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Original Article

The use of berberine in the treatment of diabetes: The available evidence and expert opinion

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Nutritional supplements have been increasingly used in the prevention and treatment of a variety of chronic disorders including diabetes. Research evidence has been increasing suggesting the usefulness of several supplements including fenugreek, cinnamon, and lipoic acid in the management of diabetes.

During the previous decades, berberines, a plant alkaloid that can be obtained from Rhizoma Coptidis and Coptis Chinensis Franch have been reported mostly by Chinese researchers to have beneficial effects in diabetes. This paper reviews the available evidence supporting the use of berberine in diabetes with the aim of providing expert opinion.

Expert opinion: The available evidence suggests that berberine has anti-diabetic effects through improving insulin secretion and it can also improves lipids profile. Berberine has been reported to have pancreatic β-cells protective and can increase peripheral tissues insulin sensitivity. It can also stimulate glycolysis, and thus it can improve insulin resistance. In addition, it can inhibit intestinal α-glucosidase and reducing absorption of glucose decrease. However, the available evidence research also suggests the usefulness of several other supplements including fenugreek, cinnamon, and lipoic acid in the management of diabetes. Therefore, the choice of diabetic supplement depends to some extent on the availability and cost. It seems that berberine is the most available and cost effective diabetic supplement in China, however, it is not in other counties in the world including Iraq.

Key words: Diabetic supplements, berberine, expert opinion.

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Introduction:

Nutritional supplements have been increasingly used in the prevention and treatment of a variety of chronic disorders including diabetes. Research evidence has increasing suggesting the usefulness of several supplements including fenugreek, cinnamon, and lipoic acid in the management of diabetes [1, 2, 3].

A hypoglycemic effect of berberine has been reported as early as 1986 [4], and in 1988, Ni reported that the use of berberine in sixty patients with diabetes type-2 was associated with a therapeutics effect [5].

In 2003, Zhou et al reported an experimental study on cultured 3T3-L1 pre-adipocytes which showed that berberine can improve 3T3-L1 pre-adipocytes proliferation and reduce the accumulation of lipid drops and can also inhibit the terminal differentiation of adipocyte. Therefore, Zhou et al suggested that berberine can be useful in the management of diabetes type-2 associated with obesity [6].

In 2004, Leng and colleagues from China reported an experimental study on rats with streptozotocin-induced impaired glucose tolerance. Berberine treatment was associated with anti-diabetic effects through improving insulin secretion and lipids profile [7].

In 2008, Yin and colleagues from China reported which included two groups of patients. The first group included 36 with recent development of diabetes type 2 who received either berberine or metformin (500 mg 3 times daily) for three months. Berberine treatment was associated with a hypoglycemic effect that was similar to the hypoglycemic effect associate with metformin treatment.

Berberine treatment was also associated with marked reduction in glycosylated hemoglobin (HbA1c) ($P<.01$), fasting and postprandial blood glucose ($P<.01$), and plasma triglycerides ($P<.05$).

The second group included 48 patients with poorly controlled diabetes (Type 2) who received berberine for months. Berberine treatment was associated with a decrease in fasting blood glucose, postprandial blood glucose, glycosylated hemoglobin (HA1c) ($P<.001$). Berberine was also associated with improvement in insulin resistance and. Lipids profile.

Twenty patients (34.5%) reported temporary gastrointestinal adverse effects [8].

Also, in 2008, Zhang et al from China reported a study which included 116 patients with diabetes type 2 associated with dyslipidemia who received either berberine 1000 mg a day or placebo for three months. Berberine treatment was associated with reduction in fasting and post-load plasma glucose, and glycosylated hemoglobin (HbA1c). Berberine treatment was also associated with improved lipids profile.

The main side effect associated with berberine treatment was the occurrence of mild to moderate constipation in five patients [9].

In 2015, Lan et al from China conducted a meta-analytic study which included 27 controlled clinical studies with 2569 patients. The meta-analysis showed that berberine can have a beneficial therapeutic effect in diabetes type 2, hyperlipidemia and hypertension, and it is generally not associated with serious side effect [10].

In 2018, Li et al from China reported a study which included 114 patients with diabetes type 2 (46 males, 68 females) aged 55 years (±14). 57 patients were treated only with hypoglycemic medications (Controls), and 57 patients received also berberine 400 mg, 3 times a daily for six months. Berberine treatment was associated with lowering of systolic pressure, and reduction of glycosylated

hemoglobin, blood urea nitrogen, high sensitive C-reactive protein, Erythrocyte sedimentation rate, and estimated glomerular filtration rate. Berberine was safe and was not associated with adverse effects. Therefore, Li et al suggested that berberine may help in improving diabetic renal disease [11].

In 2019, Liang et al from China conducted a systematic review and meta-analysis which included 28 studies with 2313 patients with diabetes type 2. The study showed that berberine can be more useful when combined with hypoglycemic medications [12].

In 2021, Guo et al from China conducted a systematic review and meta-analysis which included 46 studies studying the use of berberine in diabetes type 2. This study confirmed the safety of berberine and its usefulness as adjunctive therapy for improving diabetic control and lipids profile [13].

In 2022, Hu et al from China conducted a systematic review and meta-analysis which included 25 experimental studies on animals' models studying the effect of berberine in diabetic nephropathy. This study showed that berberine can improve renal function and reduce blood urea nitrogen, creatine, and proteinuria. In addition, berberine can reduce inflammation indicators including IL-6 and TNF-α, and also indicators oxidative stress including superoxide dismutase activity and malondialdehyde content. Furthermore, berberine was associated with a beneficial effect on lipids profile. The favorable effects of berberine in diabetic nephropathy were attributed to possible anti-fibrotic, anti-inflammatory, and anti-oxidative stress effects.

In 2023, Panigrahi and Mohanty from India reported a placebo-controlled study which included 34 pre-diabetic patients who received either berberine 1500 mg daily in three divided doses or placebo for 12 weeks.

Berberine treatment was associated with marked (Clinically and statistically significant) reduction in all markers of glycemic control in association with reduction of fasting plasma glucose and 2 hr-oral glucose tolerance test. Treatment was not associated with any adverse effect [15].

Expert opinion

The available evidence suggests that berberine has anti-diabetic effects through improving insulin secretion and it can also improve lipids profile. Berberine has been reported to have pancreatic β-cells protective and can increase peripheral tissues insulin sensitivity. It can also stimulate glycolysis, and thus it can improve insulin resistance. In addition, it can inhibit intestinal α-glucosidase and reducing absorption of glucose decrease. However, the available evidence research also suggests the usefulness of several other supplements including fenugreek, cinnamon, and lipoic acid in the management of diabetes. Therefore, the choice of diabetic supplement depends to some extent on the availability and cost. It seems that berberine is the most available and cost effective diabetic supplement in China, however, it not in other counties in the world including Iraq.

Conflict of interest: None.

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