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• Review

Screening of antidiabetic and antioxidant activities of medicinal plants

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ABSTRACT

Diabetes is a common metabolic disorder characterized by abnormally increased plasma glucose levels. Postprandial hyperglycemia plays an essential role in development of type-2 diabetes. Inhibitors of carbohydrate-hydrolyzing enzymes (such as α-glucosidase and α-amylase) offer an effective strategy to regulate/prevent hyperglycemia by controlling starch breakdown. Natural α-amylase and α-glucosidase inhibitors, as well as antioxidants from plant-based sources, offer a source of dietary ingredients that affect human physiological function in order to treat diabetes. Several research studies have investigated the effectiveness of plant-based inhibitors of α-amylase and α-glucosidase, as well as their antioxidant activity. The aim of this review is to summarize the antidiabetic and antioxidant properties of several medicinal plants around the world. Half inhibitory concentration (IC_{50}, for enzyme suppression) and half effective concentration (EC_{50}, for antioxidant activity) values of less than 500 μg/mL were defined as the most potent plant-based inhibitors (*in vitro*) and are expected to provide interesting candidates for herbal treatment of diabetes, as foods, supplements, or refined drugs.

Keywords: medicinal plants; α-amylase; α-glucosidase; antioxidant; review

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1 Introduction

Diabetes mellitus is currently a growing global health concern. The estimated number of 171 million diabetics worldwide in 2000 is expected to increase to at least 366 million by the year 2030[1]. The incidence and prevalence of diabetes are increasing, especially in developing and newly industrialized countries. About 90% of all cases of diabetes in developed and developing countries are non-insulin-dependent diabetes mellitus, also known as type-2 diabetes (T2D), or adult-onset diabetes. These diagnoses are typically in adults more than 30 years of age[2], and are usually characterized by postprandial hyperglycemia, an abnormal rise in blood sugar following a meal[3]. T2D is complicated by several factors integral to the disease process such as insulin resistance, hyperinsulinemia, impaired insulin secretion, reduced insulin-mediated glucose uptake and utilization[4]. Many efforts have been made to search for other effective and safe enzyme inhibitors from natural materials in order to control diabetes[5].

In enterocytes of the small intestine, carbohydrate can be absorbed only as monosaccharides (glucose and fructose). Human pancreatic α-amylase (E.C. 3.2.1.1) is the main enzyme in the digestive system and is responsible for hydrolysis of starch, glycogen and various oligosaccharides to smaller oligosaccharides including maltose, maltotriose, and a number of α-(l-6) and α-(1-4) oligoglucans. α-Glucosidase, locating in the brush border of the small intestines, further breaks down disaccharides, making them available for intestinal absorption[6]. This process of dietary starch

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digestion happens quickly and results in postprandial rise in blood sugar. The rise in postprandial blood glucose level is associated with the activity of digestive enzymes (α-amylase and α-glucosidase) in the small intestine[7]. Therefore, inhibition of these two enzymes could play a role in controlling diabetes by slowing down the digestion of starch and extending intestinal carbohydrate holding time. This would be followed by a decrease in the rate of glucose absorption and a subsequent reduction in the rate of increase of postprandial blood glucose[1]. This could be a promising approach for the control of T2D[5], and forms the basis of many current clinical antidiabetic agents. Several synthetic inhibitors or antidiabetic agents, such as acarbose, miglitol and voglibose may reduce the absorption rate of glucose by slowing down carbohydrate digestion, causing a decrease in postprandial serum glucose level[8]. However, many of these synthetic hypoglycemic agents are non-specific, fail to prevent the development of diabetic complications and cause side effects[9]. Some of these side effects include gastrointestinal bloating, abdominal discomfort, diarrhea and flatulence[10]. An alternative approach may include natural products that display effective inhibitory activity against α-amylase and α-glucosidase with fewer side effects[11,12]. Numerous medicinal plants have showed some relationship to the inhibition of carbohydrate processing enzymes[12,13].

