

Application Of Functional Food in Blood Glucose Regulation

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Abstract. Currently, as living standards continue to improve globally, the prevalence of diabetes is rising. This has led to diabetes becoming a significant global public health concern. Diabetes and its associated complications have a significant impact on human health. Traditionally, oral drugs and insulin injections are taken as the efficient ways to fight against diabetes, while always accompanied with adverse effects under certain conditions, which further underscores the importance of developing alternative treatments, among those, the functional foods based on natural active substances draw great attention, as their moderate efficiency and convenient administration manner. This paper presents a review of the glucose-regulating functional factors, including polysaccharides, polyphenols, flavonoids, and bioactive peptides with hypoglycaemic effects. It introduces the hypoglycaemic-related mechanisms of these factors and discusses the current shortcomings of research in this field, as well as future trends. This review provides insights that can inform the research and development of glucose-regulating functional foods.

Keywords: Diabetes, Hypoglycemic, Polysaccharide, Polyphenol, Active peptide.

1. Introduction

Diabetes is a lifelong metabolic disease characterized by chronic high blood sugar, which is usually associated with hereditary factors and lifestyle changes. According to China diabetes Market Report: 2024-2032, China is the country with the highest number of people with diabetes in the world. This disease has now reached epidemic levels among the adult population. About 30 years ago, less than 1% of Chinese adults suffered from diabetes. Previously, the incidence of diabetes has risen to about 12%. More seriously, diabetes can also cause a variety of complications, such as diabetes nephropathy, metabolic cataract, cardiovascular complications of diabetes, etc. Diabetes can be roughly divided into type 1 diabetes and type 2 diabetes. Of these, the proportion of type 2 diabetes is relatively high, accounting for around 90%. The type 1 diabetes is usually associated with beta cells inside pancreas being destroyed that are unable to produce insulin or can only secrete small amount of insulin. This type of diabetes often occurs in adolescents, and requires lifelong use of exogenous insulin for treatment. Type 2 diabetes usually occurs because insulin receptor cells are not sensitive to insulin, resulting in a decrease in insulin secretion or human's body resistance to insulin. This type of disease may occur at all ages, but most of it occurs in adults, who can be treated with some medications or insulin injections, but these methods may cause some side effects. Studies have proved that chronic metabolic diseases such as diabetes can be prevented and controlled, and that diet plays an extremely important role in the prevention and control process [1]. Therefore, it is very important to search for ingredients that can lower blood sugar in existing foods in nature for the development and application of functional foods for blood sugar regulation, which can assist patients in controlling blood sugar and reduce the risk of complications. Many experiments have shown that ensuring a balanced and healthy diet is the basis of diabetes treatment, and is also a necessary control measure at all stages of diabetes's natural course. Correct diet can achieve stable sugar control, reduce blood sugar fluctuations, and prevent complications of diabetes [2]. People have been paying attention to the research, development and application of food for blood glucose regulation. For example, at the beginning, we started with some sugar free and low sugar foods, from focusing on the proportion of carbohydrates in food to focus on food with low blood sugar generating index foods, and the rapid development of full nutrition food substitutes for preventing and treating diabetes. In addition, according to the current increasingly in-depth research, some food functional ingredients that have a

potential role in blood sugar regulation key targets, such as natural polysaccharide, polyphenols, flavone, bioactive peptide, etc[2]. With the continuous improvement of relevant research, the research and development system of blood glucose regulating food is also increasingly scientific, standardized, normalized. This paper will provide an overview of polysaccharide, polyphenols, flavone, bioactive peptide and other aspects, the mechanisms of action of glucose in the blood, to provide some references for the development of blood sugar control foods.

