Carbohydrate Polymers 144 (2016) 474–494

Contents lists available at ScienceDirect

Carbohydrate Polymers

journal homepage: www.elsevier.com/locate/carbpol

Review

Mechanisms underlying the effect of polysaccharides in the treatment of type 2 diabetes: A review

Jianjun Wu, Songshan Shi, Huijun Wang, Shunchun Wang*

The MOE Key Laboratory for Standardization of Chinese Medicines and the SATCM Key Laboratory for New Resources and Quality Evaluation of Chinese Medicines, Institute of Chinese Materia Medica, Shanghai University of Traditional Chinese Medicine, 1200 Cailun Road, Shanghai 201203, PR China

ARTICLE INFO

Article history:
Received 27 October 2015
Received in revised form 18 January 2016
Accepted 14 February 2016
Available online 18 February 2016

Keywords:
Diabetes mellitus
Type 2 diabetes
Polysaccharides
Anti-diabetic
Beta cell
Mechanism

ABSTRACT

Type 2 diabetes mellitus, a common metabolic and endocrine disorder worldwide, causes severe health and economic problems. At present, pharmacotherapy involving synthetic diabetic agents is clinically administered for diabetic therapy, which has certain side effects. Fortunately, various natural polysaccharides have anti-diabetic activity and use of these polysaccharides as adjuncts to conventional therapies is increasing in developing countries. A literature search was conducted to obtain relevant information of anti-diabetic polysaccharide from electronic databases, namely PubMed, Web of Science, ScienceDirect, and Springer, for the period 2011–2015. In total, 114 types of polysaccharides from 78 kinds of natural sources, namely plants, fungi, algae, animals, and bacteria, have shown anti-diabetic properties. In vivo and in vitro experiments have shown that administering these polysaccharides has hypoglycaemic effects and alleviates β-cell dysfunction in addtion to eliciting other anti-diabetic activities which are equally efficient to even more efficient than those of synthetic diabetic agents.

Contents

* Corresponding author. Fax: +86 21 5132 2519.
E-mail address: shunchunwang@126.com (S. Wang).

http://dx.doi.org/10.1016/j.carbpol.2016.02.040
0144-8617/

1. Introduction

On September 14, 2014, the International Diabetes Federation announced that diabetes affects over 387 million people worldwide, caused 4.9 million deaths in 2014, and causes one death every 7 s. In 2014, diabetes expenditure reached US $612 billion, accounting for 11.1% of the total world health care expenditure on adults. In 1998, diabetes was predicted to affect 286 million people worldwide by 2030 (Harris et al., 1998), reflecting that the increase rate is faster than that expected. The prevalence of diabetes is increasing worldwide, and the number of cases is predicted to increase to approximately 592 million (1 in every 12 people) by 2035 (Guariguata et al., 2014).

Diabetes mellitus (DM) is a chronic disease occurring when the body no longer produces adequate insulin or when it cannot use the produced insulin effectively. Diabetes has three main types. Type 1 diabetes (T1DM), formerly called insulin-dependent DM, is typically caused by autoimmune destruction of the insulin-producing pancreatic β cells; the mechanism underlying this phenomenon remains unclear. Type 2 diabetes (T2DM), formerly called non-insulin-dependent DM, is a complex metabolic and endocrine disorder characterised by high blood sugar causing insulin resistance (IR) and relative insulin deficiency (Liao, 2011; Puri & Hebrok, 2012; Tahrani, Bailey, Del Prato, & Barnett, 2011). Gestational DM (GDM) is characterised by high blood glucose levels in pregnant women without previously diagnosed diabetes. T2DM accounts for approximately 90% of DM cases, with the remaining 10% primarily being T1DM and GDM. The present review focuses on T2DM.

T2DM, a critical risk factor for cerebral infarction, cardiovascular disease (Mazzone, Chait, & Plutzky, 2008), blindness, and kidney failure, is caused by the joint influence of lifestyle and genetic components. Because of the association of the aforementioned factors, IR occurs several years before T2DM onset. Lifestyle factors, including overweight, obesity, physical inactivity, poor diet, and stress, act in conjunction with key genes, such as *PPARG*, *IRS1*, *IGF1*, *FTO*, *TCF7L2*, *KCNJ11*, *WFS1*, *HNF1B* and *CDKN2B*, to impair β-cell functioning (Bonnefond, Froguel, & Vaxillaire, 2010; Nolan, Damm, & Prentki, 2011; Prokopenko, McCarthy, & Lindgren, 2008; Ridderstrale & Groop, 2009; Schäfer, Machicao, Fritsche, Häring, & Kantartzis, 2011). Inadequate insulin secretion for overcoming IR characterises the transition from impaired glucose tolerance to T2DM.

