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Review

Antidiabetic dietary materials and animal models

Sunan Wang [a], Fan Zhu [b,*]

[a] Canadian Food and Wine Institute, Niagara College, 135 Taylor Road, Niagara-on-the-Lake, Ontario L0S 1J0, Canada
[b] School of Chemical Sciences, University of Auckland, Private Bag 92019, Auckland 1142, New Zealand

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ABSTRACT

The ever-increasing occurrence of diabetes worldwide demands cost-effective anti-diabetic strategies. Food-based materials have great potential as efficient anti-diabetic agents. Focusing on the literatures of the recent 5 years, this review summarizes the methods, findings, and limitations of each research involving non-medicinal foods (individual and mixed) and diabetic animal models. Various types of fruits, vegetables, legumes, cereals, spices, beverages, oilseeds, and edible oils showed antidiabetic effects in different animal models. Animal feeding trials rarely had identical designs in food doses, feeding schedules, and routes of administration, as well as biochemical markers for antidiabetic evaluation. Various possible cellular and metabolic targets were speculated for the anti-hyperglycemic effects of the dietary materials, and the molecular mechanisms of action remain to be better explored. Short-term (maximum 16 weeks) antidiabetic studies have been established. Limited safety/tolerability data are available for antidiabetic dietary materials. Findings from current animal studies present a generic antidiabetic dietary pattern associated with plant-based whole foods, which agrees well with the findings of epidemiological studies.

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* Corresponding author.
E-mail address: fzhu5@yahoo.com (F. Zhu).

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1. Introduction

Among the diet-related non-communicable chronic diseases, diabetes mellitus, after cardiovascular diseases, cancers, chronic respiratory diseases, ranks fourth in prevalence worldwide (Schwarz et al., 2013). The global incidence of diabetes reached 387 million in 2014. Diabetes caused approximately $612 billion USD dollars in global health expenditure in 2014 (IDF, 2014). By 2030, the projected top 10 countries with high diabetes prevalence from the highest to the lowest are: India ($79.4 million); China ($42.3 million); USA ($30.3 million); Indonesia ($21.3 million); Pakistan ($13.9 million); Brazil ($11.3 million); Bangladesh ($11.1 million); Japan ($8.9 million); Philippines ($7.8 million); Egypt ($6.7 million) (Wild, Roglic, Green, Sicree,; King, 2004). The majority of people (77%) with diabetes live in low- and middle-income countries worldwide (IDF, 2014; Wild et al., 2004). One strategic initiative is, therefore, to develop affordable diabetes prevention and treatments.

Most diabetic patients do not achieve and maintain euglycemia with those traditional therapies such as the use of oral antidiabetic agents (Levetan, 2007). The main variables associated with the unsatisfied responses are the low efficacy and tolerability of antidiabetic drugs, unhealthy lifestyle intervention, and lack of adherence to therapy. Antidiabetic drugs (i.e., metformin) are costly with undesirable side effects. Levetan (2007) concluded that all 10 widely used oral antidiabetic drugs had side effects. These drugs lead to a certain degree hypoglycemia (occasionally life-threatening), weight gain, edema gastrointestinal complaints, lactic acidosis (associated with a high mortality rate), hypersensitivity, liver toxicity, and renal dysfunction (Levetan, 2007). The side effects can be minimized with the reduction in drug dose, when combined therapies or alternative treatments are applied. A number of non-medicinal foods have claimed to be antidiabetic agents of high potential. These foods are particularly advantageous for their "generally recognized as safe" status and economic viability.

Recently-documented foods with antidiabetic potential fall into a few broad categories, including fruits (Gondi, Basha, Bhaskar, Salimath, & Rao, 2015; Gondi & Rao, 2015), vegetables (Clouatre, Rao, & Preuss, 2011; Hafizur, Kabir, & Chishti, 2012; Shukla et al., 2011; Zhao et al., 2011), legumes (Lomas-Soria et al., 2015; Yao, Cheng, & Ren, 2014), cereals (Brockman, Chen, & Gallaher, 2013; Minaiyan, Ghannadi, Movahedian, & Hakim-Elahi, 2014), oilseeds (Ghule, Jadhav, & Bodhankar, 2012; Maknia, Fetouia, Gargourib, El Garouia, & Zeghala, 2011), beverages (Islam, 2011; Yamamoto, Tadaishi, Yamane, & Oishi, 2015), edible oils (Al-Amoudi & Abu Araki, 2013). These foods differ with regard to the physiological effects on the diabetic animal models applied. For example, flax and pumpkin seed powder mixtures regulated hepatic glucose metabolism, lipid metabolism, and antioxidant defense system of alloxan-induced diabetic mice (Maknia et al., 2011). Barley flour improved insulin resistance of Zucker diabetic fatty rats (Brockman et al., 2013). Mango peel powder ameliorated diabetic nephropathy in streptozotocin-induced diabetic mice (Gondi et al., 2015). In addition to the type of diabetic animal models, variables associated with antidiabetic effects of food materials include food form and dose, dose schedules, routes of administration and chemical constitutions of foods. Anti-hyperglycemic effects of the crude food extracts on diabetic models were simply demonstrated in several studies. Dose-dependent antidiabetic effects were observed while time-dependent effects of the treatments were little reported. Molecular approaches to reveal the mechanisms of action behind these antidiabetic foods are limited.

