Alternative natural therapeutic plants and diabetes mellitus

Mohamed S. Abd El Hafeez [1], *

[1]*Pharmacognosy Department, Faculty of Pharmacy, Egyptian Russian University, Badr City, Cairo-Suez Road, 11829, Cairo, Egypt.*

*Corresponding author(s): Mohamed S. Abd El Hafeez, E-mail: mohamed-sayed@eru.edu.eg

ABSTRACT

Diabetes mellitus (DM) is a main health badly-behaved, that is not considered a disease of largely developed countries. The occurrence of diabetes is gradually growing far and wide, most obviously in developing countries. The majority of anti-diabetic formulations/medicines prescribed attempt to stabilize or lower blood glucose levels. In addition to traditional medications, some individuals employ complementary or alternative therapies to treat diabetes. Many phytochemical or herbal compositions are highly useful in diabetes control and treatment. Natural antidiabetic drugs exhibit several mechanisms of action. α-glucosidase inhibition, inhibition of aldose reductase, inhibition of α-amylase stimulation of insulin secretion from β-cells, antioxidant activity, and numerous other mechanisms. This mini-review was performed on the four selected herbal drugs, Mango leaves (*Mangifera indica* L., Family Anacardiaceae), leaves of Rosemary (*Rosmarinus officinalis* L., Family Lamiaceae), grains of Barley (*Hordeum vulgare* L. Family Poaceae) and *Delonix regia* leaves (*Delonix regia* L, Family Fabaceae) which are growing in Egypt.

Keywords: Diabetes mellitus, IDF, natural products.

1-Introduction

Diabetes mellitus is a main health problem, that is not considered a disease of wealthy countries. The occurrence of diabetes is gradually growing everywhere, most obviously in developing countries.

Worldwide, the number of individuals with diabetes has more than doubled during the past 30 years. The latest universal estimate from International Diabetes Federation (IDF) in 2021 stated that 536 million persons with diabetes mellitus and that by 2045 the number will be 783 million (**1**). according to (IDF), in 2021 over 39 million persons in Middle East and North Africa (MENA) region had diabetes, and it is expected that the number will reache 82 million in 2045. Egypt is the state with the major number of diabetes persons (8.3 million). In 2021, the IDF ranked Egypt as the 8th country in the world in the number of patients with diabetes, with the occurrence estimated to be about 15.1% mid adults among 20-79 years and yearly death of 373.00. It is alarming that diabetes occurrence in Egypt has enlarged within a quick period and it is predictable the number will jump to 16.7 million by 2045 (**1**).

Definition:

Diabetes mellitus is a collection of metabolic diseases in which blood sugar is high, because the pancreas does not produce sufficient insulin, or because cells do not reply to the insulin that is formed. The long-lasting hyperglycemia of diabetes is linked with long-standing damage, dysfunction, and failure of different organs. Numerous pathogenic progressions are involved in the progress of diabetes. These range from autoimmune destruction of the *β*-cells of the pancreas with subsequent insulin shortage to anomalies that result in a confrontation with insulin action (**2**).

Types of Diabetes

There are several types of *Diabetes Mellitus*; **Type I,** also identified as Insulin Dependent Diabetes Mellitus (IDDM), which is genetic and treated by insulin, and **Type II**, Non-Insulin Dependent Diabetes Mellitus (NIDDM) **Table 1**, which occurs in old people and is treated by controlling the diet and oral anti-diabetic drugs.

The chief signs of these types are; the increased need for liquids, increased urinary output, ketonemia, and ketonuria. In **Type I** (IDDM), the insulin–producing cells in the pancreas are lost as a consequence of an attack from the body's immune system. The result is a total lack of self–produced insulin and patients have to take it every day **(2)**.

IDDM is not linked to obesity and is exacerbated by ketosis and acidity. In type II diabetes (NIDDM), the amount of insulin produced is insufficient, or the body's cells do not respond to its presence. If the *β*-cells have not been emptied, NIDDM is frequently associated with normal shape and insulin content. The precise causes of pancreatic failure and loss of insulin cellular acceptance are unknown, however, they are linked to illness, environmental, and/or nutritional factors **(3)**.

