biochemistry, Risk Factors, Diagnosis, Complications and Comprehensive Management. *Diabetology* 2021, 2;36–50.
6. Yedjou, C.G.; Grigsby, J.; Mbemi, A.; Nelson, D.; Mildort, B.; Latino, L.; Tchounwou, P.B. The Management of Diabetes Mellitus Using Medicinal Plants and Vitamins. *Int. J. Mol. Sci*. 2023, 24 ;01-14.
7. Matalqah SM and Al-Tawalbeh DM: Medicinal plants potential against diabetes mellitus: Review article.Int J Pharmacognosy 2019; 6(2): 39-53.
8. Deka H,Choudhury A,Dey BK. "An Overview on Plant Derived Phenolic Compounds and Their Role in Treatment and Management of Diabetes".Journal of Pharmacopuncture 2022;25(3):199-208.
9. Malviya N, Jain S, Malviya S.ANTIDIABETIC POTENTIAL OF MEDICINAL PLANTS.Acta Poloniae Pharmaceutica-Drug Research.2010. Vol. 67 (2): 113-118.
10. El-Attar N.E, Moustafa BM, Awad WA. "Deep Learning Model to Detect Diabetes Mellitus Based on DNA Sequence". *Intelligent Automation & Soft Computing*.2022:31(1);325-338.
11. Banday MZ, Sameer AS, Nissar S. Pathophysiology of diabetes: An overview. Avicenna J Med 2020;10:174-88.
12. Alam U, Asghar O, Azmi S and Malik RA.General aspects of diabetes mellitus.*Handbook of Clinical Neurology*, Vol. 126 (3rd series); *Diabetes and the Nervous System*.2014:211-222.
13. Westman EC. "Type 2 Diabetes Mellitus: A Pathophysiologic Perspective".*Frontiers in Nutrition*. 2021:8;01-05.
14. Farmaki P, Damaskos C, Garmpis N, Garmpi A, Savvanis S and Diamanti E.Complications of the Type 2 Diabetes Mellitus.*Current Cardiology Reviews.* 2020,:16 (4); 249-251.
15. Banwari M, Kawathekar N & Jain G. Pathophysiology and treatment of type 2 diabetes mellitus: A Review.Journal Of Coastal Life Medicines .2023; 1 (11);1171-1193.
16. C. Burns and I. Sirisena.Type 2 Diabetes: Etiology, Epidemiology, Pathogenesis, Treatment.Springer International Publishing Switzerland.2016; 601-617.
17. Alejandro EU, Mamerto TP, Chung G, Villavieja A, Gaus NL, Morgan E, Pineda-Cortel MRB. Gestational Diabetes Mellitus: A Harbinger of the Vicious Cycle of Diabetes. *International Journal of Molecular Sciences.* 2020; 21(14):5003;01-21.
18. Dwivedi M, Raj Pandey AR.Diabetes Mellitus and Its Treatment: An Overview.*Journal of Advancement In Pharmacology*.2020:1(1);48-58.
19. Ojo OA,Ibrahim HS,Rotimi DE, Ogunlakin AD, Ojo AB. Diabetes mellitus: From molecular mechanism To pathophysiology and pharmacology.*Medicine in Novel Technology and Devices*.2023:19;100247.
20. Rozzo, Nancy. "Pathophysiology of Diabetes Mellitus". *Nursing Student Class Projects (Formerly MSN)*.2020;429; 1.
21. Del Chierico, F.; Rapini, N.;Deodati, A.; Matteoli, M.C.;Cianfarani, S.; Putignani, L.Pathophysiology of Type 1 Diabetes and Gut Microbiota Role. *Int. J. Mol.Sci.* 2022, 23 ;01-12.
22. C. Michael Gibson. 31 August 2020.Diabetes mellitus type 1 pathophysiology.10 October 2024. https://www.wikidoc.org/index.php/File:Type-1-diabetes_pathophysiology.jpg
23. Galicia-Garcia U, Benito-Vicente A, Jebarib S, Larrea-Sebal A, Siddiqi H, Uribe KB, Ostolaza H and Martín C.Pathophysiology of Type 2 Diabetes

