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Review Article

The Effectiveness of Selected Saudi Medicinal Plants in the Management of Diabetes Mellitus: A Review

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Abstract

Diabetes mellitus is a chronic metabolic illness which is distinguished by a long-term hyperglycaemic condition. In so many communities it is devastatingly inflicts a major socio economic problem in humans, especially to the adversely attacked patients. Saudi Arabia is known to be one of the top countries worldwide with the sharpest penetration and high prevalence of diabetes. The conventional treatment of diabetes involves a sustained reduction of homeostatic blood glucose levels using different synthetic drugs. Medicinal plants are natural sources, they have fewer side effects, and they offer evidence for the synthesis of novel and improved medicines for the treatment of diabetes. This review provides useful information and analyzed the results reported in the literature related to the hypoglycemic effect of selected Saudi medicinal plants that are potentially and scientifically validated.

Keywords: Diabetes; Saudi Arabia; Prevalence; Medicinal Plants

Introduction

Diabetes mellitus (DM) is a chronic metabolic illness which is distinguished by a long-term hyperglycaemic condition [1,2]. According to contemporary and universally trajectory of DM disease and by the year 2040, there will be about 642 million diabetic subjects [3]. In so many communities it is devastatingly inflicts a major socio economic problem in humans, especially to the adversely attacked patients. As a metabolic disorder, DM is the underlying precipitant of many crucial debilitating diseases especially the nephropathy, peripheral polyneuropathy, retinopathy, atherosclerosis, peripheral arterial disorder, coronary artery disease, and cerebrovascular disorder [4-9]. The prevalence of end stage renal disease is higher amongst patients with DM [10].

The financial burden related to diabetes resulted mainly from both the expenses of medical treatment as well as the expensive toll of reduced efficiency linked to diabetes-associated morbidity and mortality [11]. Currently, different therapeutic approaches are enacted and applied to suppress and ultimately control the disease using synthetic anti-diabetic drugs in addition to the strict life style modification. Unfortunately, most of the available anti-diabetic drugs are associated with many adverse drug reactions, costly and not readily affordable to the majority of the affected population [12]. Medicinal plants and the potential alternative remedies are safer, active, and inexpensive options when compared to the oral hypoglycaemic agents [13]. The main active constituents of these antidiabetic herbs that engaged to have hypoglycaemic effect are mostly glycosides, alkaloids, terpenoids, flavonoids, carotenoids and saponins [14-17]. Many medicinal plants extracts have shown their ability to treat DM by stimulating the pancreatic beta cells to secrete insulin both *in vivo* and *in vitro* studies [18, 19]. Thus, the objectives of this review were undertaken to validate the base line

data of traditional use of selected Saudi medicinal plants in the control and treatment of diabetes which would provide an alternative lucrative platform for a scientific basis for the evidently subsequent standardization and commercialization of these medicinal plants as antihyperglycemic natural products.

Global prevalence and incidence of DM

Type-1 DM outlines approximately 10% of all patients with DM, attacking nearly 20 million persons worldwide [20,21]. Type-2 DM is the dominant type of DM and represent 90% of DM cases [22-24]. Globally, by 2030, there will be about 439 million persons with DM [25,26]. The number is supposed to rise to 642 million by 2040 [25]. Worldwide, the high incidence of DM is expected to be present in the Middle East and North Africa region [27]. Saudi Arabia is among the top 10 countries mostly affected by DM with 31.6% prevalence [28-30].

