



Efficacy of berberine on diabetic patients

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ABSTRACT :

The body uses glucose as its primary energy source. On the other hand, excessive blood sugar levels can cause a number of dangerous side effects, such as problems with the kidneys, eyes, and cardiovascular system. The state in which there is an excess of blood sugar is known as elevated blood sugar. Hyperglycemia is a complication of diabetes mellitus, a metabolic disorder that has been linked to several deaths. As a result, numerous therapies and precautions have been implemented to combat diabetes mellitus. Numerous oral medications are used to treat diabetes, including rosiglitazone, metformin, and sulfonylureas. Nevertheless, a few of these medications come with a lot of hazards or shouldn't be used by particular populations. Here, we talked about the antidiabetic mechanism of the naturally occurring substance berberine. Furthermore, we discovered that berberine had anti-inflammatory and antioxidant properties, and that the presence of oxidative stress and inflammation itself impacts the development of diabetes mellitus.

Keywords: Berberine, Dibetes, AMPK,

1. Introduction

1.1 DIABETES

A blood sugar (glucose) level that is too high results in diabetes. It arises when your body isn't reacting to the effects of insulin appropriately or when your pancreas produces too little or no insulin at all. People of all ages are affected by diabetes. All types of diabetes are treatable with medicine and/or lifestyle modifications, and the majority are chronic (lifelong).

The primary source of glucose, or sugar, is found in the carbs in food and beverages. It serves as your body's primary energy source. All of the cells in your body receive glucose from your blood to utilize as fuel (23).

1.1.1 Types of diabetes

Type 1 diabetes:

Type 1 diabetes, also referred to as juvenile diabetes, is a condition in which the body is unable to manufacture insulin.

The hormone insulin is in charge of metabolizing blood sugar so that the body can use it. A type 1 diabetes diagnosis can come from an early diagnosis in childhood.

Insulin must be given on a regular basis to those with type 1 diabetes. People can use an insulin pump or shots to do this.

Type 1 diabetes does not have a treatment. After being diagnosed, a patient must take insulin, monitor their blood sugar levels on a regular basis, and manage their disease by adopting certain lifestyle changes (20).

Type 2 diabetes:

Insulin is neither produced nor used by the body efficiently in people with type 2 diabetes.

The most prevalent kind of diabetes is type 2, according to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Trusted Source. It is closely related to obesity.

It's possible that someone with type 2 diabetes doesn't require insulin. Medication, together with healthy eating and exercise habits, can help control the illness in many situations.

Anyone can get type 2 diabetes, even adults and children (20).

Gestational diabetes:

Pregnant women without diabetes before to becoming pregnant may acquire newly emerging hyperglycemia, which is a sign of gestational diabetes mellitus (GDM), a metabolic disorder of pregnancy that often goes away after giving birth. The incapacity of the mother pancreas to adapt to the elevated insulin demand during pregnancy explains the etiology of gestational diabetes mellitus. The body becomes less sensitive to insulin during pregnancy, which causes the pancreatic beta cells to produce more insulin. These beta cells emit insulin, which is essential for stimulating peripheral

tissue uptake of glucose, decreasing hepatic glucose synthesis, and regulating adipose tissue lipid release (21).