*Corresponding Author: **Sajid Khan.**

Mellitus.*International Journal of Molecular Sciences.* 2020; 21: 01-34
24. Jessica E.B.F. Lima, Natalia C.S. Moreira, Elza T. Sakamoto-Hojo.Mechanisms underlying the pathophysiology of type 2 diabetes: From risk factors to oxidative stress, metabolic dysfunction, and Hyperglycemia.*Mutation Research/Genetic Toxicology and Environmental Mutagenesis.* 2022 ;874-875;01-13.
25. Padhi S, Nayak AK, Behera A. Type II diabetes mellitus: a review on recent drug-based therapeutics.*Biomedicine & Pharmacotherapy*. 2020;131;01-23.
26. Gajera D, Trivedi V. Detailed Review on Gestational Diabetes Mellitus with Emphasis on Pathophysiology, Epidemiology, Related Risk Factors, and its Subsequent Conversion to Type 2 Diabetes Mellitus.Horm Metab Res 2023; 55: 295–303.
27. Sharma, A.K.; Singh, S.;Singh, H.; Mahajan, D.; Kolli, P.;Mandadapu, G.; Kumar, B.; Kumar,D.; Kumar, S.; Jena, M.K. Deep Insight of the Pathophysiology of Gestational Diabetes Mellitus. *Cells*. 2022: 11; 01-19.
28. Saeedi P. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. DIABETES RESEARCH AND CLINICAL PRACTICE.2019: 157; 01-10.
29. The anterior segment of the eye in diabetes - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Age-sex-distribution-of-181-patients-with-diabetes-malefemale-ratio-is-1210_fig1_225086712 [accessed 15 Oct 2024].
30. Pradeepa R, Mohan V. Epidemiology of type 2 diabetes in India. Indian J Ophthalmol 2021;69:2932-8.
31. India Science, Technology and Innovation Portal, Exploring Diabetes Epidemic in India,9 August 2024. https://www.indiascienceandtechnology.gov.in/featured-science/exploring-diabetes-epidemic-india
32. Sapra A, Vaqar S, Bhandari P. Diabetes Mellitus. [Updated 2019 Dec 9].Treasure Island (FL): StatPearls Publishing; 2020 Jan. https://www.researchgate.net/publication/339297854
33. Afroj A. Shaikh et al., Int. J. Res. Pharm. Sci., 2022, 13(1), 102-109.
34. Sitobo Z, Navhaya LT, Makhoba XH. Medicinal plants as a source of natural remedies in the management of diabetes. *INNOSC Theranostics and Pharmacological Sciences.* 2024;7(3):01-13.
35. Shabil, M.; Bushi, G.; Bodige, P.K.; Maradi, P.S.; Patra, B.P.; Padhi, B.K.; Khubchandani, J. Effect of Fenugreek on Hyperglycemia: A Systematic Review and Meta-Analysis. *Medicina* 2023, 59, 248:01-14.
36. Baset ME, Ali TI, Elshamy H. Anti-diabetic effects of fenugreek (Trigonella foenum-graecum):A comparison between oral and intraperitoneal administration - an animal study. INTERNATIONAL JOURNAL OF FUNCTIONAL NUTRITION. 2020 :1(2) ; 01-09.
37. Haxhiraj, M.; White, K.; Terry, C. The Role of Fenugreek in the Management of Type 2 Diabetes. *Int. J.Mol. Sci*. 2024 : 25;01-15.
38. Sivakumar T, Deepa B.A critical review on Antidiabetic Potential of Herbal plants and its their bioactive components. Journal of University of Shanghai for Science and Technology. 2023: 25(01) ;303- 314.
39. Nasir A, Fatma G,Neshat N and Ahmad MA. Pharmacological and therapeutic attributes of garlic (*Allium sativum Linn.*) with special reference to Unani medicine-A review. Journal of Medicinal Plants Studies 2020; 8(3): 06-09.
40. Batiha G El-Saber, Beshbishy A.M.; Chemical Constituents and Pharmacological Activities of Garlic (*Allium sativum L.*): A Review. *Nutrients*. 2020; 12,872;01-21.
41. Chakraborty A.J.; Uddin T.M.; Allium cepa: A Treasure of Bioactive Phytochemicals with Prospective Health Benefits.Evidence-Based Complementary and Alternative Medicine. 2022; 2022;01-27.
42. Esakki A, Ramadoss R, Ananthapadmanabhan L, et al. Quantification of the Anti-diabetic Effect of Allium cepa. Cureus 2024:16(4):01-06.
43. Wang, H.; Teng, Y.; Li, S.; Li, Y.; Li, H.; Jiao, L.; Wu, W.UHPLC-MS-Based Serum, and Urine Metabolomics Reveals the Anti-Diabetic Mechanism of Ginsenoside Re in Type 2 Diabetic Rats. *Molecules* 2021, 26, 6657;01-17.
44. Przeor, M. Some Common Medicinal Plants with Antidiabetic Activity, Known and Available in Europe (A Mini-Review).*Pharmaceuticals* 2022, 15, 65;01-25.
45. Alam S, Sarker MMR, Sultana TN, Chowdhury MNR, Rashid MA, Chaity NI, Zhao C, Xiao J, Hafez EE, Khan SA and Mohamed IN. Antidiabetic Phytochemicals from Medicinal Plants: Prospective Candidates for New Drug Discovery and Development.Front. Endocrinology 2022:13 ;01-35.
46. Govindarajan S, Babu S.N.; Vijayalakshmi M.A.Aloe vera carbohydrates regulate glucose metabolism through improved glycogen synthesis and downregulation of hepatic gluconeogenesis in diabetic rats. *Journal of Ethnopharmacology* 2021;281;01-12.
47. Babu S.N, Govindarajan S, Noor A.Aloe vera and its two bioactive constituents in alleviation of diabetes –proteomic & mechanistic insights. *Journal of Ethnopharmacology* 2021:280;01-09.

