1. Introduction

Diabetes mellitus (DM) is one of the most common metabolic disorders worldwide with an estimated 143 million people suffering from the disease [1]. This number may double by 2030 [2]. Although understanding of the pathophysiological processes involved in DM has increased, with great feats achieved in the management of DM, yet serious diabetic complications still confront patients and physicians [3]. Diabetes mellitus is characterized by chronic hyperglycemia (very high blood glucose levels) and disturbances of carbohydrate, fat and protein metabolism associated with absolute or relative deficiency in insulin secretion or insulin action [4-5]. On the basis of aetiology and clinical presentation, DM is classified into two; type 1 diabetes mellitus also called insulin-dependent diabetes mellitus (IDDM) and type 2 which is the non-insulin dependent diabetes mellitus (NIDDM). The effects of DM include long term damage, dysfunction and failure of various organs, especially the eyes, kidneys, livers, hearts, and blood vessels [6].

In the treatment of diabetes, many oral hypoglycemic agents like sulfonylureas, meglitinides, thiazolidines, D-phenylalanine and α-glucosidase inhibitors are used in addition to insulin treatment action along with appropriate diet and exercise [5]. However, none can be termed as an ideal one, due to their toxic side effects and sometimes diminution in response after prolonged use [7]. The limitations and side effects associated with existing synthetic oral hypoglycemic agents had necessitated the search for newer drugs. As a result, natural agents from plants and plant products have been the alternative target to source for new antioxidant and antidiabetic agents based on their traditional use.
2. Hyperglycemia and oxidative stress

A relationship has been established between hyperglycemia, oxidative stress and numerous pathways which can lead to the development of diabetic complications. Four of these pathways are very important: activation of protein kinase C isoforms, increased hexosamine pathway flux, increased advanced glycation end-product (AGE) formation [8-9], and increased aldose-reductase pathway flux [10]. Oxidative stress has been implicated to play a central role in these pathways. Oxidative stress occurs as a result of excessive formation of reactive oxygen species (ROS) and reactive nitrogen species (RNS) collectively described as free radicals. Free radicals are highly unstable and have the ability to attract electrons from macromolecules such as carbohydrates, protein, lipid and DNA [11]. Excessive ROS can cause structural deterioration and instability of the macromolecules, consequently affecting proper cellular signaling pathways, gene regulation and function [12]. Although, the human system has check-in mechanisms to deal with oxidative damage and free radical formation through endogenous and exogenous antioxidants, however, when the rate of formation of ROS overwhelms the detoxifying ability of the antioxidants, oxidative stress can occur [11, 13-14].

The increase in oxidative stress in diabetes mellitus could be attributed to elevated blood glucose levels, which upon auto-oxidation generates free radicals and damages the cell membrane through peroxidation of membrane lipids [15] and protein glycation [16]. Chronic hyperglycemia results in oxidative stress via auto-oxidation of glucose in the presence of transition metals [17]; decreased activities of antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase [18]; increased oxidative phosphorylation [19], glycosylation of proteins [17]; and activation of the hexosamine pathway [20]. Hyperglycemia-induced oxidative stress has been demonstrated to result in beta cell dysfunction and death [21-22], as well as in fibrosis of pancreatic islets [23-24]. It has also been established that hyperglycemia increases mitochondrial ROS production, which could represent a key event in the development of diabetic complications [19, 25].

Hyperglycemia has been reported to induce oxidative insult and apoptosis in diabetic liver and renal tubular cells [26-27]. Hyperglycemia leads to increased levels of ROS and D-glucose which has been shown to be capable of inducing apoptosis through the activation of Bax-caspase pathway [28]. Caspases are a family of cysteine proteases known to be the effectors of apoptosis. Upon activation of Bax by free radicals, caspases are activated, which alter mitochondrial function by reducing the electrochemical gradient across the mitochondrial membrane leading to the release of mitochondrial cytochrome C into cytoplasm [28-29]. Studies had shown that movement of Bax into the mitochondrial membrane is accompanied by a significant increase in the activities of caspase-3 and caspase-9 [30-32].