2. Blood Glucose Regulation Factors

2.1. Polysaccharides and their hypoglycemic effect

Polysaccharides, are composed of multiple monosaccharide molecules, typically comprising more than 10 monosaccharide units linked by glycosidic bonds. These monosaccharides may be identical or vary in structure, forming macromolecular carbohydrates. Polysaccharides possess a multitude of functions and are characterised by low toxicity and a vast range of sources. Among these, the hypoglycaemic effect of polysaccharides represents a particularly popular avenue of research. Polysaccharides are widely distributed in the natural world, occurring in plants, animals and microorganisms. Consequently, polysaccharides are typically classified according to their source, with plant, animal and microbial polysaccharides being the most common categories. Plant polysaccharides encompass a multitude of varieties, which are primarily classified as starch, cellulose, hemicellulose, pectin, and glycogen, among others. To date, a greater number of plant polysaccharides have been identified as possessing hypoglycaemic properties. These include pumpkin polysaccharides, yam polysaccharides, lily polysaccharides, yucca polysaccharides, and cactus polysaccharides, among others [3]. Animal polysaccharides are distributed in almost all animal tissues and organs, including glycogen, chitin, heparin, chondroitin sulphate, hyaluronic acid, and others, which have been demonstrated to possess favourable biological activities [3]. Polysaccharides extracted from animals with hypoglycaemic effects include sea cucumber polysaccharides, loach polysaccharides, rhubarb fish polysaccharides, and so forth. The category of microbial polysaccharides encompasses a range of substances derived from bacteria, fungi, and algae. Among these, polysaccharides extracted from shiitake mushrooms, reishi mushrooms, honey mushrooms and other fungi have been observed to possess hypoglycemic properties.

2.2. The mechanism of polysaccharides for the treatment of type 2 diabetes

2.2.1 It can delay glucose absorption

Polysaccharides can inhibit the activity of enzymes related to the hydrolysis of carbohydrates, delay the absorption of glucose, and reduce postprandial blood glucose. Some studies have demonstrated that polysaccharides extracted from *Boletus edulis* can effectively inhibit the activities of α -glucosidase and α -amylase at higher concentrations, with an inhibition rate of approximately 20% and 40%, respectively. Additionally, when the polysaccharides of *Boletus edulis* are at a concentration of 5 mg/mL, they also exhibit strong inhibition of lipase or from, with an inhibition rate of 30% [4]. The polysaccharide extracted from the cockle mushroom substrate has two main fractions with a monosaccharide composition of mannose:glucose:galactose=2.03:9.52:1 and fucose:galactose=1:5.21[4]. These fractions have been demonstrated to exert a certain inhibitory effect on α -amylase in in vitro experiments, which in turn reduces the diffusion of glucose. Furthermore, polysaccharides extracted from matsutake mushrooms have been demonstrated to possess remarkable potential in glycaemic regulation. Their capacity to markedly inhibit α -glucosidase and α -amylase activities has been substantiated in in vitro experiments [4].

2.2.2 It is imperative to safeguard pancreatic β -cells and facilitate insulin secretion.

Insulin is the sole hormone in the human body that exerts a hypoglycaemic effect. It is a protein hormone secreted by pancreatic β -cells. Damage to the structure or function of pancreatic islet β -cells results in insufficient insulin secretion, which in turn leads to the development of diabetes mellitus

[5]. The administration of varying doses of yucca polysaccharide was employed to investigate its potential role in the management of STZ-induced type 2 diabetes. Following the assessment of blood parameters, it was observed that yucca polysaccharide exhibited the capacity to stimulate insulin secretion, safeguard pancreatic islet cells, facilitate tissue repair, uphold the normal glucose metabolic pathway, and consequently, contribute to the reduction of blood glucose levels. The study conducted by Yang Jie and colleagues established a high-fat feed diabetic rat model and administered Astragalus polysaccharide during the same period [3]. After two months, the pancreatic cell tissues of the rats were observed, and the results demonstrated that the morphology and structure of the pancreas had undergone alterations, the number of pancreatic islet cells had increased significantly, and the degree of pancreatic islet β -cells had been reduced due to damage. It can therefore be concluded that erythrocyte polysaccharide has the capacity to promote the proliferation of pancreatic cells, increase the number of pancreatic cells, restore cell function and further promote the secretion of insulin, thereby achieving the objective of lowering blood glucose.

2.2.3 Improvement of insulin sensitivity

Glucose transporter protein is closely related to the occurrence and development of insulin resistance. Furthermore, it is a signalling molecule downstream of phosphorylation in diabetic rats, which can reflect the degree of insulin resistance to a certain extent. In a study conducted by Yu Zhuqin et al, rats with a high-fat diet and a STZ diabetes model were administered kelp and sea cucumber polysaccharides [3]. The results demonstrated that polysaccharides enhanced the expression of glucose transporter protein, resulting in a reduction in blood glucose levels and an improvement in insulin resistance. The results demonstrate that kelp polysaccharides and sea cucumber polysaccharides can enhance the expression of glucose transporter proteins, optimise glucose utilisation in peripheral tissues and subsequently mitigate insulin resistance, thereby reducing blood glucose levels. In a study conducted by Wang Yi [3], a high-fat feed-induced diabetic mouse model was employed, and the mice were administered flavonoid polysaccharides. The results demonstrated a decline in insulin levels and an increase in the level of the insulin receptor substrate IRS-2 in the mice. The results of this study indicate that polysaccharides derived from *Rhizoma Polygoni Multiflori* can facilitate the elevation of IRS-2 levels and enhance insulin secretion, which in turn can contribute to a reduction in blood glucose levels.