*Corresponding Author: **Sajid Khan.**

48. Hithesh Gowda H S, Karthik S.A Pharmacological review on *Cassia Auriculata. J. innov. Ap pl. pharm. Sci*, 7(3) 2022, 113-117.
49. Shanmugam, H., & Venkatesan, R. S. Determination of antihyperglycemic activity of ethanolic crude leaf extract of *cassia auriculata* in the streptozocin induced male wistar albino rats. *International Journal of Health Sciences.* 2022; 6(S3), 5617–5630.
50. Salma BJanhavi P,Muthaiah S.Ameliorative Efficacy of the Cassia auriculata Root Against High-Fat- Diet + STZ-Induced Type-2 Diabetes in C57BL/6 Mice. *ACS Omega* 2021, 6, 492−504.
51. Mughal S.S., A review on potential antioxidant effects of Cumin *(Cuminum cyminum),* phytochemical Profile and its uses. Global Scientific Journal 2020,8(9);01-19.
52. Ghods M., Karimi S., Salari S., Alem E., Bahmani P., Karimi A., Saeedpour A., Noormohamadi M., Jahromi S. R. Anti-diabetic effect of a combination of black seed *(Nigella sativa)* and Cumin *(Cuminum cyminum),* a two-step study from bench to bed. Functional Food Science. 2023; 4(2):55-68.
53. Kesevan, R.K., Norakma, M.N, Total phenolic content and anti-diabetic activity of dried and fresh leaves of *Ocimum sanctum (Linn). Food Research* 2023, 7 (Suppl. 4): 139 - 145.
54. Almatroodi SA, Alsahli MA, Almatroudi A, Rahmani AH. *Ocimum sanctum*: Role in Diseases Management Through Modulating Various Biological Activity. Pharmacogn J.2020;12(5):1198-205.
55. Gulhane N.S., Ghode C.D., Jadhao A.G.and Patil P.A.Study of medicinal uses of *Ocimum sanctum* (Tulsi). Journal of Pharmacognosy and Phytochemistry 2021; 10(2): 1427-1431.
56. Gajera H.P, Hirpara D.G. Exploring the antioxidant and antidiabetic potentials of *Syzygium cumini L.* landraces: phytochemicals, bioactive constituents and pathway enrichment analysis.International Journal of Food Science and Technology 2024;01-11.
57. Komal V. Mahindrakar & Virendra K. Rathod.Antidiabetic potential evaluation of aqueous extract of waste *Syzygium cumini* seed kernel's by in vitro α-amylase and α-glucosidase inhibition, Preparative Biochemistry & Biotechnology.2020;01-10.
58. Rashid, F.; Javaid, A.; Mahmood-ur-Rahman; Ashfaq, U.A.; Sufyan, M.; Alshammari, A.; Alharbi, M.; Nisar, M.A.; Khurshid, M.Integrating Pharmacological and Computational Approaches for the Phytochemical Analysis of *Syzygium cumini* and Its Anti-Diabetic Potential. *Molecules* 2022, 27;01-16.
59. Singh P, Dhankhar J, Kapoor RK, Kumar D, Bhatiya S, Al-Harrasi A, Sharma A. *Ficus benghalensis*—A comprehensive review on pharmacological research, nanotechnological applications, and patents. J Appl Pharm Sci, 2023; 13(10):059–082.
60. Navneet Kumar Verma et al.: Medicinal Uses, Phytochemistry, and Pharmacological Actions Ficus Benghalensis and *Ficus Religiosa*.International Journal of Medical and Pharmaceutical Research 2023;4(3);350-353.