3. Levels of antioxidant action

The antioxidants acting in the defense systems act at different levels such as preventive, radical scavenging, repair and de novo, and the fourth line of defense, i.e., the adaptation.
According to Lobo et al. [33], the first line of defense is the preventive antioxidants, which suppress the formation of free radicals. Although the precise mechanism and site of radical formation in vivo are not well elucidated yet, the metal-induced decompositions of hydroperoxides and hydrogen peroxide must be one of the important sources. To suppress such reactions, some antioxidants reduce hydroperoxides and hydrogen peroxide beforehand to alcohols and water, respectively, without generation of free radicals and some proteins sequester metal ions. Glutathione peroxidase, glutathione-s-transferase, phospholipid hydroperoxide glutathione peroxidase (PHGPX), and peroxidase are known to decompose lipid hydroperoxides to corresponding alcohols. PHGPX is unique in that it can reduce hydroperoxides of phospholipids integrated into biomembranes. Glutathione peroxidase and catalase reduce hydrogen peroxide to water.

The second line of defense is the antioxidants that scavenge the active radicals to suppress chain initiation and/or break the chain propagation reactions. Various endogenous radical-scavenging antioxidants are known: some are hydrophilic and others are lipophilic. Vitamin C, uric acid, bilirubin, albumin, and thiols are hydrophilic, radical-scavenging antioxidants, while vitamin E and ubiquinol are lipophilic radical-scavenging antioxidants. Vitamin E is accepted as the most potent radical-scavenging lipophilic antioxidant.

The third line of defense is the repair and de novo antioxidants. The proteolytic enzymes, proteinases, proteases, and peptidases, present in the cytosol and in the mitochondria of mammalian cells, recognize, degrade, and remove oxidatively modified proteins and prevent the accumulation of oxidized proteins.

The DNA repair systems also play an important role in the total defense system against oxidative damage. Various kinds of enzymes such as glycosylases and nucleases, which repair the damaged DNA, are known [33].

There is another important function called adaptation where the signal for the production and reactions of free radicals induces formation and transport of the appropriate antioxidant to the right site [34].

4. Antioxidants and diabetes mellitus treatment

The human system employs the use of endogenous enzymatic and non-enzymatic antioxidant defense systems against the onslaught of free radicals and oxidative stress [35-36]. Enzymatic antioxidants include superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase. Non-enzymatic antioxidants include vitamins A, C, and E, glutathione, alpha-lipoic acid, carotenoids, and coenzyme Q. Other antioxidants include biflavonoids, minerals (copper, zinc, manganese, and selenium), and cofactors (folic acid, vitamins B1, B2, B6 and B12). These antioxidants work synergistically with each other using different mechanisms against different free radicals and stages of oxidative stress [37]. Hyperglycemia has been reported to impair the endogenous antioxidant defense systems in many ways during diabetes in addition to generating free radicals [18, 38]. The involvement of hyperglycemia-mediated oxidative damage in diabetes mellitus has led to the hypothesis that drugs that
improve glycemic index and/or oxidative stress will be beneficial in the treatment of diabetes mellitus and its complications.

Majority of the drugs currently used in the treatment of diabetes mellitus have antioxidant activities in addition to their primary pharmacological activity. For example, aminoguanidine has been shown to exhibit free radical scavenging properties and inhibit lipid peroxidation [39-43] although clinical trials were discontinued in Europe and in the United States due to its long term toxicity. Troglitazone lowered hydroperoxides and decreased SOD activity in type 2 diabetic rats [44]. Glibenclamide, a sulphonylurea in addition to its glucose lowering effect possesses antioxidant properties due to its ability to restore liver catalase and superoxide dismutase in diabetic rats [45]. Also, repaglinide used in the treatment of type 2 diabetes mellitus exhibited antioxidant properties and inhibited protein peroxidation by upregulating glutathione reductase and glutathione levels in diabetic rabbits in addition to its insulin releasing effects [46].

Several in vivo studies have been carried out to ascertain the effects of antioxidants on experimental diabetic models [47-53]. Most of these studies reported the beneficial role of antioxidants against specific biomarkers of oxidative stress and provided the foundation for clinical trials embarked on later [54-60]. Majority of the studies were not designed specifically to assess the effects of antioxidant use in diabetic patients and none has been carried out yet on antioxidant-rich plant products despite the large evidence supporting its use. Medicinal plants and antioxidant-rich plant products definitely hold promise in this area in the near future.

