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REGULAR ARTICLE

Role of various flavonoids: Hypotheses on novel approach to treat diabetes

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Abstract Basically flavonoids are naturally occurring phenolic compounds that are distributed in plants. They contain wide range of biological activity and lot of research has been carried out on their potential role in treating diabetes and other diseases. Most importantly the flavonoids and their related natural compounds are known to encompass antidiabetic potential, demonstrated in various animal models. Such beneficial flavonoids are less utilized on account of its deprived solubility, decreased bioavailability; first pass metabolism and intestinal degradation. However, flavonoids are capable of improving, stabilizing and long sustaining the insulin secretion, human islets and pancreatic cell respectively. In this article we propose, remarkable antidiabetic activity of flavonoids as well as few approaches on nanoparticulate systems in diabetes induced animal models. The proposed nanoparticulate system of flavonoids is projected to improve the solubility, bioavailability, by passing the first pass metabolism and decreasing susceptibility to intestinal environment as compared to pure flavonoid isolates. Further, this hypothesis exemplifies to enhance the efficacy of flavonoids in a novel way of antidiabetic treatment.

Introduction

The most ubiquitous part of plant constituents are flavonoids, so far about 8000 varieties of flavonoids have been identified [1]. The flavonoids are bioactive phenols with low molecular weight and play a major role in the cell synthesis [2–5]. Flavonoids are highly present in fruits, vegetables, nuts, seeds, stem, flowers tea etc., [6]. As for as diabetes mellitus is concern, flavonoids play a vital role in all aspects and its mechanism is well known [7].

Diabetes is a metabolic disorder leads to hyperglycemia and hindrance in carbohydrate, protein and fat metabolisms resulting in deprived insulin profile [8]. The effective control of

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Table 1 Remarkable endeavors to surmount the limitations of various flavonoidal nanoparticulate system.

S. No	Endeavors	Flavonoids	Result	Refs.
1	β-cyclodextrin nanoparticles of propolis extract	Kaempferol, rutin, quercetin, apigenin, acacetin, chrysin	Lower release pattern of flavonoids from β-cyclodextrin cavity	[11]
2	Enhancement of dissolution of kaempferol nanoparticles	Kaempferol	Improved solubility of kaempferol	[12]
3	Biodegradable poly-D,L-lactide (PLA) nanoparticles of quercetin	Quercetin	Biphasic release of nanoparticles followed by sustained slow release	[13]
4	Stevioside pluronic-F-68 copolymer PLA-nanoparticles	Stevioside (non caloric sweetener)	Increased intestinal absorption, biocompatibility and bioavailability and caused a controlled release	[14]
5	PLGA Nanohydrogel matrix for oral delivery of flavonoid	Silymarin	Enhanced dissolution and Bioavailability	[15]

Table 2 Remarkable endeavors to surmount the limitations of various flavonoidal isolates in animal models.

S. No.	Endeavors	Flavonoids	Result	Refs.
1	*Averrhoa carambola* isolated flavonoid on glycogen synthesis and insulin secretion	Apigenin-6-C-β-L-fucopyranoside	Increased insulin secretion and potentiated glucose-induced insulin secretion in hyperglycemics rats	[16]
2	*Acacia auriculiformis* poly flavonoids on antidiabetic factor	Gallic acid, caffeic acid, catechin, rutin, quercetin, myricetin and kaempferol	Significant suppression on α-amylase and α-glucosidase.	[17]
3	Effect of *Bauhinia forficate* on serum glucose	Kaempferol-3,7-O-(α)-rhamnoside	Hypoglycemic effect was observed in alloxan induced diabetic rats	[18]
4	Icariin in diabetic rats on mitochondrial oxidative stress	Icariin	Improvement in overall complication of diabetes in steptozotocin induced rats	[19]
5	Kaempferitrin on glucose uptake on skeletal muscles	Kaempferitrin	Insulin-mimetic role of kaempferitrin in glucose homeostasis	[20]
6	Isolates from *Euonymus alatus* in glucose uptake	Kaempferol and quercetin	Potential ameliorated hyperglycemia observed, due to glucose uptake in mature 3T3-L1 adipocytes	[21]
7	An isolate exposure on chronic hyperglycemic β-cell	Kaempferol	Restoration of high glucose-attenuated intracellular cAMP and ATP production	[22]
8	Flavonoid isolate as insulinomimetic on glycemia and glucose uptake	Kaempferitrin	Lowering blood glucose level and ^{14}C uptake of glucose in peripheral muscles of rat	[23]
9	Inhibition of intestinal and renal Na-glucose cotransporter	Naringenin	Inhibition of intestinal glucose uptake and renal glucose reabsorption was observed	[24]
10	Combined effect of flavonoid in type 2 diabetic rat	Naringin and hesperidin	Synergistic insulin releasing effect	[25]
11	Antidiabetic activity of isolate in normoglycemic rats	Naringenin	Diminishing the carbohydrate absorption from intestine and reduced post prandial glucose levels	[26]
12	Enhancement of bioavailability and anti-diabetic efficacy	Berberine	Increased bioavailability and a promising alternative for diabetes therapy	[27]

blood glucose level is an effective strategy in reducing clinical complications of diabetes mellitus remarkably. Besides optimal control of blood glucose level alone, could not prevent complications and it promotes to hypothesize an alternative treatment approaches essentiality [9]. Even though there is no cure for diabetes, the pharmacological and non-pharmaco-