61. Logesh R, Sathasivampillai S.V.,, Varatharasan S, Rajan S, Das N, Pandey J, Devkota H.P.; *Ficus benghalensis* L. (Moraceae): A review on ethnomedicinal uses, phytochemistry, and pharmacological activities, *Current Research in Biotechnology* 2023;6; 01-09.
62. Oyelere S.F.A detailed review on the phytochemical profiles and anti-diabetic mechanisms of *Momordica charantia*. *Heliyon* 2022; 8 ;01-11.
63. R,Mustafa G,Mahrosh HS.Molecular Docking and Simulation Studies of Antidiabetic Agents Devised from Hypoglycemic Polypeptide-P of *Momordica charantia*.BioMed Research International 2021;01-15.
64. Xu, B.; Li, Z.; Zeng, T.; Zhan,J.; Wang, S.; Ho, C.-T.; Li, S. Bioactives of *Momordica charantia* as Potential Anti-Diabetic/Hypoglycemic Agents. *Molecules* 2022, 27;01-17.
65. Mahomoodally, M.F.; Aumeeruddy, M.Z.; Legoabe, L.J.; Montesano, D.; Zengin, G. *Nigella sativa* L. and Its Active Compound Thymoquinone in the Clinical Management of Diabetes: A Systematic Review. *Int. J. Mol. Sci.*2022, 23; 01-26.
66. Vijayakumar, S., Divya, M., Vaseeharan, B. et al. Biological Compound Capping of Silver Nanoparticle with the Seed Extracts of Blackcumin (*Nigella sativa*): A Potential Antibacterial, Antidiabetic, Antiinflammatory, and Antioxidant. J Inorg Organome t Polym 2021 31, 624–635.
67. Wariyapperuma WANM, Kannangara S, Wijayasinghe YS, Subramanium S, Jayawardena B.In vitro anti-diabetic effects and phytochemical profiling of novel varieties of *Cinnamomum zeylanicum* (L.) extracts. *PeerJ* :2020 ;8;01-18.
68. Christiany C,Sudraja S.E,Rahayu I.The Potency of *Cinnamomum Zeylanicum* to Prevent Diseases: A Review.Eureka Herba Indonesia 2021 ;2 (1); 49-58.
69. Pandey S, Patel D, Mishra P, Tiwari R.Morphological, phytochemical and pharmacological study of *Helicteres isora* (Marorphali).International Journal of Research in Pharmacy and Pharmaceutical Sciences 2021,6(3); 13-17.
70. Hoque M, Md. Hossain F, Tusher STI, Md. Aktaruzzaman and Afrida Hasan. Few promising medicinal plants as anti-diabetic agent. *International Journal of Pharmacognosy and Life Science* 2024; 5(1): 93-101.
71. Amalkar, S. V., Hatwar, P. R., Bakal, R. L., & Kohale, N. B. (2024). Advance in gold

*Corresponding Author: **Sajid Khan.**

nanoparticle-mediated drug delivery system. *GSC Biological and Pharmaceutical Sciences*, *28*(3), 169-179.

72. Dafe, V. N., Hatwar, P. R., Bakal, R. L., Kubde, J. A., & Jumde, K. S. (2024). Transdermal insulin delivery via microneedle technology, patches, and pumps offers a promising alternative to traditional subcutaneous injections for diabetes management. *GSC Biological and Pharmaceutical Sciences*, *29*(1), 233-242.
73. Hatwar, P. R., Bakal, R. L., Dumare, A. A., Dere, M. D., & Hage, P. D. (2023). TARGETED DRUG DELIVERY SYSTEM FOR THE TREATMENT OF CANCER.

*Corresponding Author: **Sajid Khan.**