Table (1): Common differences between type I and II diabetes

Feature	Type I diabetes	Type II diabetes
Onset	Sudden	Gradual
Age at onset	Any age (mostly in young)	Mostly in adults
Body habitus	Thin or normal	Often obese
Ketoacidosis	Common	Rare
Auto antibodies	Usually present	Absent
Endogenous insulin	Low or absent	Normal, decreased or increased

Gestational Diabetes Mellitus (GDM):

1- GDM is well-defined as any degree of glucose intolerance that begins or is first seen during pregnancy.

2- Although the majority of cases end with delivery, the criteria apply whether or not the problem persists following pregnancy.

3- This criterion aided in the development of a standardized technique for the identification and classification of GDM, but its limitations were acknowledged for many years.

4- As the continuous obesity and diabetes epidemic has resulted in a rise in type II diabetes in women of reproductive age, the number of pregnant women with undiagnosed type II diabetes has grown **(4)**.

Symptoms of Diabetes:

The symptoms of the two major forms of diabetes are essentially identical, but their severity varies. The initial symptoms of untreated diabetic patients are attributed to elevated blood glucose levels. **Figure 1**, As a result,

1- there is a loss of glucose in the urine, which increases urine output, resulting in dehydration, thirst, and increased water consumption.

2- Despite an increase in desire and food consumption, insulin insufficiency eventually leads to weight reduction.

3- Diabetic individuals who are untreated experience exhaustion, nausea, and vomiting. They are more prone to bladder, skin, and vaginal infections.

4- Blood sugar fluctuations can cause hazy vision. Furthermore, extremely high blood sugar levels might cause unconsciousness and even death **(5)**.
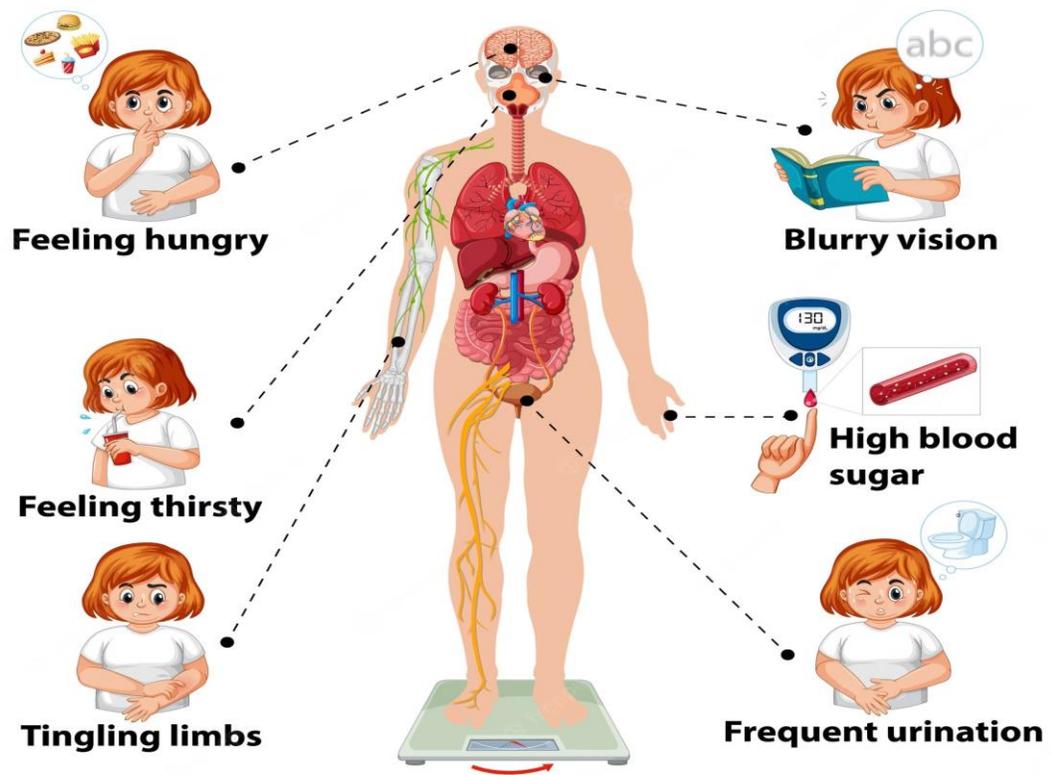
DIABETES SYMPTOMS

Figure 1: symptoms of diabetes www.freepik.com

Risk Factors and Causes of Diabetes:

Several studies have been conducted to determine the cause of diabetes. Diabetes has been discovered to be a complex, diverse condition that is influenced by a variety of factors including:

1- hormones

2- genetics

3- obesity

4- ethnicity

5- age

6- biochemical factors (6).

