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The Role of Herbal Medicines in the Treatment of Diabetes: A Short Review

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Running Title: *Diabetes and Herbal Medicine*

Abstract: ***The metabolic disorder, Diabetes Mellitus (DM), is rapidly growing to bea grave global concern. Despite the development of several synthetic drugs, none of these molecules have been able to effect a total cure. The intake of certain synthetic agents on a continuous basis sometimes results in serious side effects, inducing a persistent demand for non - toxic, inexpensive drugs. Throughout human history, traditional treatments have proven to be highly valued as a medicinal source. From recent studies, herbal extracts have been shown to offer some degree of protection against the diabetes mellitus - related complications. This review discusses some herbal drugs that are effective in the treatment, as well as prevention of complications arising from diabetes.***

Keywords: Diabetes, treatment, herbal, hypoglycemia risk, Saud Arabia

1. Introduction

Recognized as ranking high among the major public health hazards, Diabetes mellitus (DM) is a global issue. Over the last thirty years, the World Health Organization (WHO) reported a rapid rise in the incidence of DM, in all countries, regardless of the income bracket of the individual [1]. From the estimates of the most recent International Diabetes Federation (IDF), Diabetes Atlas 2019, around 463 million people (9.3 %) of the adult population worldwide, between the ages of 20 and 79 years, live with this disease. Alarmingly, it has been projected that the number of adults between 20 and 79 years living with diabetes will be about 578.4 million adults (10.2 %) by 2030, and will exceed 700 million (10.9 %) by 2045 [2, 3]. In light of many earlier reports, 10 million more adults have diabetes at present, while 34 million more adults are under the threat of developing the disease, and 19 million more adults are undiagnosed diabetics [4, 5]. However, it is encouraging to know that diabetes can be managed very well by following correct treatment and control [6]. Apart from taking medication and related treatments, diabetes can be well managed if accurate awareness, education, and self - management methods are implemented. Further, although there is considerable evidence that type 2 diabetes (T2D) is disease that is easily preventable or even capable of being delayed, there is now increasing evidence of the possibility of remission of the T2D vialifestyle changes, albeit only for some types of individuals [2, 7].

The disturbing escalation in diabetes is posing a critical socioeconomic issue, particularly in several of the developed and developing nations. In order to tackle this difficulty, much research is under way by many multinational pharmaceutical companies which are on an aggressive path to develop competitive drugs. Among these, therapeutic processes using natural products are offering medicinal herbs or fruit sources as safe, effective, and quite inexpensive substitutes for synthetic medications. At present, interest in herbal remedies is increasing because these do not have the side effects that oral hypoglycemic agents (therapeutic agents) inflicton patients with DM. Traditionally, the use of herbal medicines which are drawn from plants, play a crucial part in the treatment of DM [8]. Therefore, a scientific study of the effect of traditional herbal remedies in the treatment of diabetes may supply important clues in the development of alternative drugs and therapeutic techniques. Finding suitable substitutes is significant as the current therapies appear inadequate to check or limit all the pathological characteristics of the disease, apart from the high expenditure involved and poor availability of the present treatments, specifically in many of the developing nations, and particularly for the rural populace living there [9]. Folk medicine apparently uses an estimated count of an excess of 1000 plant species to treat diabetes. The biological activities of the plant products that find use as alternative medications for the treatment of diabetes arise from the chemicals they are contain. Most herbal or plant products have an abundance of phenolic compounds, flavonoids, terpenoids, and coumarins, among other component chemicals, which enable the blood glucose levels to decrease [10, 11]. In the present review article, a few medicinal plants with hypoglycemic properties are described, and their action mechanisms are explained.

2. Methods

The literature search for this review required investigation into the PubMed, Scopus, Google scholar, and Google archives to draw out the relevant data. After reviewing the titles and abstracts, the bibliography of the articles chosen was examined. The keywords listed included, diabetes, herbal medicines, treatment of diabetes mellitus, diabetes complications, type 2 diabetes, and type 1 diabetes, and relevant articles alone were identified. These words were used, either individually or combined with others, to facilitate a literature search on a large scale.