Prevalence and economic burden of diabetes in Saudi Arabia

From the geographical and geological point of view it shows that the KSA without comparison is the largest country in the Arabian Peninsula and in the Middle East comprising alone about four-fifth of the Arabian Peninsula which has the population of more than 33.3 million citizens [31]. Saudi is known to be one of the top countries worldwide with the sharpest penetration and high prevalence of diabetes [25,30]. In Saudi Arabia, approximately 4004 participants out of 16917 were confirmed to be diabetics [32]. Moreover, the incidence of DM was more predominant amongst Saudis females in the civilized modern societies [27]. Type I DM is the most widespread among the young individuals that places KSA in the 5th position around the world in penetration levels in children [33]. In terms of the total population of children with IDDM, the position of the country is 7th in world ranking [33]. In terms of town versus rural societies, the prevalence is 25% vis-à-vis 19.5%, respectively, from the data of 2014 [34]. In a contemporary recent report the prevalence of diabetes in Saudi Arabia was found to be about 14.8% among men and 11.7% among women leading to (53.0% and 47.8% among men and women of age 55–64 years, respectively) which sounds the alarm and raised the awareness that 40.2% of these men and 48.4% of women were previously undiagnosed for diabetes. Moreover, 22.9% of diabetic men and 23.4% of women were being treated, but their blood glucose levels remained uncontrolled [35].

Globally Diabetes as a scary formidable menace it imposes a large economic toll on the afflicted individuals, the national healthcare systems and evidently the economy of all countries. Economically, KSA takes a great chunk of its health budget on diabetes. A substantial percentage the country's spending on the health sector goes into the control of the disease. The 2010 allocation of $ 0.9 billion represented a significant margin of the over 9 billion dollars the health sector spent in that year [28]. The overall monetary cost is estimated to be skyrocketing reaching about $6.5 billion by the 2020 reflecting an increase of $5.6 billion (or 7 times higher than the cost in 2010) within the next 10 years [28]. Although diabetes imposes a large economic burden on national healthcare budget the estimated medical healthcare expenditures attributed to diabetes including an array of the indirect costs associated with diabetes. These costs comprise a wide spectrum such as absenteeism, lost productivity from disease-related complications, unemployment due to disability and early mortality by the disease. The spectre of ddiabetes social cost is aggravated by affected individuals pain, sufferings and unprofessional care provided by caregivers in addition to healthcare systems administrative costs, furthered by the cost of medications, clinician training programs, initiatives research and infrastructural development [28,32].

Adverse effect of synthetic anti-diabetic drugs

Diabetes mellitus causes many complications of kidney and heart ailments, which resulted in the obstruction of patients to perform work hence it does constitute an added economic burden to the society. The economic toll associated with DM is substantiated by twin factors embodying the direct costs of medical care as well as indirect costs of an overall diminished productivity evidently tied to diabetic ailments that emanate from morbidity and mortality [11]. There are several synthetic drugs categories that are involved in the treatment of DM including, biguanides (metformin), sulfonylureas (glyburide), meglitinides (Nate glinide), thiazolidinediones (pioglitazone), alpha-glucosidase inhibitors (acarbose), incretin-based therapies (exenatide) and dipeptidyl-peptidase IV (DDP-4) inhibitors (sitagliptin) [36-38].

The use of the synthetic drugs in the treatment of DM is accompanied with diverse array of side effects including lactic acidosis, abdominal pain, diarrheal caused by metformin; hypoglycaemia, weight gain, jaundice, hepatitis and cardiac side effects caused by

sulfonylureas drugs; water retention, peripheral edema and increased fracture risks caused by pioglitazone; in addition to the bloating caused by acarbose [12,39,40]. Moreover, metformin and acarbose are used cautiously in renal impaired patients while thiazolidinediones are contraindicated in cardiac disease patients [41,42]. Insulin may have different side effects including increased lipid reserves, weight gain, lipoatrophy, and hypoglycemic coma [43].

Medicinal plants

The conventional treatment of diabetes involves a sustained reduction of homeostatic blood glucose levels using different drugs, such as metformin, sulfonylurea and thiazolidinediones [44]. However, these synthetic drugs do not adequately inhibit the development of the associated complications, not easily accessible and not affordable by the majority of people in developing countries and furthermore, they may cause a plethora of side effects. Hence, there is a demand for potential alternative therapies to manage diabetes mellitus and its associated complications [12,44].

Since eons of time, the medicinal plants did represent the core of traditional medicines that have been practiced a long time ago in folk medicine and are easily available as a source of treatment all over the world [45]. At present, numerous medicines owe their basis to these medicinal plants since they were defined as plants having comparable properties as synthetic pharmaceutical medicines. The oldest evidence on paper about the use of medicinal plants for making drugs was discovered and dated back in Nagpur, about 5000 years ago [46]. Research has demonstrated that the medicinal plants were still used as traditional medicine to treat fever and malaria worldwide [47-49].