- Type I diabetes is thought to be caused by a mix of genetic vulnerability and environmental variables, and despite the substantial investigation into potential

biological, pharmacological, dietary, and behavioral causes, none has yet been identified as the cause.

- Type II diabetes risk factors are better understood. Although there is a significant hereditary component, the majority of instances occur in the context of risk factors such as age, obesity, and physical inactivity.

- Although smoking has been demonstrated to raise the risk of diabetes, increasing body fat is by far the most significant risk factor.

- A high sugar and fat intake, for example, has also been related to an increased risk of type II diabetes.

- Gestational diabetes risk factors include, in addition to family history, age, obesity, and physical inactivity, as well as excessive weight gain during pregnancy (7).

Diagnosis of diabetes:

The sugar tolerance test, often known as the glucose tolerance test (GTT), is an important blood sugar test for identifying diabetes.

1- Diabetes is classified as normal, mild, moderately severe, or severe based on the patient's blood sugar level.

2- This test is commonly performed in the morning after a night's fast, although it can also be performed four or five hours after the last food was consumed. Fasting blood sugar levels are measured using blood samples.

3- After obtaining the blood sample, the patient is administered 1.75 g of glucose/kg body weight orally, and blood samples are obtained at half, one, and two-hour intervals to assess the blood sugar level. In the normal scenario, the blood sugar level climbs to around 150 after an hour, then begins to decline, and returns to normal after two hours.

4- In diabetics, the sugar level rises higher at 200-300 mg and remains high for a longer period, i.e., 3-6 hours. Furthermore, the peak value is obtained over a longer period (2 hours).

5- The peak of the curve in non-diabetics is frequently between half and one hour. Sodium fluoride (100 mg/ml) must be added to the blood shortly after collection for sugar measurement.

6- This is done to prevent blood enzymes from changing the amount of glucose in the blood during storage.

7- However, within limitations, the glucose concentration in the blood responds to several biochemical and physiological activities. Stress, meal size, sugar content, rate of digestion, and drugs that modify glucose absorption and metabolism all allow sugar levels to be altered at various stages along the glucose cycle in the body. (3).

Mechanism of natural antidiabetic drugs:

The majority of anti-diabetic formulations/medicines prescribed attempt to stabilize or lower blood glucose levels. In addition to traditional medications, some individuals employ complementary or alternative therapies to treat diabetes. Many phytochemical or herbal compositions are highly useful in diabetes control and treatment **(6).** Herbal medicines are the leading major actors among accessible therapies, particularly in rural areas, due to their ease of availability, few side effects, and low cost **(5).Figure 2.**

Natural anti-diabetic drugs have a variety of mechanisms of action, including increasing insulin sensitivity, inhibiting gluconeogenesis and glycogenolysis in the liver, stimulating glycogenesis, increasing glucose uptake in adipose and skeletal muscle tissues, inhibiting glucose absorption in the intestine, improving glucose metabolism, and lowering lipid peroxidation and oxidative stress **(8, 9).**