5. Role of flavonoids in diabetes mellitus

The presence of polyphenolic compounds such as flavonoids, phenols, flavonols, and proanthocyanidins in plants is associated with the antioxidant and antidiabetic potentials [61]. A number of studies have reported on the beneficial effect of flavonoids in diabetes mellitus [62-63]. Examples of flavonoids include quercetin, rutin, diosmin, luteolin, lycopene, catechins and cinnamic acids.

5.1. Quercetin

Quercetin (3,3′,4′,5-7-penta- hydroxyflavone), belongs to the class flavonol, a member of the flavonoid family and is widely distributed in plants. Quercetin and rutin are the flavonoids most abundantly consumed in foods [64]. Sources of quercetin include brassica green vegetables, carrots, berries, onions, apple, legumes, green tea, citrus fruits, red wines etc [65]. Quercetin has been shown to prevent oxidative stress [66] by different mechanisms, including scavenging free radicals [67], inhibiting xanthine oxidase [68], lipid peroxidation, and chelating metal ions [69]. Quercetin is a powerful antioxidant, proven by in vitro [70] and in vivo studies [71]. Quercetin ameliorated the damage caused by oxidative stress in pancreatic tissues in rats, by directly quenching lipid peroxides and indirectly enhancing the production of endogenous antioxidants [72].
Quercetin reduces intestinal glucose absorption by inhibiting GLUT 2 in CaCo-2 intestinal cells [73-74]. Quercetin has been extensively investigated in diabetic rat models in recent times. It decreases the fasting blood glucose and improves glucose tolerance [75]; protects against oxidative damage and preserves pancreatic beta cell integrity [76]. Kobori et al. [77] reported that quercetin alleviated diabetic symptoms and liver injury in diabetic patients. Quercetin blocks tyrosine kinase thereby interfering with insulin signaling and the propagation of the biological actions of the hormone [78-79]. Quercetin elevated insulin secretion in insulin-secreting cell line induced by glucose and glibenclamide [80] by mediating ERK1/2 pathway [81]. Insulin resistance was improved in genetically obese Zucker rats upon administration of quercetin [82]. Quercetin also reduced maltose-induced postprandial hyperglycemia in type 2 diabetic patients by inhibiting intestinal alpha glucosidase activity [83]. Several mechanisms of action of quercetin in diabetes have been postulated and those included: decreases lipid peroxidation, increases antioxidant enzymes activity like superoxide dismutase (SOD), glutathione peroxidase (GPX), and catalase [76]. Other mechanisms are inhibition of insulin-dependent activation of phosphoinositol-3 kinase (PI-3K) [84], increase adiponectin levels [85], and decrease the intestinal maltose activity [27].
5.2. Rutin

Rutin \[2-(3,4\text{-dihydroxyphenyl})-5,7\text{-dihydroxy}-3-[\alpha\text{-Lrhamnopyranosyl}-(1\rightarrow6)-\beta\text{-D-gluco pyranosyloxy}]4\text{Hchromen-4-one}\] is abundantly present in onions, apples, tea and red wine [86]. The name rutin originated from the plant \textit{Ruta graveolens}. Rutin exhibits multiple pharmacological activities including antibacterial, antitumour, antidiabetic, anti-inflammatory, antidiarrhoeal, antiulcer, antimutagenic, myocardial protecting, vasodilator, immunomodulator and hepatoprotective activities [87]. It is a potent antioxidant and anti-inflammatory agent that has the potential to provide a lot of health benefits [88].

![Figure 3. The chemical structure of rutin.](image)

Rutin by its ability to scavenge free radicals and to inhibit lipid peroxidation, prevents streptozotocin-induced oxidative stress and protects pancreatic beta cells resulting in increased insulin secretion and decreased blood glucose levels. Rutin effectively reduced the increased levels of thiobarbituric acid reactive substances and hydroperoxides in the diabetic state \textit{in vivo} [89] and \textit{in vitro} [90]. Rutin reduces hyperglycemia and dyslipidemia while inhibiting the progression of liver and heart dysfunction in diabetic rats [91]. It also significantly decreases elevated reactive oxygen species while increasing endogenous antioxidant enzymes in kidney of diabetic rats and may consequently control or prevent the development of diabetic nephropathy [92]. When Rutin supplementation tablets (500mg) was administered simultaneously with their regular medication for 60 days to patients with type 2 diabetes mellitus, the hypertension, total cholesterol and low-density lipoproteins (LDL) were markedly attenuated. Rutin also decreased the levels of fasting blood glucose, systolic and diastolic blood pressure and improved lipid profiles in the diabetic subjects [93]. Rutin found in \textit{Morus alba} leaves, possesses significant, dose-dependent antidiabetic activity in a type 2 diabetic rat model [94].