Thus, the science of medicine now gives logical emphasis to the use of medicinal plants in the state of the art for the treatment of chronic diseases like diabetes. There are also various medicinal plants that help people in lowering their high blood sugar levels [50]. *Avicennia marina, Allium cepa, Ficus benghalensis, Rhizophora mucronata, Allium sativum, Pterocarpus marsupium and Gymnema sylvestre*, were studied for their active hypoglycemic properties [51]. These plants also have shown a direct effect on the pancreas and able to enhance insulin blood level [52]. They improve the function of the pancreas by increasing the insulin secretion or reducing the absorption of glucose in the intestine [15]. Medicinal plants also help to maintain the optimum enzymatic reactions in the body therefore, facilitating effective breakdown and synthesis of glucose.

Moreover, medicinal plants contain high levels of saponins, flavonoids, carotenoids, glycosides, antioxidants, terpenoids, and alkaloids needed in the human body. Aside from the anti-diabetic effects of medicinal plants, they also help the body to perform essential metabolic functioning [53]. Considerable scientific research evidence suggests that under oxidative stress situations, reactive oxygen species (ROS) are produced albeit, it is believed that the equilibrium between the oxidation and antioxidation processes results in causing human diseases including diabetes [54]. Since medicinal plants are natural sources, they have fewer side effects, and they offer evidence for the synthesis of novel and improved medicines for the treatment of diabetes [55].

Selected Saudi medicinal plants used for the control of diabetes

It is worthy to note that there are many Saudi medicinal herbs used by healers and herbalist folklore medicine in the treatment of diabetes. The majority of these medicinal plants have not been adequately studied. Moreover, their mechanism of action is not thoroughly understood. The objective of this review focuses on the selected Saudi medicinal plants that are potentially and scientifically validated.

Avicennia marina

Avicennia marina is a member of *Avicenniacea* family that belongs to the genus *Avicennia* [56] which is known as "Grey mangrove". In Saudi Arabia, *A. marina* is widely omnipresent along the Central Red Sea coast where it forms one of the dominant varieties of mangrove [57]. Traditionally, *A. marina* was used for the treatment of ulcer, small pox lesions and snake bites in folk medicine [58]. It was also used to treat scabies and other skin problems besides, its wood is utilised for house building, charcoal production, furniture making, firewood and construction of the sailing boats. Moreover, its branches can be used as stakes for hedges [58].

Avicennia marina contains saponins as phytoconstituents and can activate catalase (CAT) while its antidiabetic effects include β-cells stimulation to release insulin [59]. Rahbaria., *et al* [60]. studied the *A. marina* effects on hormonal profile of diabetic rat's and found a protective effect of this plant. The author concluded

that the use of *A. marina* might prove to be effective in alleviating hormonal imbalances and damage to ovarian tissue in patients suffering from diabetes [60].

Rhizophora mucronata

Rhizophora mucronata is a wind-pollinated tree with potential antidiabetic properties. It is also identified as "red mangrove," and it belongs to *Rhizophoraceae* family. It grows on the tidal creeks banks, on low coastal regions in estuaries and overflowed by usual every day high tides [61]. In Saudi Arabia, it is widely distributed along the Red Sea coast where organic substances are conveyed from the Gulf waters and shore of the Red Sea, between Jizan in the south and Dibain in the north [62]. *R. mucronata* provides fuel and charcoal and it is used for firewood. Previously, it was used to treat haematoma, ulcer, hepatitis, elephantiasis, and diarrhoea. It also possesses antiplasmodial, antioxidant, anti-human immunodeficiency virus (HIV), and hepatoprotective [63-65].

Sur., *et al*. [54] have studied *R. mucronata* for its antidiabetic as well as its antiradical properties and concluded that it did exhibit a strong antioxidants and antidiabetic properties since it helps improve the high blood glucose levels via its antiradical activity. Pandey., *et al*. [65] have also reported about the hypoglycemic effects of leaves of *R. mucronata* in the management of diabetes. In a similar study Haque., *et al*. [66] observed a considerable decrease of postprandial hyperglycemia following sugar intake by this plant's bark. Similarly, Hardoko., *et al*. [67] and Ramu and Vijayakumar [68] documented its antidiabetic effects.