Alkaloids, terpenoids, phenolics, flavonoids, and a variety of other types of plant secondary metabolites all exhibit promising anti-diabetic properties. These organic components might exert their effects via several methods. for instance, α-glucosidase inhibition **(10)** inhibition of aldose reductase **(11)**, inhibition of α-amylase **(12)** stimulation of insulin secretion from β-cells **(13),** antioxidant activity **(14)**, and numerous other mechanisms **(9).**
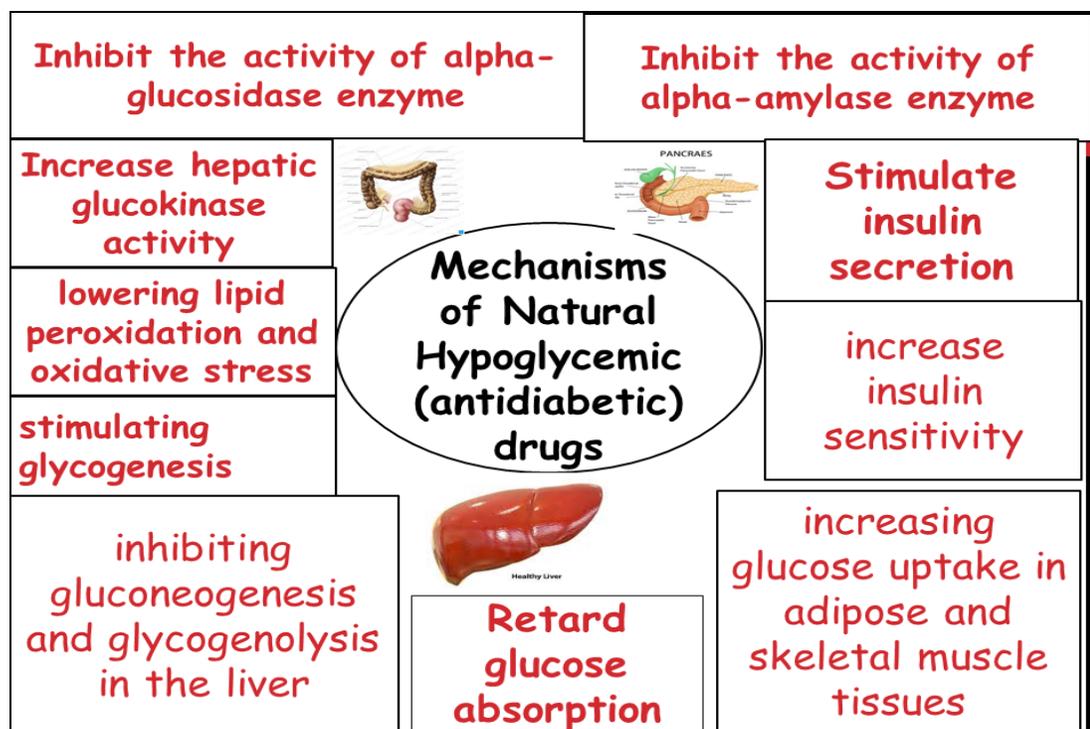
Figure 2: Mechanisms of natural hypoglycemic drugs

The anti-diabetic potential of several herbal plants has been extensively investigated and demonstrated because diabetes is a worldwide disease that necessitates lifetime monitoring and therapy. For the effective treatment and control of diabetes, many of these plant extracts are utilized either alone or in combination with traditional therapy approaches. Alternative therapeutic medications are becoming more and more well-liked as a result of the expensive expense of chemical prescriptions, their lifelong dependence, and their negative side effects. A variety of natural antidiabetic drugs exhibit several mechanisms of action e.g. stimulate insulin secretion (Aloes, *Biophytum sensitivum)*, inhibition of α-glucosidase (*Colvillea racemosa* (**15**), retard glucose absorption, increase hepatic glucokinase activity (*Myrica sangzhia)* and promote glucose uptake (*Ginseng, Bittermelon, Cinnamon*)(**6**).

This review was performed on the four selected herbal drugs, Mango leaves (*Mangifera indica* L., Family Anacardiaceae), leaves of Rosemary (*Rosmarinus officinalis* L., Family Lamiaceae), grains of Barley (*Hordeum vulgare* L. Family Poaceae) and *Delonix regia* leaves (*Delonix regia* L, Family Fabaceae). The review focused on data reported concerning the biological effects especially those responsible for anti-diabetic and antioxidant effects (**16.**

Mango leaves

analysis the impact of *Mangifera indica* leaf aqueous extract on rats with normoglycemia, glucose-induced hyperglycemia, and diabetes produced by streptozotocin (STZ). The findings showed that *Mangifera indica* leaf aqueous extract has a hypoglycemic activity that could be linked to a decrease in glucose absorption in the intestine **(17).**

