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Mini Review

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with Small-Bowel Glucose/
Antiabsorption and Sugar
Digestion Enzymes' Inhibition
Actions: New Strategy to
Relieve Hyperglycemia and
Diabetes

HATASO, USA

Natural Bioactive Compounds with Small-Bowel Glucose/Antiabsorption and Sugar Digestion Enzymes' Inhibition Actions: New Strategy to Relieve Hyperglycemia and Diabetes

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Abstract

Intestinal glucose absorption/inhibition activity by natural bioactive compounds is considered a new strategy for prevention/treatment of uncontrolled hyperglycemia and diabetes as well as chronic human metabolic disorders. This mini review provides scientific evidence of the contribution of natural bioactive nutrients to inhibit glucose absorption in the small bowel. Many studies were realized on intestinal glucose transport *in vitro* and on postprandial glucose levels *in vivo*. In this context, the main designated constituents are (+)-catechin, (–)-epicatechin, (–)-epigallocatechin, epicatechingallate, tannic acid, resveratrol, and chlorogenic acid. The therapeutic approaches are to retard the absorption of glucose by inhibition of carbohydrate-hydrolyzing enzymes such as intestinal glycosidases (α -amylase and α -glycosidase) and the inhibition of intestinal Na⁺-dependent glucose absorption mediated by reduced expression of glucose transporter (SGLT1). These studies revealed that natural bioactive compounds, as potential candidates, can be designed as natural products for the development of novel functional foods or nutraceuticals to relieve hyperglycemia/diabetes.

Keywords: Intestinal glucose absorption; Natural bioactive compounds; Hyperglycemia; Diabetes.

1. INTRODUCTION

Postprandial-glucose regulation importance in the improvement of diabetic aggravations is widely recognized based on several epidemiological researches [1]. Many α -amylase/ β -glucosidase inhibitors were suggested to control postprandial hyperglycemia, but the inhibitors of these enzymes are not capable of preventing glucose absorption when this sugar itself has been ingested. Hence, it might be important to inhibit intestinal glucose absorption as well as glucosidase or amylase actions for the regulation of postprandial blood glucose level [2]. The small intestine's ability to absorb glucose augments in patients with type 2 diabetes and in experimentally produced diabetic animals. This increase is due to the improved activity and abundance of SGLT1. Therefore, SGLT1 represents a potential target of drug development for glycemic control in hyperglycemic/diabetic patients [3].

Natural products and its derived bioactive constituents may be achievable alternatives for the prevention and treatment of hyperglycemia/diabetes and its complexions without any adverse effects. There are enormous active medicinal plants and their natural bioactive molecules that have already reported the therapeutic actions against hyperglycemia and diabetes. Numerous medicinal plants have been used for a long time to manage and prevent these metabolic disruptions and related situations [4].

2. NEW STRATEGY TO ALLEVIATE HYPERGLYCEMIA AND DIABETES

Bioactive compounds are described as constituents that modulate gastrointestinal-physiological or intestinal-epithelium activities in the animals or humans that consume them. Especially, phenolic acid, flavonoids, and tannins are bioactive compounds found in fruits and vegetables that act as antioxidants, anti-inflammatories, anticarcinogens, and protective factors against metabolic perturbations such as diabetes and hyperglycemia. Recently, much attention has been given to these bioactive food components that may be beneficial for the treatment and prevention of diabetes and hyperglycemia by various mechanisms of actions such as inhibition of glucose absorption and glucosidase activities. There are many recent studies and evidences that various bioactive compounds, including phenolic acids such as gallic acid, could help produce synergistic effects at decreasing postprandial rise in blood glucose level and offering possible diminution in the attendant side effects of this drug. Indeed,

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the combination of acarbose and gallic acid at equal proportion serves as a mild inhibitor of α -amylase and strong inhibitor of α -glucosidase. This is more so because previous works have reported the antihyperglycemic and antioxidant properties of phenolic-rich food sources. It could be of great therapeutic importance in addressing the side effects associated with acarbose in the management of type 2 diabetes mellitus (T2DM), which is linked with massive reduction of α -amylase activity [5,6]: indeed, the key enzymes that catalyze the final step in the digestive process of carbohydrates in mammals. Hence, α -amylase and α -glucosidase inhibitors can delay glucose absorption, resulting in reduced postprandial plasma glucose levels and suppressed postprandial hyperglycemia [7].

Bassoli et al. (2008) examined the actions of chlorogenic acid (CGA) on blood glucose levels and glucose tolerance. It was found that chlorogenic acid promoted a significant decrease in the plasma glucose peak in the oral glucose tolerance test, most likely by attenuating intestinal glucose absorption, indicating a possible role for chlorogenic acid as a glycemic index lowering agent and highlighting it as a component of interest for reducing the risk of developing T2DM [8]. It was reported also that CGA inhibited the activities of α -amylase and α -glucosidase and diminished the postprandial blood glucose concentration. Furthermore, chlorogenic acid suppresses postprandial hyperglycemia by inhibiting α -glucosidase. These actions resemble that of currently available α -glucosidase inhibitors such as acarbose, miglitol, and voglibose [9]. Simple phenolic acids such as *p*-coumaric acid were shown to decrease uptake of glucose into Caco-2 cells [10].

Gallocatechins (GC), including epigallocatechin gallate (EGCG) and epicatechin-3-gallate (ECG), showed to be responsible for the inhibitory actions, mainly through the reduction of Na-glucose cotransporters (SGLT1) in the intestinal epithelia and combined micelle production in the intestinal lumen. They have been found to decline the intestinal absorption of glucose in rats by encouraging dispersal of the Na⁺ electrochemical gradient, which draws glucose into the enterocytes, to reduce hepatic glucose-6-phosphatase activity and to regulate glucose homeostasis. Pradeepa and Hanumanthappa [11] demonstrated that the tannic acid was able to inhibit Na⁺/K⁺-ATPase, responsible for maintaining the sodium gradient indispensable for sodium-driven glucose transport into enterocytes [11]. Furthermore, other flavonoids such as quercetin monoglucosides, luteolin, and naringenin significantly inhibited SGLT1-mediated glucose uptake *in vitro* [12].

In the same context, several authors demonstrated that resveratrol inhibits glucose uptake in four ovarian cancer cells through the interruption of plasma membrane trafficking of the GLUT1 in an Akt/mTOR (serine/threonine protein kinase B mammalian target of rapamycin) dependent manner. Both studies can be related to the extent and importance of the Akt/mTOR pathway for glucose uptake in ovarian cancer cells and its potential as a target for pharmacological reduction by resveratrol [13].

3. CONCLUSION

This mini review has suggested that bioactive compounds derived from natural products act as a therapeutic tool against hyperglycemia and diabetes. Particularly, polyphenolic compounds appear to be significant metabolic modulators by their capability to influence intestinal glucose transporters and carbohydrate-hydrolyzing enzymes, which have been proven as potential targets for these natural constituents. The clinical studies and drug delivery strategies that are being researched promise a future in which we will finally know if this phytochemical lives up to its reputation, or if other natural components rise as better alternatives in the prevention/treatment of these infections.

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Conflict of Interest

None.

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