The direct-action effect of polysaccharides is primarily achieved through the promotion of IRS expression, phosphorylation of the insulin receptor substrate, and the increase in the level of extracellular membrane glucose transporter proteins. This ultimately leads to an enhancement in glucose uptake, which in turn reduces insulin resistance and promotes a decline in blood glucose levels.

2.3. Polyphenolic compounds and their hypoglycaemic effects

Polyphenols are beneficial natural compounds found in plants that contain multiple phenolic hydroxyl structures, such as those found in the plant epidermis, roots, stems, fruits, etc. Plant polyphenols have been demonstrated to exert a range of beneficial effects on human health, including hypoglycaemic, anti-inflammatory, and anti-tumour properties, among others. Polyphenol-containing berries, such as blueberries and strawberries, nuts, such as walnuts and almonds, and tea, including green tea and black tea, are all rich sources of polyphenols. Whole grains, such as oats and brown rice, also contain a notable number of polyphenols. The largest proportion of polyphenols is flavonoids, accounting for approximately 60%. Flavonoids are compounds with a C₆(A)-C₃(C)-C₆(B) skeleton, comprising two benzene rings with phenolic hydroxyl groups connected by a three-carbon bridge [6]. The most common flavonoids are quercetin, kaempferol and naringenin. Quercetin is a naturally occurring flavonoid found in a variety of plant and fruit species. It has been demonstrated that certain forms of quercetin possess hypoglycaemic properties. The hypoglycaemic effects of quercetin are achieved through the modulation of glucose transporter protein activity, which in turn activates the AMPK signalling pathway in skeletal muscle cells, enhancing glucose uptake and reducing hepatic glucose production. Additionally, it protects pancreatic beta cells and promotes their

regeneration. Kaempferol, which is also present in plant species, has been demonstrated to have hypoglycaemic effects. Its mechanism of action encompasses the stimulation of insulin secretion, the protection of pancreatic β -cells, and the inhibition of α -glucosidase activity, thereby achieving hypoglycaemic effects. In an in vitro study, naringenin, a dietary flavonoid, was observed to ameliorate fructose and palmitate-induced insulin resistance by improving glucose uptake via insulin stimulation and by AMPK activation of the glucose protein transporter, GLUT4, in L6 myotubes and skeletal muscle [4]. The incorporation of plant polyphenols has been demonstrated to enhance glucose-lipid metabolism by regulating the insulin signalling pathway. For example, puerarin has been demonstrated to upregulate the expression of the peroxisome proliferator-activated receptor (PPAR) and the gene encoding the cell membrane glucose transporter-4 (GLUT-4) in adipose and skeletal muscle tissues. This leads to an increase in the glucose to intracellular glucose transport and glucose consumption, which in turn reduces the concentration of glucose in the blood. Furthermore, puerarin has been shown to improve the state of hyperglycaemia and insulin resistance, IR, and to repair damaged pancreatic β -cells. Furthermore, it has been demonstrated that polyphenols derived from diverse sources can enhance insulin secretion, regulate glycolipid metabolism and exert hypoglycaemic effects by modulating the expression of genes involved in glucose-lipid metabolism via various signalling pathways [6].

Additionally, it has been shown that these compounds can repair damaged pancreatic β -cells and protect and enhance the viability of normal pancreatic islet cells.