Mangiferin helped decrease oxidative stress in rat models of streptozotocin-induced toxicity. The findings demonstrated that intraperitoneal administration of mangiferin caused a comparable reduction in oxidative stress and a significant decrease in glycosylated hemoglobin and creatine phosphokinase (CPK) levels to those of insulin treatment **(18).**

Mangiferin has been shown to have strong anti-diabetic, anti-hyperlipidemic, and antiatherogenic characteristics, indicating that it may have a positive impact on the management of diabetes mellitus accompanied by hyperlipidemia and accompanying cardiovascular problems **(19).** Mango stem bark's ethanolic extract reduced type II diabetic rats' absorption of glucose, but none of the extracts had any discernible antihyperglycemic effects on type I diabetic rats, according to research on the effects of ethanolic and aqueous extracts of mango stem barks and leaves on these rats **(20)**.

In streptozotocin-induced diabetic rats, mangiferin showed a protective effect against the advancement of diabetic nephropathy **(21).**

3*β*-taraxerol, a compound isolated from *Mangifera indica* leaves, was identified as a PI3K (phosphatidyl inositol 3-kinase) dependent dual activator of glucose transport and glycogen synthesis in 3T3-L1 adipocytes **(22).**

Diabetic rats treated with alloxan ethanolic extract of *Mangifera indica* leaves caused a drop in their blood sugar, urea, uric acid, and creatinine levels **(23).**

Diabetic individuals receiving diet advice, medicine, and a solution made from mango leaf powder showed a significant drop in blood sugar levels **(24).**

Identified benzophenones, including maclurin and iriflophenone, as important antioxidants in young mango leaves **(25)**. *in-vitro* antidiabetic and anticancer potential of the ethanolic extract of a mango leaf was shown **(26).**

The study's results strongly showed that the plant's leaf extract might have anti-diabetic properties (27). The leaf extract from young mango cv. 'Apple' has the potential to become a nutraceutical since it has the strongest anti-inflammatory and anti-diabetic properties (28) By suppressing alpha-amylase and boosting glucose uptake within the cell, ethanolic extracts of *Mangifera indica* (mango leaf) and Annona muricata (soursop leaf) have the potential to treat diabetes(29).

Rosemary leaves

in diabetic rabbits, the ethanolic extract of rosemary had an antihyperglycemic effect at doses of 100 and 200 mg/kg, which was followed by a marked rise in serum insulin levels. Furthermore, the extract was able to reduce lipid peroxidation and activate antioxidant enzymes in diabetic rabbits after a week of treatment at a dose of 200 mg/kg. It was determined that Rosmarinus officinalis extract likely has a notable anti-diabetogenic impact because of its strong antioxidant characteristics (30).

administering rosemary's aqueous extract perfusion to normal and streptozotocin-induced diabetic rats improved their lipid profiles and reduced their blood sugar levels (31). Diabetic rats' blood glucose levels were markedly lowered by R. officinalis aqueous extract (200 mg/kg body weight for 21 days) (32).

carnosic acid, at levels found in rosemary extract, stimulates muscle cell glucose uptake via AMPK (AMP-activated protein kinase) activation (33). A significant amount of pharmacological research revealed that rosemary extract and its phenolic components, particularly carnosic acid, rosmarinic acid, and carnosol, could significantly reduce the risk of diabetes mellitus by controlling lipid metabolism, inflammation, and oxidation (34).

The present study confirmed that the volatile oil of rosemary leaves could be used for management of cancer and diabetes mellitus (35).

The ethanolic extract of rosemary leaves has antidiabetic activity (36)

Barley grains

β-glucan enriched barley fraction significantly decreased cholesterol levels in hamsters when compared to rice and oat bran (37).

In rats, barley β-glucan reduced levels of triglycerides, LDL cholesterol, and total cholesterol **(36).** in diabetic rats, β-glucans exhibited anti-hyperglycemic, anti-hypertriglyceridemic, anti-hypercholesterolemic, and anti-arteriosclerotic activity **(37).**

Acute consumption of barley β-glucan was effective in reducing glucose and insulin responses in mildly insulin-resistant men **(38).**

Giving tea polyphenols (TP) and beta-glucan (BG) to diabetic rats significantly improved their blood sugar levels, serum lipid parameters (decreased triglyceride, total cholesterol, LDL-C, and increased HDL-C), lipid peroxidation (decreased malondialdehyde content), and serum antioxidant status (increased superoxide dismutase, glutathione peroxidase, and total antioxidant capacity) **(39).**