5.3. Diosmin

Diosmin (3',5,7-trihydroxy-4'-methoxyflavone 7-rutinoside) is a naturally occurring flavonoid glycoside that can be isolated from various plant sources or derived by dehydrogenation of the corresponding flavanone glycoside Hesperidin, that is abundant in the pericarp of various citrus fruits [95]. Diosmin was first isolated in 1925 from \textit{Scrophularia nodosa}. Diosmin is
considered to be a vascular-protecting agent used to treat chronic venous insufficiency, hemorrhoids, lymphedema, and varicose veins. Diosmin exhibits anti-inflammatory, antioxidant, and anti-mutagenic properties [95-97]. Clinical studies have demonstrated that diosmin can be used to treat venous leg ulcers and hemorrhoids [98]. Also, its anti-inflammatory and anti-apoptotic activity has been demonstrated in neuronal cells [99].

Figure 4. The chemical structure of diosmin.

Diosmin was found to be capable of normalizing capillary filtration rate and prevent ischemia in diabetics [100-101]. Diosmin has been shown to improve factors associated with diabetic complications. A decrease in hemoglobin A1c as well as an increase in glutathione peroxidase was observed in type 1 diabetic patients after an intervention with a diosmin-containing flavonoid mixture [102]. Diosmin and hesperidin are known to lower hepatotoxicity induced by carbon tetrachloride (CCL4) and lipopolysaccharides (LPS), minimize oxidation stress caused by nicotine, reduce blood sugar and cholesterol, and inhibit carcinogenesis of the bladder and colon [31, 103-106]. Administration of diosmin for 45 days significantly lowered plasma glucose level, increased the activities of hepatic key enzymes such as hexokinase and glucose-6-phosphate dehydrogenase in addition to decreasing glucose-6-phosphatase and fructose-1,6-bisphosphatase concentrations in streptozotocin-nicotinamide treated rats exhibiting its antihyperglycemic properties [107]. Diosmin lowered plasma glucose and increased plasma insulin levels in diabetic rats by ameliorating the oxidative stress induced by streptozotocin and nicotinamide. Activities of antioxidant enzymes (superoxide dismutase, catalase, glutathione peroxidase, and glutathione s-transferase), vitamin C, vitamin E and reduced glutathione were increased while lipid peroxidation was reduced in liver and kidney of diabetic rats upon treatment with diosmin. Diosmin was also recently reported to possess antihypertensive property by increasing the activities of antioxidant enzymes, reducing reactive oxygen species and normalizing marker enzymes in serum and tissues (liver, kidney, heart, aorta) when rats were made hypertensive by deoxycorticosterone acetate (DOCA) salt [108].

5.4. Luteolin

Luteolin (3’,4’,5,7-tetrahydroxyflavone) is a flavonoid widely distributed in the plant kingdom including several such as Reseda luteola L, Achillea millefolium L, Chamomillae recutita, Cynara scolymus, Thymus vulgaris, Limonium sinuatum [109]. Luteolin has a variety of pharmacological activities, including anti-mutagenic, anti-tumorigenic [110], anti-inflammatory [111], anti-hypertensive [112], and anti-oxidative [113] properties. It is thought to play an important role in the human body as an antioxidant, a free radical scavenger, an agent in the prevention of
inflammation, a promoter of carbohydrate metabolism, and an immune system modulator [114]. The antioxidant activity of luteolin and its glycosides has been associated with their capacity to scavenge reactive oxygen and nitrogen species [115-116], to chelate transition metals that may induce oxidative damage through the Fenton reaction [117] to inhibit prooxidant enzymes [118] and to induce antioxidant enzymes [119-120]. The antioxidant activity of luteolin has been investigated in vitro and in vivo [121-122].

Figure 5. The chemical structure of luteolin.

The antidiabetic property of luteolin was reported by Zarzuelo et al [123] where a significant decrease in glycemia levels (> 50%), a 2.5-fold increase in insulin blood levels, elevated pancreatic insulin and DNA content were observed. Luteolin is reported to inhibit alpha-glucosidase and alpha-amylase suggesting that it can suppress postprandial hyperglycemia in patients with non-insulin dependent diabetes mellitus [124]. Recently, luteolin was found to influence insulin action and production of adipokines/cytokines in adipocytes by activating the PPARγ pathway suggesting its role in preventing insulin resistance and type 2 diabetes mellitus [125].