Balanites aegyptiaca

Balanites aegyptiaca is a widespread terrestrial tree that thrive in most tropical and subtropical regions of the world. It is familiar as *Balanitaceea* [69]. The tree plant is widely used by traditional healers in rural areas of many countries [70-75]. In Saudi Arabia, *Balanites aegyptiaca* is cultivated in the western region of Hejaz to the border of Yemen [76]. It is also cultivated in King Abdulaziz University Experimental Farm at Hada Al-Sham area [77].

Balanites aegyptiaca fruits showed significant hypoglycemic effects in streptozocine-induced hyperglycemia in animals [78]. In Egyptian folk medicine, *Balanites aegyptiaca* is utilized as an oral antidiabetic remedy [75]. Rashad., *et al*. [74] reported that administration of *Balanites aegyptiaca* extract to type 2 DM patients for 2 months produced significant reduction in fasting and postprandial blood sugar levels. Another experimental study reported that *Balanites aegyptiaca* extract has antidiabetic action in type-1 DM [79]. *Balanites aegyptiaca* fruit was proved to provoke a hypoglycemic action against streptozocine-induced DM in rats [80]. Moreover, *Balanites aegyptiaca* fruit (cortex) resulted in a reduction of blood glucose level in streptozocine-induced DM in rats [81]. In another study, Baragob., *et al*. [82] demonstrated that *Balanites aegyptiaca* fruit (kernel) extract showed a significant antidiabetic action in alloxan-induced diabetes in rats.

Momordica charantia

Commonly an orbit grow on surface of the ground plant known as bitter melon, bitter melon, karela, balsam pear, or bitter gourd [83]. It grows widely in tropical areas, including parts of East Africa, Asia, the Caribbean, and South America. It belongs to Cucurbitaceae family, and it is used as food, as well as a medicine. The plant was cultivated in Hofuf oasis, Saudi Arabia for the first time. It grows on sandy soil with low organic matter content and deficient in nitrogen and phosphorus [84]. The roots of *Momordica charantia* are useful in the treatment of eye related diseases, the fruit is used to cure biliousness, blood diseases, anaemia, urinary discharges, asthma, ulcers and bronchitis [85].

Momordica charantia is a popular medical folklore plant used for the treating of diabetes-related conditions amongst the indigenous populations of Asia, South America, India, the Caribbean and East Africa [86,87]. Although, abundant data and hypotheses are available on the hypoglycemic effect of *Momordica charantia* in experimental animal models but the clinical studies in human subjects are sparse [88].

Caralluma russeliana

Caralluma russeliana is widely grown and distributed in Africa, Asia, Southeast Europe, Canary Islands, Arabian Peninsula and South Africa, it is a member of *Apocynaceae* family [89]. In Saudi Arabia it is wildly grown in Taif Governate. The plant extracts possess antidiabetic, anticancer, antioxidant, anti-inflammatory and antimicrobial characteristics [90]. Although, the hypoglycemic effect of several species of *Caralluma* were well documented and confirmed efficiently to treat DM such as *Caralluma attenuate Caralluma, tuberculata, Caralluma sinaica* and *Caralluma edulis* [91,92], However, there are few published data on the antidiabetic effect of Caralluma russeliana.

Olea oleaster

The olive tree *Olea oleaster* belongs to *Oleaceae* family. The plant is used extensively in traditional medicine in Mediterranean and European countries [93]. It has hepatoprotective [94], antimicrobial [95], anti-tumor [96] and antidiabetic effects [97,98]. In Saudi Arabia it grows in Taif, Albaha region [94,99]. Supplementation of *O. oleaster* extract significantly decreased the levels of serum glucose, triglycerides, LDL-C and VLDL- in diabetic rats (Al-Thebaiti and Zari, 2018). In a similar study, Almalki., *et al*. [100]. documented that the leaf extracts of Olea oleaster revealed ahypoglycemic action in STZ-induced diabetic rats.

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