Another problem for many patients with diabetes is oxidative stress; the difference between the generation of oxygen-derived radicals and an organism's antioxidant potential can lead to oxidative damage to cell components such as proteins, lipids and nucleic acids[14]. Components of plants, with naturally occurring antioxidant activity, can be used to control the balance between free radicals and antioxidant stress in diabetes patients, and may be a less harmful alternative to synthetic antioxidant products[15].

Traditional medicinal plants can provide valuable therapeutic effects. Various metabolic diseases such as diabetes, adiposity and cardiovascular complications can be treated by herbs, which can be readily available, affordable, easy to administer and have fewer side effects than pharmaceutical interventions[16,17]. The plant kingdom possesses a wide variety of natural substances that have antidiabetic action, and have few or no documented side effects; extracts of a number of medicinal plants have showed significant hypoglycemic properties[17,18]. Therefore, the aim of this work was to review the antidiabetic and antioxidant properties of several medicinal plants around the world. Half-maximal inhibitory concentration (IC_{50}) refers to the concentration of plant extracts that give 50% inhibition related to T2D (α-amylase and α-glucosidase). Half-maximal effective concentration (EC_{50}) refers to the concentration of a test product that yields 50% of the activity of a standard enzyme. Compounds having IC_{50} and EC_{50} less than 500 μg/mL were identified as the most potent plant inhibitors (*in vitro*) of digestive enzymes related to T2D, and most effective promoters of antioxidant activity[19].

2 *In-vitro* inhibition of α-amylase and α-glucosidase by medicinal plants

The hydrolysis of dietary starches is the main source of glucose in the blood. The enterocytes of the small intestine can only absorb monosaccharides such as glucose and fructose from our diet. Therefore, the dietary polysaccharides need to be broken down to monosaccharides before they can be absorbed. α-Amylase catalyses the hydrolysis of α-1,4-glycosidic linkages of starch, glycogen and various oligosaccharides and α-glucosidase further breaks down the disaccharides into simple sugars. Moreover, the α-glucosidase enzyme catalyzes the cleavage of glycosidic bond and subsequently liberates glucose from the non-reducing end of the oligosaccharide chain[20]. Acarbose is an inhibitor of α-glucosidase enzyme that commonly used to decrease glucose absorbance by reducing the production of this enzyme in the small intestine[21]. However, this inhibitor showed some disadvantages such as increased risk of gastrointestinal problems, inconvenient dosing and costliness. Medicinal plants play an important role in the treatment of diabetes, particularly in developing countries where most people have limited resources and poor access to modern medicine[22]. Many medicinal plants have been investigated for their suppression of glucose production from carbohydrates in the gut or glucose absorption in the intestine[23]. Recently, it has been shown that phenolics play a role in mediating amylase inhibition and therefore have potential to contribute to the management of T2D[11]. Phenolic compounds also have an inhibitory effect against α-amylase and α-glucosidase activity and therefore have potential as an effective treatment for postprandial hyperglycemia with minimal side effects[12].

Table 1 summarizes the inhibitory activities of some medicinal plants toward α-amylase and α-glucosidase, key enzymes linked to T2D (IC_{50} or EC_{50} < 500 μg/mL). Sreerama *et al*[24] have studied the enhancement of food products through the inclusion of phenolics from legume flours such as cowpea, horse gram and chickpea. These flours may provide inhibition of α-amylase and α-glucosidase enzymes and thus modulate the glycemic index of food products. Horse gram flour phenolics strongly inhibited α-amylase activity at concentrations lower than 200 μg/mL and had the lowest inhibitory activity towards α-amylase (IC_{50} = 96.4 μg/mL) compared to chickpea and cowpea (Table 1). On the other hand, the IC_{50} value of cowpea extract (52.8 μg/mL) was found to be more effective than chickpea and horse gram flours at inhibiting α-glucosidase (IC_{50} of 92.2 and 63.2 μg/mL respectively). Gulati *et al*[25]