The barley flour's protein isolate and prolamin fractions were suggested for utilization as viable candidates in the functional, nutraceutical, and pharmaceutical industries as hypoglycemic, antioxidant, and anti-diabetic compounds **(40).**

The reducing blood glucose, hepatic glucose, and lipid problems with yeast-glucan helps control glucose and lipid homeostasis in diabetic rats. To reduce the absorption of glucose and lipids, yeast glucans lowered the glucose transporters SGLT1 and GLUT2, fat emulsification, and adipogenic genetic proteins in the colon. Therefore, it might be used in anti-diabetic diets or medications **(41).**
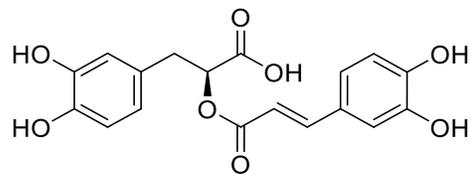
Highland barley phenolics could be used as a potential treatment agent for T2DM to enhance human health **(38) .**
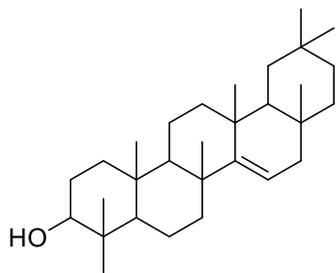
Delonix regia **leaves**

Delonix regia leaves have antidiabetic activity in which the methanolic extract in a dose of 400 mg/Kg showed significant hypoglycemic activity compared to standard glibenclamide **(13, 39)**
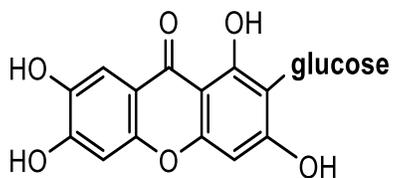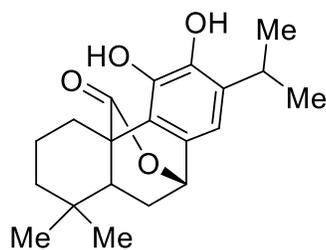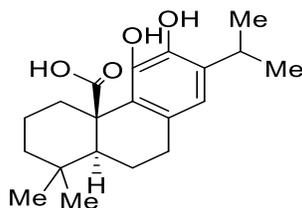
Mangiferin

Rosmarinic acid

3β-taraxerol

Carnosol

Carnosic acid

Figure 3: Some of antidiabetic compounds from natural source.

Conclusion

Diabetes mellitus (DM) is a main health problem that is no longer considered a disease in predominantly rich nations. The prevalence of diabetes is steadily increasing everywhere, most markedly in the world's middle-income countries. The high cost of chemical drugs, and lifelong dependency, along with their side effects have made alternative therapeutic medicines even more popular.

Conflict of Interest

The Authors declare no conflict of interest.

References

1.   Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, et al. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes research and clinical practice. 2022;183:109119.

2.   Eliasson M, Boström G. Chapter 5.2: major public health problems—diabetes. Scandinavian journal of public health. 2006;34(67_suppl):59-68.

3.   Singh LW. Traditional medicinal plants of Manipur as anti-diabetics. J Med Plant Res. 2011;5(5):677-87.

4.   Care D. In the same tables, the sentence "The diagnosis of GDM is made when the plasma glucose level measured 3 h after the test is $140 mg/dL (7.8 mmol/L)" is incorrect. The corrected sentence is as follows:"The diagnosis of GDM is made when at least two of the following four plasma glucose levels (measured fasting, 1 h, 2 h, 3 h after the OGTT) are met or exceeded. Diabetes Care. 2014;37:887.

5.   Singab AN, Youssef FS, Ashour ML. Medicinal plants with potential antidiabetic activity and their assessment. Med Aromat Plants. 2014;3(1):151.

6.   Awasthi A, Parween N, Singh VK, Anwar A, Prasad B, Kumar J. Diabetes: symptoms, cause and potential natural therapeutic methods. Advances in Diabetes and Metabolism. 2016;4(1):10-23.