2.4. Hypoglycaemic effects of active peptides and their mechanism of action

An active peptide is formed by two or more amino acids that are connected by a peptide bond. These peptides are typically hidden in proteins and require a series of biochemical reactions to be released before they can perform their biological function. The activity of these peptides dependent on a number of factors, including their amino acid composition, peptide chain length, and other biochemical properties. Bioactive peptides have a variety of physiological functions, including participation in human growth and development, metabolism, and hormone regulation. Additionally, they are useful for the regulation of thrombosis, hypertension, and glucose levels. The principal sources of food-derived active peptides are plants, animals, the oceans, and microorganisms. Legumes, grains, nuts, fruits, vegetables, and mushrooms are exemplary sources of plant-derived bioactive peptides, which offer the benefits of safety, resourcefulness, and ease of large-scale production, thus constituting an optimal source for the preparation of bioactive peptides [7]. Animal-derived active peptides are primarily classified into five categories: dairy-derived peptides, fish peptides, collagen peptides, livestock peptides, and silk protein peptides. These peptides are not only protein-rich and easily prepared, but they also possess biological activities such as blood pressure-lowering, blood glucose-lowering, anti-gout, and antioxidant activities [7]. At present, milk protein active peptides represent a primary area of investigation, with numerous functional foods incorporating them. For instance, the favourable impact of milk protein-derived peptides on blood glucose regulation has been extensively documented. Marine-based bioactive peptides offer a number of advantages, including a wide range of sources, diverse functions, low toxicity and high specificity, and present a promising avenue for further research. In recent years, there has been a growing interest in the potential of food-derived bioactive peptides as a means of treating diabetes. The management of T2DM typically involves weight management, dietary changes or the use of drugs to regulate blood glucose levels, restore β -cell function and enhance insulin sensitivity [7]. Dietary proteins are highly satiating and can be employed to achieve weight loss and maintain stable blood glucose levels. This is achieved by stimulating the secretion of gut hormones, increasing energy expenditure and promoting gluconeogenesis. Furthermore, wheat and buckwheat, as well as legumes such as soybeans and peas, have been demonstrated to possess a superior ameliorative effect on diabetes. The alkaline protease-treated oat protein hydrolysate (with a molecular weight of less than 5 kDa at a concentration of 1 g/kg BW) has been shown to reduce blood glucose levels in streptozotocin (STZ)-induced

diabetic mice, with its effects being observed in relation to food intake, insulin secretion and sensitivity, and gluconeogenesis [7].

3. Discussion

In recent years, the global prevalence of diabetes has increased significantly. Its pathogenesis is more complex and not yet fully defined. Insulin injections and certain medications can only control blood glucose levels and do not constitute a complete treatment for diabetes. Long-term diabetes may lead to a variety of complications, which can have a serious impact on human health. This highlights the importance of both the treatment and prevention of diabetes. This article presents an overview of the hypoglycaemic properties of natural compounds, including polysaccharides, flavonoids, polyphenols and active peptides, and outlines the associated mechanisms of hypoglycaemia. The hypoglycaemic effects of certain natural active ingredients and the mechanisms by which they operate are currently the subject of intensive investigation. Furthermore, research into functional foods is also advancing apace. The development of functional foods represents a significant area of research with the potential to play an important role in the prevention or adjuvant treatment of diabetes and its complications. However, there are still many shortcomings.

3.1. Current deficiency

A) The mechanism of action is not completely clear, although it is known that some substances have hypoglycaemic effects, but the mechanism of action is not completely clear, which will limit their entry into the clinical phase.

B) The extraction method of natural active substances and the purity of the improvement of the difficulties, these factors may lead to the effect of different effects.

C) The safety of these drugs has not been studied in enough clinical trials, and the safety of long-term use of these substances has not been confirmed, and it is not known whether there will be adverse reactions.

D) The consumption of functional foods based on natural active substances may interact with the medication that diabetic patients are being treated with, potentially affecting the therapeutic effect or human health.

E) Some functional foods based on natural substances may neglect the balance of nutrition due to an excessive focus on the effect of lowering blood sugar.

F) Publicity and regulatory issues. In comparison with prescription drugs, the regulation of functional foods based on natural active substances is more lenient, which may result in the exaggerated publicity of certain foods that control glycaemia in the market.

This could mislead consumers into believing that they can fully control their blood glucose levels through the consumption of these foods alone, as well as the emergence of some counterfeit and substandard goods. It is important to be aware of these shortcomings in the course of our study. In conclusion, polysaccharides, polyphenols, flavonoids, active peptides and other natural active substances for lowering blood sugar have a beneficial effect on the development of functional foods for blood sugar regulation. However, it is important to consider the limitations of this approach. Further attention should be paid to the process of our research, and a reasonable combination of functional foods for the prevention and treatment of diabetes represents a promising avenue for future development. Furthermore, this represents a promising future trend.

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