

COMMENTARY

Herbal therapeutic strategies for diabetic retinopathy using nobiletin

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Introduction

Diabetes mellitus is one of the most challenging and prevalent metabolic diseases which results in microvascular complications such as retinopathy, neuropathy and macrovascular complications such as heart attack, stroke and peripheral vascular diseases.¹ Diabetic retinopathy (DR) is a major cause of blindness in diabetes which can be avoidable with good glycemic control. There are number of factors that contribute to vascular permeability and angiogenesis in DR including the oxidative damage of the retinal neuronal cells, vascular endothelial growth factor (VEGF), prostaglandins, cyclooxygenase-2 (COX-2) and nitric oxide (NO) synthase.² Despite the standards of care, laser photocoagulation and pars plana vitreous surgery for DR, recent successful use of several molecules is bringing a paradigm shift in favor of pharmacotherapy.³ There is an increasing interest in natural products in pharmacotherapy as the chemical diversity of natural products has better matches than the diversity of synthetic compounds.⁴ Flavonoids, a common group of plant polyphenols are known for their antioxidant, anti-inflammatory, anti-angiogenic activities also shown their potential in the prevention and treatment of various ocular diseases.⁵

Nobiletin and diabetic retinopathy

Parker and Addepalli⁶ investigated the effects of four weeks treatment of nobiletin, a citrus flavonoid on DR in streptozotocin induced diabetic rats. Outcomes indicated that treatment with nobiletin could be beneficial in amelioration of DR in experimental animals. Though there are number of studies showing the inhibitory activity of nobiletin on Matrix Metalloproteinase (MMP)-2 and MMP-9, they were mainly focused on various cancer treatments.^{7,8} The approach of using nobiletin in the treatment of DR is a timely and significant approach. There are only limited investigations available on the use of flavonoids in blood retinal barrier permeability for e.g. diosmin and eriodictyol significantly ameliorates retinal edema by protecting the blood retinal barrier and reducing retinal vascular permeability.^{9,10} The

Histopathological analysis on retinal thickness and retinal barrier permeability with nobiletin could be commendable and indicate direct and hard end point.

In a situation, where the exact mechanism by which hyperglycemia causes blindness remains incompletely understood, this study clearly indicates that the mechanism of action of nobiletin is not by glucose lowering mechanism. This reveals a less complicated direction for a more complex question. In addition, the results showed lower doses of nobiletin (10mg/kg) did not have any significant effect on blood retinal barrier permeability compared to higher dosage (25 mg/kg). This leads to further investigation on the dosage, bioavailability and the ocular concentrations of nobiletin. It is noteworthy to recall that the drug delivery to the ocular tissues is still a challenging task.

Future directions

This article is highly recommended for its new approach in showing the therapeutic implications of nobiletin for the treatment of DR. It provides a valuable perspective for future investigations to use other bioflavonoids in the prevention and treatment of DR. In addition, the results from this study navigates the further research on the mode of drug delivery via topical or local administration to yield effective concentrations at much lower doses. Above all, this article supports the fact that the use of phytochemicals is inevitable in order to increase the therapeutic activity and reduce toxicity in diabetes treatment.

Conflict of interest

None

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