5.5. Lycopene

Lycopene is a carotenoid present in tomatoes (Lycoperisicon esculentum). It can be found in many fruits and vegetables like water melon, pawpaw and pink grape fruit. Lycopene is a potent antioxidant according to in vitro and human studies, inactivating hydrogen peroxide and nitrogen dioxide [126] and reducing the susceptibility of lymphocyte DNA to oxidative damage [127]. The presence of many conjugated double bonds in lycopene may account for its antioxidant properties [128]. Lycopene quenches singlet oxygen and traps peroxyl radicals [129]. The singlet quenching ability has been reported to be twice as high as that of beta carotene and 10 times higher than that of alpha tocopherol and butylated hydroxytoluene (BHT) [130-132]. Lycopene is also a potent neuroprotective [133], anti-proliferative, anti-cancer [134], anti-inflammatory [135] and hypocholesterolemic agent [136]. The mechanisms of action against reactive species for lycopene has been proposed to be by adduct formation, electron transfer to radicals and allylic hydrogen attraction [137-141].
Lycopene values in serum were found to be significantly lower in patients suffering from type-2 diabetes and impaired glucose metabolism [142-143]. Also, according to data from phase I of the Third National Health and Nutrition Examination Survey (1988-1991), lycopene was found to be inversely related to fasting serum insulin suggesting a possible role for lycopene in the pathogenesis of insulin resistance and diabetes [144]. Lycopene was also found to be useful in the management of neuropathy, a complication of diabetes mellitus, by attenuating cold allodynia and thermal hyperalgesia in streptozotocin induced diabetic rats [145].

5.6. Catechins

Tea (Camellia sinensis L) is the most widely consumed beverage in the world, next to water [146-147]. Tea contains catechins, polyphenolic compounds belonging to the flavonoid family. The most important catechins in green tea are: epigallocatechin gallate (EGCG), epigallocatechin (EGC), epicatechin gallate (ECG) and epicatechin (EC) [148]. The antioxidant properties of catechins have been well documented [149-155]. The mechanisms of action of catechins may include free radical scavenging [149-150, 152-153], chelating metal ions to form inactive complexes [150, 152, 156-157], transferring electrons rapidly to ROS induced radical sites on DNA [158] and forming stable semi-quinone free radicals [150]. Catechins also increase the body’s endogenous antioxidants to reduce oxidative damage and decrease lipid peroxidation biomarkers in several tissues in rats [158]. Apart from their antioxidant properties, catechins are also anti-carcinogenic, anti-tumorigenic, anti-mutagenic, anti-proliferative, anti-inflammatory, anti-allergic, anti-hypertensive and chemopreventative [159].

In diabetes mellitus, the effects of catechins in vitro and in vivo studies were investigated [160-163]. In rat models of diabetes, catechins have been demonstrated to have ameliorative effects on biomarkers of oxidative stress on diabetic erythrocytes [164] and on erythrocyte Na/H antiport [165].
5.7. Cinnamic acids

Cinnamon, used extensively since ancient times in food as a herb or spice, has been shown to ameliorate the symptoms of metabolic syndromes, such as insulin resistance and elevated levels of glucose and lipids [166]. Cinnamon bark contains cinnamic acid, cinnamaldehyde and cinnamic alcohol [167]. Cinnamic acid has been reported to exhibit several pharmacological properties including hepatoprotective [168], antioxidant [169] and anti-diabetic properties [170].

Cinnamic acid was recently reported to be capable of preventing advanced glucated end-products (AGEs)-mediated diabetic complications. It inhibited the formation of AGEs in a bovine serum albumin (BSA)/fructose system, as well as reduced the levels of fructosamine, the formation of N-(carboxymethyl) lysine (CML) and the level of amyloid cross beta-structure [167]. Sinapic acid is a 4-hydroxy-3, 5-dimethoxy cinnamic acid derivative. It is widely distributed in edible plants such as cereals, nuts, oil seeds and berries [171]. Sinapic acid is a potent antioxidant [172]. Sinapic acid possesses potential anti-hyperglycemic effects, through an increase in insulin production associated with a subsequent increase in the activity of
glcolytic enzyme, hexokinase and decrease in the activity of gluconeogenic enzymes, glucose-6-phosphatase and fructose-1, 6-bisphosphatase [173].