Achillea

Achilleamillefolium L. (Asteraceae), commonly called yarrow (milenrama), is frequently employed in folk medicine for the treatment of gastrointestinal disorders (both

inflammatory and spasmodic), hepatobiliary ailments, as well as overactive cardiovascular and respiratory conditions. [12]. From recent studies done, evidence was found for a substantial decrease in the blood glucose, serum liver enzymes, triglycerides, and total - and LDL - cholesterol levels in the groups using the Achilleamillefolium extract, when compared with the groups not using it. In fact, Sadeghi et al., recorded similar findings in the blood glucose of male rats that received treatment with Achilleawilhelmsii [13]. Another study reported similar outcomes for the use of the Achilleamillefolium extract [14]. Hyperglycemia, in patients with DM, is recognized to aggravate the oxidative stress [15]. The Achilleamillefolium*in vivo* exerts antidiabetic influence, through multitarget action mechanisms, and involves symptoms of antihyperglycemia (αglucosidases inhibition), hypoglycemia (insulin secretion), and potential insulin sensitizer actions (PPARγ/GLUT4 overexpression) [12].

Basil leaves

Among the plants that possess essential oils, besides polyphenols, phenolics, flavonoids and phenolic acids, Basil (Ocimumbasilicum) is one of the most noteworthy. Belonging to the mint family, this annual is indigenous to the tropics. Basil exhibits positive results against some viral, fungal, and bacterial infections. The leaves of this plant are useful for treating fevers, coughs, flu, asthma, bronchitis, influenza and diarrhea, although its principal use in pharmacology is for anti - diabetic activity [16]. The reports of one study done in diabetic rats revealed that basil leaf extract showed promise in decreasing the blood glucose levels and advanced glycation end products. From earlier studies, it was clear that both metformin or basil leaves could be used to reduce the blood glucose level, and both appear to have the same effect; in fact, Eddouks M and Kumar S have reported that basil leaves are able to act as an anti - diabetic agent, and heighten the insulin sensitivity [17, 18].

Olive oil

The Mediterranean diet uses extra virgin olive oil as the main dietary fat source. From recent studies it is clear that a diet rich in olive oil lowers the glucose levels and, hence, can prevent the onset of diabetes. As it is high in monounsaturated fatty acids (MUFA), tyrosol, secoiridoids and lignans, extra virgin olive oil, when included in the diet may offer benefits that help in the prevention, progress, and advancement of this disease, more than refined olive oil [19]. A recent meta - analyses of the Randomized Controlled Trials (RCT) showed that in general, when T2D patients consistently replaced the consumption of carbohydrates (~5–10% of total energy intake) with monounsaturated fatty acids as a particular dietary compound, their metabolic risk factors were positively affected [4, 20, 21].

Nigella sativa

For many centuries, Nigella sativa (black seeds) has been a well - known herb, popular in the diet of several communities. This annual plant, from the family Ranunculaceae, is common in Europe, the Middle East, and Western Asia. The benefits of using Nigella sativa in diabetic animals has been reiterated in many earlier studies. The strong antidiabetic effects of Nigella sativa observed were considered possibly due to itsinsulinotropic activity and its antioxidant abilities, which reduce the oxidative stress and safeguard the integrity of the pancreatic β - cell mass. Itsextrapancreatic action, specifically the inhibition of hepatic gluconeogenesis by Nigella sativa, is responsible for the glycemic control it exerts [22]. One study reported that Nigella sativa is effective in diabetes control as an adjuvant for oral antidiabetic drugs [23].

Radish

Radish (Raphanussativus) is a root vegetable grown and consumed worldwide and is considered part of the human diet. Radishes come in different skin colors (red, purple, black, yellow, and white through pink), while their flesh is typically white. Besides, the edible root in the radish varies throughout the world in terms of flavor, size, and length, [24]. Radish has been identified as having antidiabetic effects, making it favorable for those with diabetic conditions. This may be due to its ability to enhance the antioxidant defense mechanism and reduce the accumulation of free radicals, affect hormonal - induced glucose hemostasis, promote glucose uptake and energy metabolism, and reduce the glucose absorption in the intestine [24].

Cinnamon

The Cinnamon, a well - known spice derived from the inner bark of the tree scientifically termed Cinnamomum, has been proclaimed as a natural insulin sensitizer. The insulin - sensitizing effect of cinnamon has been determined both in the *in vitro* cell line research using adipocytes, and in the *in vivo* studies on animals. At first, the bioactive compound isolated from cinnamon was categorized as a methylhydroxychalcone polymer (MHCP), which imitates insulin [25]. In an earlier study, the results revealed that the consumption of 1, 3, or 6 g of cinnamon per day lowers the serum glucose, triglyceride, LDL cholesterol, and total cholesterol in individuals with type 2 diabetes; further, it recommends that cinnamon be included in the diet of such patients in order to minimize the risk factors related to diabetes and cardiovascular conditions [26]. In another study, the cinnamon extract appears to moderately lower the concentrations of plasma glucose during fasting, in diabetic patients having poor glycemic control [27].

