



Contents lists available at ScienceDirect

Journal of Traditional and Complementary Medicine

journal homepage: <http://www.elsevier.com/locate/jtcme>

An update on natural compounds in the remedy of diabetes mellitus: A systematic review

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ARTICLE INFO

Article history:

Received 21 June 2017

Received in revised form

15 August 2017

Accepted 16 August 2017

Available online xxx

Keywords:

Herbal medicine
Insulin secretion
Insulin resistivity
Active component
Diabetes control

ABSTRACT

Herbal medicine, phytomedicine or botanical medicine are synonymous, utilizes plants intended for medicinal purposes. Medicinal use of herbal medicine in the treatment and prevention of diseases including diabetes has a long history compared to conventional medicine. Diabetes is one of the major public health concerns over the world. Diabetes or hyperglycemia is considered to be one of the common public health hazard; optimal control of which is still not possible. Persistent hyperglycemia or uncontrolled diabetes has the potential to cause serious complications such as kidney disease, vision loss, cardiovascular disease, and lower-limb amputations which contributed towards morbidity and mortality in diabetes. There are various approaches to treat and prevent diabetes as well as its secondary complications, one of it is herbal medicines. However, the selection of herbs might depends on several factors, which include the stage of progression of diabetes, types of comorbidities that the patients are having, availability, affordability as well as the safety profile of the herbs. This review focuses on the herbal and natural remedies that play the role in the treatment or prevention of this morbid disorder – diabetes, including their underlying mechanisms for the blood glucose-lowering property and the herbal products already been marketed for the remedial action of diabetes.

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1. Introduction

Use of herbal products are not only limited to dietary uses, such as food, nutrition, etc., it has its distinct role in remedy of several diseases. Herbal medicine, sometimes known as phytomedicine or botanical medicine, utilizes different parts of the plants, including its flowers, fruits, seeds, leaves, berries, bark and roots intended for medicinal purposes.¹ The use and delivery of herbal medicine as

dosage form in treating and preventing of diseases has a long history started with use in Mesopotamia in 2600 B.C.,² although the oldest record on practice of medicinal plants for drug preparation was engraved on a Sumerian clay slab, created over 5,000 years ago.³ The use of medicinal plants are still continuing in this modern era, and it has been estimated that approximately one fourth of prescription medicines worldwide are derived from plants.¹ World Health Organization has also reported the use of traditional medicine for primary health care needs in most countries.⁴ Herbal products in Malaysia have molded an essential component in the medicine system, where the Malaysian market for herbal products stands at approximately RM4.6 billion with a 15–20% annual projected growth rate.⁵ Therefore increased interest of Malaysians' for the use herbal medicines lead to tremendous growth of the Malaysian herbal product market.

Herbal medicine is one of the subgroups of complementary and alternative medicinal (CAM) therapies. Many patients consider

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Peer review under responsibility of The Center for Food and Biomolecules, National Taiwan University.

<https://doi.org/10.1016/j.jtcme.2017.08.012>

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CAM over conventional therapies due to dissatisfied outcomes from the conventional therapies, higher treatment costs and increased side effects of modern medicines. Therefore, the active ingredients of the medicinal plants are directing towards its particular use in diseased condition, may be applied in complex formulation of one or more plants. The use of traditional herbal medicines is more associated with patient conception and less paternalistic compared to allopathic medicine in general.^{6–9} Moreover, traditional herbal medicines may be used in combination with or as alternative to the conventional allopathic medicines. Thus, there are thousands of medicinal plants for the treatment of a range of diseases. There are several complications which are targeted to treat with herbal medications, including cancer, memory impaired condition, liver disorder, peptic ulcer and other gastrointestinal disorder, inflammatory disorder, hypertension and other cardiovascular disease, diabetes mellitus, hyperlipidemia, tuberculosis, dermatological infections, along with undefined muscular pains and other diseases related to urinary tract, respiratory tract and central nervous system.^{6–19} The worldwide utilization of herbal medicines are summarized in Fig. 1. In this article, we aim to focus the potential herbal medications as an effective and sustainable alternative for the treatment of diabetes. In due course of the study, we have done extensive literature search to provide a summarized database on available herbal treatments in the control and treatment of diabetic condition.