6. Selected antioxidant-rich natural plants with antidiabetic potentials

6.1. *Sclerocarya birrea*

*Sclerocarya birrea* (Family: Anacardiaceae) is a medium-size-to-large deciduous tree widely used for the treatment of proctitis, dysentery, and diarrhea in South Africa and Africa at large and its antimicrobial and antiparasitic properties has been documented [174-175]. *Sclerocarya birrea* is widely used as traditional remedy against diabetes in Africa [176] and has a significant hypoglycemic effect [177]. The methanolic extracts of different parts of the tree such as the leaves, fruit juice, roots and stem-bark has antioxidant properties [61] due to high contents of flavonoids and polyphenolic compounds.

![Sclerocarya birrea plant](image)

**Figure 9. Sclerocarya birrea plant**

6.2. *Prosopis glandulosa*

*Prosopis glandulosa* (Family: Fabaceae) commonly known as Honey mesquite is a small to medium height tree or shrub that is thorny and branching near the ground found mostly in southern parts of India. The bark and leaves are used by the tribes and native medical practitioners to treat various ailments such as leprosy, dysentery, bronchitis, asthma, leucoderma, piles, and tremors of the muscles, tumors, eye diseases and rheumatism [178]. It is commonly found in the dry, arid regions of the northern and north-western Cape of South Africa. Literature studies have indicated that the plant contains flavan-3-ol dimer, mesquitol [179-180] and catechin [181]. Phytochemical screening of leaves from *Prosopis glandulosa* indicates the presence of alkaloids, glycosides, flavonoids, phenolic compounds, steroids and terpenoids [182].
6.3. *Tamarindus indica*

*Tamarindus indica* Linn (Family: caesalpinioceae) is a plant that grows naturally in tropical and subtropical regions and has become an important plant for food, herbs in many parts of the world [183]. Literature studies reported *Tamarindus indica* as a traditional medicine for the management of diabetes mellitus in human and experimental animals [184-185]. Siddhuraju [183] reported the potential antioxidant activity of *Tamarindus indica* seeds isolating the antioxidant components 2-hydroxy-3,4-dihydroxyacetophenone, methyl 3,4- dihydroxybenzoate, 3,4-dihydroxyphenylacetate and oligomeric proanthocyanidins. Phenolic compounds such as procyanidin B2, epicatechin, procyanidin trimer, procyanidin tetramer, procyanidin pentamer, procyanidin hexamer, polymeric tannins, polymeric tannins are also present in the seeds of *Tamarindus indica* [186]. It has been postulated that the antidiabetic property of *Tamarindus indica* observed in experimental animals may be due to the presence of the antioxidant-rich compounds [187].
7. Conclusion

The pathophysiology of most of the diseases affecting mankind today (diabetes mellitus inclusive) seems to have a common denominator, namely oxidative stress. Although, it is a wide topic with several theories, mechanisms, sites and targets of action, reactive oxygen species (ROS) have been implicated in the management of many diseases. As a result, antioxidants have received overwhelming attention in recent years with many outstanding achievements. Most therapeutic agents and drugs are either antioxidants or act primarily to prevent the formation of excess ROS. Therefore it is not surprising to note that natural products with antioxidant properties from plant origin are again gaining prominence in research circles all over the world.

Currently, a lot of therapeutic agents with different modes of action have been designed to combat hyperglycemia; the efficacy and effectiveness of these agents are limited due to several reasons. Individual agent with particular mechanism of action can only act on part of the pathogenic process and only to a partial extent [188-189]. Also, several defects in the pathophysiology of diabetes remain unresolved, and therefore, result in the inability to single out a drug target to focus on as human systems are too interwoven and complex to be fully understood through conventional experimental protocols [190]. However, combination of natural products and phytomedicines from different plants present in most traditional medicines appears to take a different, more holistic approach. These medicinal preparations contain a variety of natural products that act synergistically on a variety of targets through different mechanisms fighting the disease in a more efficient manner. Consequently, the conventional, unidirectional therapeutic method in the management of diabetes seems to be gradually replaced by a more holistic, multidimensional approach.

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