7.   Organization WH. World health statistics 2016: monitoring health for the SDGs sustainable development goals: World Health Organization; 2016.

8.   Modak M, Dixit P, Londhe J, Ghaskadbi S, Devasagayam TPA. Indian herbs and herbal drugs used for the treatment of diabetes. Journal of clinical biochemistry and nutrition. 2007;40(3):163-73.

9.   Prabhakar PK, Doble M. Mechanism of action of natural products used in the treatment of diabetes mellitus. Chinese Journal of Integrative Medicine. 2011;17(8):563.

10.   Benalla W, Bellahcen S, Bnouham M. Antidiabetic medicinal plants as a source of alpha glucosidase inhibitors. Current diabetes reviews. 2010;6(4):247-54.

11.   de la Fuente JÁ, Manzanaro S. Aldose reductase inhibitors from natural sources. Natural product reports. 2003;20(2):243-51.

12.   Etxeberria U, de la Garza AL, Campión J, Martínez JA, Milagro FI. Antidiabetic effects of natural plant extracts via inhibition of carbohydrate hydrolysis enzymes with emphasis on pancreatic alpha amylase. Expert opinion on therapeutic targets. 2012;16(3):269-97.

13.   Khan D, Sharif A, Zafar M, Akhtar B, Akhtar MF, Awan S. Delonix regia a folklore remedy for diabetes; attenuates oxidative stress and modulates type II diabetes mellitus. Current pharmaceutical biotechnology. 2020;21(11):1059-69.

14.   Salimifar M, Fatehi-Hassanabad Z, Fatehi M. A review on natural products for controlling type 2 diabetes with an emphasis on their mechanisms of actions. Current diabetes reviews. 2013;9(5):402-11.

15.   Abd El Hafeez MS, El Gindi O, Hetta MH, Aly HF, Ahmed SA. Quality Control, Anti-Hyperglycemic, and Anti-Inflammatory Assessment of Colvillea racemosa Leaves Using In Vitro, In Vivo Investigations and Its Correlation with the Phytoconstituents Identified via LC-QTOF-MS and MS/MS. Plants. 2022;11(6):830.

16.   Kumar M, Saurabh V, Tomar M, Hasan M, Changan S, Sasi M, et al. Mango (Mangifera indica L.) leaves: Nutritional composition, phytochemical profile, and health-promoting bioactivities. Antioxidants. 2021;10(2):299.

17.   Aderibigbe A, Emudianughe T, Lawal B. Antihyperglycaemic effect of Mangifera indica in rat. Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives. 1999;13(6):504-7.

18.   Muruganandan S, Gupta S, Kataria M, Lal J, Gupta P. Mangiferin protects the streptozotocin-induced oxidative damage to cardiac and renal tissues in rats. Toxicology. 2002;176(3):165-73.

19.   Muruganandan S, Srinivasan K, Gupta S, Gupta P, Lal J. Effect of mangiferin on hyperglycemia and atherogenicity in streptozotocin diabetic rats. Journal of ethnopharmacology. 2005;97(3):497-501.

20.   Bhowmik A, Khan LA, Akhter M, Rokeya B. Studies on the antidiabetic effects of Mangifera indica stem-barks and leaves on nondiabetic, type 1 and 2 diabetic model rats. ||| Bangladesh Journal of Pharmacology. 2009;4(2):110-4.

21.   Li X, Cui X, Sun X, Li X, Zhu Q, Li W. Mangiferin prevents diabetic nephropathy progression in streptozotocin-induced diabetic rats. Phytotherapy Research. 2010;24(6):893-9.

22.   Sangeetha KN, Sujatha S, Muthusamy VS, Anand S, Nithya N, Velmurugan D, et al. 3β-taraxerol of Mangifera indica, a PI3K dependent dual activator of glucose transport and glycogen synthesis in 3T3-L1 adipocytes. Biochimica et Biophysica Acta (BBA)-General Subjects. 2010;1800(3):359-66.

23.   Kemasari P, Sangeetha S, Venkatalakshmi P. Antihyperglycemic activity of Mangifera indica Linn. in alloxan induced diabetic rats. J Chem Pharm Res. 2011;3(5):653-9.