Polysaccharides, which have the general formula $C_x(H_2O)_y$, are polymeric carbohydrate molecules composed of long chains of monosaccharide units bound together by glycosidic linkages and, on hydrolysis, provide the constituent monosaccharides or oligosaccharides. Monosaccharides have a general formula of $(CH_2O)_n$ where n is three or greater. Examples of monosaccharide include glucose, galactose, mannose, arabinose, fructose, rhamnose and xylose. Because the repeating units in a polysaccharide backbone are usually six-carbon monosaccharides, the general formula of polysaccharide can also be represented as $(C_6H_{10}O_5)_n$, where n is a high number between 40 and 3000. The polysaccharide structure can be linear or highly branched (Zong, Cao, & Wang, 2012). The function of polysaccharides in living organisms is typically either related to structure (e.g., cellulose and chitin) or storage (e.g., starch and glycogen). Moreover, polysaccharides are extremely complex and not encoded in the genome; therefore, until recent decades, they have gradually been determined to have various biological functions, such as antioxidant (Ji et al., 2014), immunomodulation (Sun, Wang, & Zhou, 2012), antitumour (Ruijun et al., 2015), radioprotection (Chen, Zhao et al., 2011), antidiabetes (Tong, Liang, & Wang, 2008), hepatoprotection (Liu et al., 2015), antimicrobial (Cheng et al., 2013), and antifatigue (Tan et al., 2012) functions.

Numerous studies have indicated that polysaccharides exhibit anti-diabetic effects through a variety of mechanisms. The present review discusses natural anti-diabetic polysaccharides derived in the past 5 years, and mechanisms underlying their multiple anti-diabetic activities are classified in the following sections.

2. Polysaccharides targeting β-cell dysfunction

T2DM is characterised by an absolute or relative lack of insulin secretion from pancreatic β cells, resulting in poorly regulated blood glucose levels. Pancreatic β cells compensate for IR by increasing insulin secretion before progression to T2DM. β-Cell dysfunction and T2DM that follow this period of β-cell compensation may result from an inadequate expansion of the β cell mass and inadequate production of insulin (Kasuga, 2006; Nolan et al., 2011). The exact mechanisms underlying T2DM are unknown; however, the role of lipotoxicity (Biden, Boslem, Chu, & Sue, 2014) and glucotoxicity (Paul, Jamie, Phuong Oanh, Yoshito, & Hiroki, 2003) in the development of obesity and T2DM has been recognised. Growing evidence has shown that inflammation (Donath & Shoelson, 2011; Du, 2011) and oxidative stress (Dabhi & Mistry, 2015; Mehta, Rasouli, Sinha, & Molavi, 2006) cause impairment of pancreatic β cell structure and function and IR and, consequently, cause T2DM. Compounds that improve the aforementioned conditions suggest positive effects on the pancreas or liver and potentially prevent and treat T2DM.

2.1. Polysaccharides having hypoglycaemic and hypolipidaemic effects

The impaired glucose tolerance in addition to a gradual loss of β-cell function frequently observed in patients with T2DM has been attributed to glucose toxicity and lipotoxicity of different magnitudes. The notion that chronic exposure to hyperglycaemia can lead to irreversible cellular dysfunction has led to the concept of glucose toxicity. Hyperglycaemia, causing an increase in the number of reactive oxygen species (ROS) in β cells, causes subsequent damage to cellular components (Yki-Järvinen, 1992). Although the pancreatic lipid content is not associated with β cell dysfunction in youth-onset T2DM (Wicklow et al., 2013), pancreatic islet lipotoxicity is considered a major factor for T2DM onset and development. Elevated circulating serum fatty acid levels and disordered lipid metabolism cause β-cell dysfunction and are risk factors for T2DM (Janikiewicz, Hanzelka, Kozinski, Kolczynska, & Dobrzyn, 2015).

An aqueous extract of *Acacia tortilis* polysaccharide (AEATP) obtained from gum exudates contains D-galactose, D-glucose, L-rhamnose, and D-glucuronic acid, and exhibited an anti-diabetic effect in streptozotocin (STZ)-induced diabetic rats. AEATP significantly reduced fasting blood glucose (FBG) and glycated haemoglobin levels in diabetic rats compared with glimepiride-treated diabetic mice. AEATP also improved lipid metabolism, as reflected by reduced levels of total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL), and very LDL (VLDL) and an increased level of high-density lipoprotein (HDL). Moreover,