Previously reviews addressed some specific antidiabetic foods (Adams et al., 2011; Srinivasan, 2005) and antidiabetic plants (Chan, Ngoh, & Yusoff, 2012; Saravanamuttu & Sudarsanam, 2012). Reviews focused on medicinal dietary materials (Eddouks, Chattopadhyay, & Zeggwagh, 2012; Teng et al., 2012; Ma, Hsieh, & Chen, 2015; Surya et al., 2014). Others were particularly interested in particular food constitutes, such as phenolics (Asgar, 2013) and polysaccharides (Xiao et al., 2012; Simpson & Morris, 2014). This mini-review updates information to reflect recent 5 years on antidiabetic potentials of non-medicinal whole foods (mostly plant-based individual and mixed) as proved by animal feeding trials. Whole food materials, rather than individual components, were placed into the special attention, due to the lower cost and feasibility for daily use. Common healthy products with antidiabetic such as tea are not included here as they have been much studied previously. Frequencies of citation were also considered in the selection of research articles. This review also features commonly used diabetic animal models in food research. Streptozotocin- and alloxan-induced mice represent non-obese models, while high fat/fructose-induced mice, Zucker diabetic fatty rats, and KKAy mice represent obese models. Future research directions are suggested. Food therapy to treat diabetes may decrease the risks of other diseases such as atherosclerosis, carcinogenesis, and osteoporosis, which is beyond the focus of this review (González-Castejón & Rodriguez-Casado, 2011; Singh et al., 2015). This review may shed light on the development of low-cost food-derived alternative and complementary therapies for diabetes.

2. Diabetes and diabetic complications

Impaired insulin secretion or sensitivity leads to diabetes. It can be categorized as type 1, type 2, and gestational diabetes. Type 1 diabetes is known as insulin-dependent diabetes mellitus or juvenile diabetes. Type 2 diabetes is known as non-insulin-dependent diabetes mellitus or adult-onset diabetes. Type 1 diabetes typically occurs when pancreas fails to stimulate enough insulin due to the degeneration of pancreatic β-cells. Type 2 diabetes typically occurs when the cells fail to respond to insulin properly as a result of insufficient insulin secretion and/or insulin resistance in peripheral and liver tissues (Adams et al., 2011; Cryer, Davis, & Shamoon, 2003; Inzucchi & Sherwin, 2005; Kahn, 2003). Gestational diabetes (beyond the focus of this review) only occurs among pregnant women, who have high blood glucose levels. A genetic susceptibility is linked to type 1 diabetes (rarely type 2 diabetes), while behavioral and environmental factors (including diet) are linked to type 2 diabetes (Inzucchi & Sherwin, 2005; Newsholme, Keane, de Bittencourt, & Krause, 2013; Sadiku, 2012).

The acute and chronic diabetic complications are associated with the majority of individuals with type 1 or type 2 diabetes. The acute diabetic complications can be hyperglycemia (exceptionally high blood glucose), hypoglycemia (low blood glucose), and increased water intake and polyuria (abnormally large production of urine). The chronic diabetes complications include microvascular diseases (due to damage to small blood vessels) and macro-vascular diseases (due to damage to the arteries). Diabetic retinopathy (retinal dysfunction), diabetic nephropathy (kidney dysfunction) and diabetic neuropathy (nerve dysfunction) are typical microvascular diseases. Coronary artery disease, peripheral arterial disease, and stroke are considered macrovascular diseases (Adams et al., 2011; Cryer et al., 2003; Forbes & Cooper, 2013; Kahn, 2003).

3. Diabetic animal models

Numerous diabetic animal models have been established to reflect the pathogenesis and progression in human diabetes (Lenzen, 2008; Ishii, Ohta, & Sasase, 2012; Katsuda, Ohta, Shinohara, Bin, & Yamada, 2013). Diabetic model animals can exhibit abnormalities of insulin sensitivity, glucose and lipid metabolisms, and also represent a certain level of retinal, kidney, and liver dysfunctions.

According to diabetes-inducing methods, diabetic models most recently applied can be grouped as 1) diet/nutrition-induced obese models; 2) chemical-induced diabetic non-obesity models; and 3) surgical diabetic and transgenic/knocked-out diabetic models (Table 1). These diabetic models (even within the same group) vary in genetic background and diabetic characteristics. Table 1 details the animal origin, inducing methods, and diabetic symptoms of each model. An