24.   Patnaik R. Mango leaves in treating diabetes: A strategic study. Int J Innov Res Dev. 2014;3(12):432-41.

25.   Prommajak T, Kim SM, Pan C-H, Kim SM, Surawang S, Rattanapanone N. Identification of antioxidants in young mango leaves by LC-ABTS and LC-MS. Chiang Mai University Journal of Natural Sciences. 2014;13(3):317-30.

26.   Ganogpichayagrai A, Palanuvej C, Ruangrungsi N. Antidiabetic and anticancer activities of Mangifera indica cv. Okrong leaves. Journal of advanced pharmaceutical technology & research. 2017;8(1):19.

27.   Saleem M, Tanvir M, Akhtar MF, Iqbal M, Saleem A. Antidiabetic potential of Mangifera indica L. cv. Anwar Ratol leaves: medicinal application of food wastes. Medicina. 2019;55(7):353.

28.   Chewchinda S, Suriyaphan O, Kanchanadumkerng P, Sato H, Sato V. Comparison of antioxidant and α-glucosidase inhibitory activities in different cultivars of five mango (Mangifera Indica L.) leaf extracts. CMUJ. Nat Sci. 2021;20(1):e2021014.

29.   Ogbonna CC, Iwuji SC, Ndubuka GI, Oladimeji NAT, Okafor SA. In-vitro Antidiabetic Assessment of Bioactive Phytochemicals in Locally used Mango and Soursop Leaves.

30.   Bakırel T, Bakırel U, Keleş OÜ, Ülgen SG, Yardibi H. In vivo assessment of antidiabetic and antioxidant activities of rosemary (Rosmarinus officinalis) in alloxan-diabetic rabbits. Journal of ethnopharmacology. 2008;116(1):64-73.

31.   Al-Jamal A-R, Alqadi T. Effects of rosemary (Rosmarinus officinalis) on lipid profile of diabetic rats. Jordan J Biol Sci. 2011;4(4):199-204.

32.   Khalil OA, Ramadan KS, Danial EN, Alnahdi HS, Ayaz NO. Antidiabetic activity of Rosmarinus officinalis and its relationship with the antioxidant property. African Journal of Pharmacy and Pharmacology. 2012;6(14):1031-6.

33.   Naimi M, Vlavcheski F, Murphy B, Hudlicky T, Tsiani E. Carnosic acid as a component of rosemary extract stimulates skeletal muscle cell glucose uptake via AMPK activation. Clinical and Experimental Pharmacology and Physiology. 2017;44(1):94-102.

34.   Bao T-Q, Li Y, Qu C, Zheng Z-G, Yang H, Li P. Antidiabetic effects and mechanisms of rosemary (Rosmarinus officinalis L.) and its phenolic components. The American journal of Chinese medicine. 2020;48(06):1353-68.

35.   Ahamad J, Uthirapathy S, Mohammed Ameen MS, Anwer ET. Essential oil composition and antidiabetic, anticancer activity of Rosmarinus officinalis L. leaves from Erbil (Iraq). Journal of Essential Oil Bearing Plants. 2019;22(6):1544-53.

36.   Malek A, M Sadaka M, Hamo S, Al-Mahbashi HM. Evaluation of Antidiabetic Activity of Rosmarinus officinalis var. prostratus Growing in Syria in Alloxan Diabetic Rats. Current Bioactive Compounds. 2021;17(2):187-93.

37.   Kahlon T, Chow F, Knuckles B, Chiu M. Cholesterol lowering effects in hamsters of b-glucan enriched barley fraction, dehulled whole barley, rice bran, and oat bran and their combinations. Cereal Chem. 1993;70(4):435-40.

38.   Deng N, Zheng B, Li T, Liu RH. Assessment of the phenolic profiles, hypoglycemic activity, and molecular mechanism of different highland barley (Hordeum vulgare L.) varieties. International journal of molecular sciences. 2020;21(4):1175.

39.   Rahman M, Hasan N, Das AK, Hossain T, Jahan R, Khatun A, et al. Effect of Delonix regia leaf extract on glucose tolerance in glucoseinduced hyperglycemic mice. African Journal of Traditional, Complementary and Alternative Medicines. 2011;8(1).