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MINI REVIEW

Diabetes Mellitus and Natural Products: Recent Updates

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Abstract

Diabetes mellitus is an epidemic, with an estimated prevalence of 463 million people worldwide and is thought to increase to 700 million by 2045. Despite the numerous pharmacological choices dietary lifestyle still remains as the cornerstone of diabetes. Oxygen consumption inherent in cell growth leads to the generation of a series of reactive oxygen species (ROS) also called as free radicals. In addition to harmful effects, ROS also have some beneficial roles in immune system activation and maintain the homeostasis of body. Imbalance between the free radicals and antioxidants leads to oxidative stress that results in the development of pathological condition, and diabetes is one among them. Diabetes mellitus represents an important disease to study the adverse effects of oxidative stress and its treatment. Numerous studies worldwide reported the mechanistic aspects of diabetes progression at biochemical and molecular levels including the altered functions of pancreatic β -cells in hyperglycemia, the effect of oxidative stress on β -cells, role of oxidative stress in diabetes and linked pathophysiology as well as antioxidant therapy based randomized human clinical trials. From eternity plants have been an ideal source of drugs/pharmaceuticals and have directly or indirectly yielded essential medicines used for diverse etiology. In modern era, antioxidants of natural origin have gained growing attention over chemically synthesized products in the defense against diabetes because of their established advantages, low toxicity, and ease of entry using dietary supplements. For example, metformin, the widely used hypoglycemic drug was discovered by the traditional approach of using *Galega officinalis*. On the whole, herbal prescriptions are attaining recognition because of several benefits such as a relatively lower occurrence of side-effects at optional dosages, improved acceptance by patients, comparatively low cost, and acceptance due to a long traditional use.

Keywords: *Diabetes mellitus, Natural products, Reactive oxygen species, Traditional uses*

1. Introduction

Diabetes mellitus is a complex disease that is portrayed by mounting risk of developing metabolism linked adverse complications in patients. It is a progressive metabolic disorder of glucose metabolism that ultimately leads to micro- and macrovascular modifications causing chronic impediments affecting various organs in body. According to an estimate, 387 million people are diabetic and the number is projected to dramatically increase beyond 640 million people by 2040 across the globe (1). It is classified as type-1 diabetes, type-2 diabetes, gestational-diabetes, and specific types of diabetes attributable to other reasons (2). Among these, type-2 diabetes is the most frequent and number of affected patients is increasing every year. It is characterized by cellular resistance to insulin activity and deficiency in insulin secretion. There are many oral anti-diabetic drugs used to manage

type-2 diabetes mellitus but most of them have poor efficacy and undesirable effects including hypoglycemia, osteoporosis, fluid retention and heart failure which limit their clinical relevance. Therefore, the development of prospective therapeutic agents with superior efficacy to fight its ill effects and complications is still needed (3). Traditional systems of medicines have been used globally for diabetes therapy along with complications associated with it. These medicines work to delay the progress of diabetes associated complications and amend the metabolic aberrations. However, many phytoconstituents that exhibited anti-diabetic efficacies are being isolated and they have demonstrated higher efficacy than the synthetic drugs (4).

2. Plant Product as Anti-diabetic Agents

Natural products are commonly used for the treatment of diabetes since time immemorial. Dietary supplements with

combined antiglycation and antioxidant nutrients can put forth their effects on glucose metabolism consequently playing noteworthy role in diabetes managements. Several natural products have been used globally for managing blood glucose levels in diabetic patients (5; 6; 7). *Senna auriculata* Roxb is one of the most commonly used medicinal plants in Sri Lanka (8). For cure of diabetes, *Bauhinia forficata* is extensively used ethnomedicinal plant in South America (9). Studies have been published about antidiabetic activity of *Abelmoschus esculentus* L. The plant is native of Africa (10). The mode of anti-diabetic action comprises of inhibition of α -glucosidase and α -amylase in the intestine, stimulation of insulin secretion and pancreatic β -cell proliferation, alteration of glucose uptake and the expression of glucose transporters, control of insulin resistance and regulation of oxidative stress (11; 12). *Caralluma europaea*, a leafless, succulent and angular plant is one of the Moroccan medicinal plants widely used in traditional medicine in Morocco, Libya, Egypt, Italy, Spain, Algeria and Tunisia. Aerial parts of this plant are mainly used as a juice or powder in case of diabetes and to treat goiter and cyst (13). Quercetin is a flavonoid of natural origin that suppresses oxidative stress, enhances glyoxalase pathway activity, hinders the formation of advanced glycation end products, boosts the activities of antioxidant enzymes catalase and superoxide dismutase (SOD). It also restores the vitamin C and vitamin E levels in blood. It also defends neuronal cells against hyperglycemia-induced oxidative stress, inflammation and apoptosis (14; 15; 16). Similarly, mangiferin increases glucose utilization and has antioxidant and anti-inflammatory activities and augments the activity of glyoxalase-I in neurons exposed to chronic increased glucose while reduces microglia activation and associated inflammation in mice after prolonged therapy (17; 18; 19). A novel curcumin derivative J147 designed to enhance curcumin bioavailability has been reported to exert neuroprotective activity. Curcumin is an integral part of *Curcuma longa*. J147 lessens inflammation by diminishing activation of tumour necrosis factor-(TNF)-pathway in mice treated with streptozotocin (20), supporting that different curcumin and J147 possess potent antioxidant activity having ability to restrict other diabetic complications. Resveratrol is also a flavonoid that decreases astrocytic activation and transcription of TNF and interleukin 6 (IL-6) in the hippocampal region of diabetic rats (21). It also reduces malondialdehyde and oxidized glutathione levels in diabetic rats and also enhances the action of SOD and catalase. *Ficus deltoidea* extract also augments superoxide dismutase and glutathione peroxidase levels, while diminishing malondialdehyde. Similar activities have been published for saffron extracts with antidiabetic activity, which also alter the anti-inflammatory pathways. Extracts of *Scoparia dulcis* also raise activities of SOD, catalase or glutathione-S-transferase or glutathione peroxidase while lessens glutathione in diabetic rats. Similar results have been explained for chrysin, a phytoconstituent isolated from *Passiflora incarnata* also reduces oxidative stress by decreasing catalase levels, SOD and glutathione in diabetic rats (22; 23; 24; 25). Numerous natural product-derived anti-diabetic medications are now available in the market. These include Glyoherb[®], Metformin[®], Diabecon[®], and Diabeta Plus[®], each of them having mul-

multiple active ingredients (26). Clinical studies are gradually picking up. Between 2005 and 2016, numerous studies related with diabetes were published which included 16 clinical studies (27). The imbalanced glucose homeostasis imposes serious health consequences and that is why diabetes mellitus is one of the most important health problems in the world. Recent studies have also paved the way for discovery of new natural compounds with antidiabetic efficacy which could be a great promise (6; 28; 29). The available antidiabetic drugs have unavoidable detrimental side effects. Safety concerns of individuals have resulted in a current top-priority health-issue-seeking better medication of diabetes.

3. Conclusion

Plants have been an ideal source of drugs/pharmaceuticals and have directly or indirectly yielded essential medicines used against the diseases of diverse etiology. In modern era, antioxidants of natural origin have gained attention over chemically synthesized products in the defense against diabetes because of their established advantages, low toxicity, and ease of entry using dietary supplements. Herbal prescriptions are attaining recognition because of several benefits such as a relatively lower occurrence of side-effects at optional dosages, improved acceptance by patients, comparatively low cost, and acceptance due to a long traditional use.

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