2. Clinical overview of diabetic mellitus

Diabetes is a chronic disease characterized by hyperglycemia, and is categorized into two types: Type I Diabetes Mellitus (T1DM) and Type II Diabetes Mellitus (T2DM). In T1DM, β -cells of the pancreas are damaged, leading to a decreased insulin supply to the circulation. Patients will be fully dependent on exogenous insulin administration for existence. Contrarily, T2DM has been observed in majority of diabetic patients (85%) and results in peripheral insulin resistance, thereby results in decreased insulin sensitivity to the skeletal muscles, adipose tissues and liver (Fig. 2).²⁰ Another category of diabetes can also be categorized in pregnant women

without previously diagnosed diabetes, known as gestational diabetes mellitus. Factors such as aging, obesity, physical inactivity, population growth and urbanization can gradually leads to steady increase in the number of patients with diabetes. In year 2000, prevalence of diabetes worldwide among adults is estimated to be approximately 171 million,²¹ whereas the number has been increased to 422 million (approximately 1 in every 11 people) in 2014.²² The prevalence of diabetes in the world is expected to be doubled to approximately 366 million in year 2030 due to demographic changes in people of more than 65 years old and most importantly, adaptation of sedentary life style by the people in the urban areas of the world.²¹ If this disease left untreated it can lead to acute fatal complications including diabetic ketoacidosis and coma due to exceptional increase in blood glucose. Additional dreadful consequences of diabetes include vascular complications due to damage of the vessels for high glucose level, may result in macrovascular and microvascular disorders. Consequences of microvascular complications are retinopathy, neuropathy, etc., whereas, macrovascular complications lead to cardiovascular complications. Other complications for chronic diabetic conditions include dementia, sexual dysfunction, depression and lower-limb amputations.²⁰

Different categories of antidiabetic medications are there in the market for the remedial action, which includes insulin analogues, sulphonylureas, biguanides, dipeptidyl peptidase-4 inhibitors, thiazolidiones, α -glucosidase inhibitors, etc, where the mechanism of counteracting this increased glucose level is different for different categories (Fig. 3).²² However, long term treatment and side effect of the available hypoglycemic medications leading towards huge demand for efficacious, decreased side effects and affordable agents for the treatment of diabetic condition.

3. Herbal remedy in diabetes

Complementary or alternative treatments using herbal medicines draw the attention of many diabetic patients. Numerous common herbs are claimed to reduce blood glucose level, therefore the possibility of having better glycemic control or being less

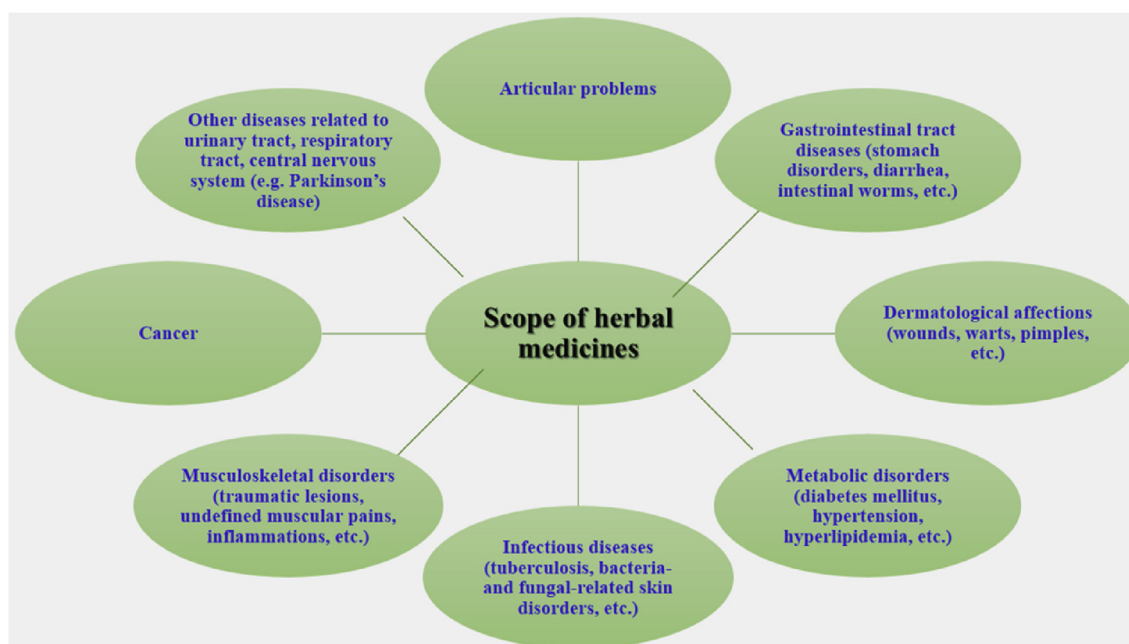


Fig. 1. The traditional utilization of herbal medicines in different field of medical field.

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