Ginger

Ranked high among the most extensively and globally consumed spices, ginger (Zingiberofficinale, Roscoe Zingiberaceae) has been shown recently to have the potential of treating DM [28]. Zingiberofficinale (ginger) exhibits highly beneficial properties of glycemic control in individuals with diabetes mellitus. The action mechanisms involved are related to the inhibition of the critical enzymes governing the metabolism of carbohydrates and heightened insulin release/sensitivity, causing a rise in the uptake of glucose in the peripheral adipose tissues and those of the skeletal muscles. The principal lipid - lowering influence of ginger also helps in the improvement of the insulin - resistant state. One of the protective effects ginger exhibits against diabetic - related complications is also a vital facet of the advantages it offers. More information to facilitate good understanding of the metabolism of ginger, particularly its pungent properties, comes from the pharmacokinetic and bioavailability studies. There are sufficient studies on acute

and chronic toxicity to demonstrate the safety, overall, of ginger as a complementary agent for hyperglycemic control [28, 29].

Armillariamellea

An edible, ubiquitous fungus, Armillariamellea is extensively distributed in northeastern China. Prior studies showed that the polysaccharides contained in A. mellea possess potential biological properties, mainly related to their anti - inflammatory, anti - oxidative, and immunomodulatory roles. The polysaccharides from A. mellea have also been reported to promote glucose - induced insulin secretion through free radical scavenging in pancreatic cells treated with alloxan [30].

Anthocyanins

The group of naturally present pigments called Anthocyaninsare responsible for the red - blue color observed in several grains, fruits, and vegetables. In comparison with the other flavonoids, the dietary consumption of anthocyanins is on the high side, due of their wide distribution among the plant foods. Several studies suggest the potential influence that this flavonoid family exerts in lowering the incidence of cardiovascular disease, cancer, hyperlipidemia, and other insulin resistance - linked diseases by the consumption of anthocyanin - rich foods [31]. Sound knowledge of the anthocyanins in terms of their absorption and metabolism is vital to understanding the way they control this disease. In the published data a suggestion is made that blood glucose may be lowered by the anthocyanins through the improvement of the insulin resistance, protection of the β cells, increase in the insulin secretion, and decrease in the digestion of sugars taking place in the small intestine. The action mechanisms are mainly associated with their antioxidant properties, although enzymatic inhibition and other pathways may also be pertinent [32]. From several *in vitro* and *in vivo* studies, a plethora of mechanisms are indicated, through which the anthocyanins can either preventT2D - linked pathologies or reverse them, including the advancement of the antioxidant and anti - inflammatory activities, enhancement of the insulin resistance, as well as hypolipidemic and hypoglycemic actions [33].

Cudraniatricuspidata

Extensively used as a constituent in oriental medicine, this small tree of the Moraceae family, Cudraniatricuspidata, has many benefits. From many studies, the C. tricuspidata extract (CTe) has been demonstrated to exhibit a number ofpositive effects, such asthe inhibition of pancreatic lipase, production of lipopolysaccharide - induced nitric oxide, formation of prostaglandin E2 in the macrophages, proliferation of the IL - 1β - induced rheumatoid synovial fibroblasts, and creation of matrix metalloproteinase [34]. Earlier studies recommended the use ofCTe as a good substitute for synthetic drugs to treat diabetes. These studies revealed that the hydrophilic extracts which contain thestrong PTP1B inhibitors may offer promise as reagents to develop novel drugs that provide antidiabetic and anti - obesity, health - enhancing benefits [34].

Rhinacanthusnasutus

A member of the Acanthaceae family, Rhinacanthusnasutus (R. nasutus) (Linn) is used in the treatment of a variety of diseases such as eczema, herpes, pulmonary tuberculosis, hepatitis, diabetes, hypertension, and several skin conditions **[35]**. Employed as a treatment measure for myriad health conditions, the compounds isolated from this herb (apart from using the herb as such) can control infections which are neurological, viral, and bacterial in origin, as well as skin disorders, and sugar levels in individuals with diabetes [36].

3. Conclusion

Right through human history herbal medicines have been extensively used for their medicinal properties. Several of these are available, at present, as commercial supplements and are recommended for their benefits to public health, either as a preventive or in the treatment of particular diseases. In general, there is relatively high public interest in the potential advantages that herbal supplements offer for the metabolism of carbohydrates. The benefits of herbal extracts are that if they are proven at a clinical level to effectively improve the metabolism and/or risk factors, these extracts, which typically are available easily, can potentially support the general public in dealing with diabetes.

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