1.1.2 Symptoms of diabetes (22)

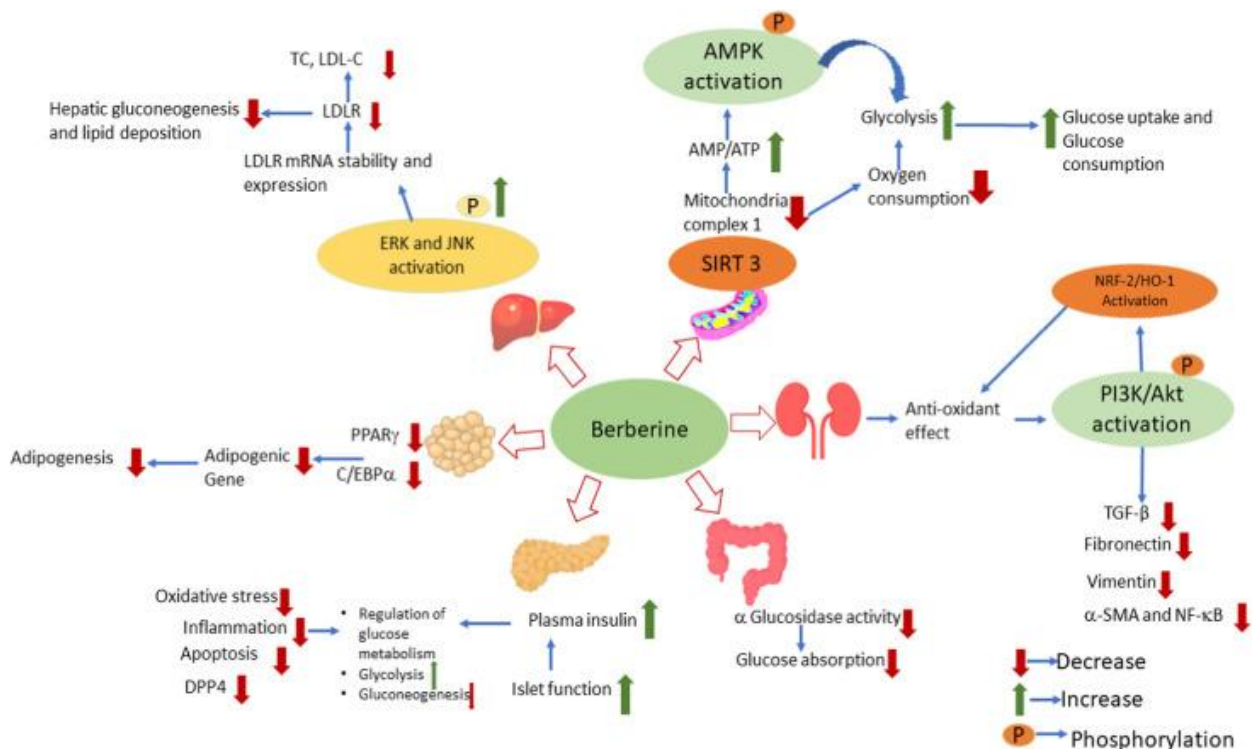
- Increased thirst (polydipsia) and dry mouth.
- Frequent urination.
- Fatigue.
- Blurred vision.
- Unexplained weight loss.
- Numbness or tingling in your hands or feet.
- Slow-healing sores or cuts.
- Frequent skin and/or vaginal yeast infections.

2. Efficacy of berberine on diabetic patients :

The primary potent bioactive ingredient in many Traditional Chinese Medicine systems and Indian Ayurvedic formulations is berberine. The usefulness of these traditional remedies against tumors, inflammation, hyperlipidemia, and diabetes has been demonstrated in the literature. Berberine has been shown in pharmacological trials to be a glucose-lowering drug that is dependent on hyperglycemia (1). The majority of the studies were poorly constructed, although berberine was said to have similar blood glucose-lowering effects to metformin or sulphonylureas. Berberine has so far been examined in a number of clinical trials. In individuals with recently diagnosed type 2 diabetes, our study demonstrated that berberine (0.5 g t.i.d.) administered at the start of each meal was able to lower fasting blood glucose (FBG) and postprandial blood glucose (PBG)(7). Moreover, it has been demonstrated that berberine targets several signaling pathways in order to achieve its antidiabetic effects. One well-established mechanism of action of berberine to reduce blood glucose levels is activation of the AMPK signaling system. (1)

Recent research has demonstrated that berberine directly binds to KCNH6 potassium channels to function as an insulin secretagogue. Long-term glucose-dependent cell membrane depolarization follows, eventually promoting the release of insulin. (2)

By blocking $PPAR\gamma$, $C/EBP\alpha$, and downstream target genes, BR inhibits adipogenesis. By increasing glycolysis and plasma insulin, BR enhances islet function. It also reduces gluconeogenesis by lowering oxidative stress, inflammation, apoptosis, and DPP4. Similar to this, BR increases glucose uptake and consumption by also decreasing oxygen consumption and raising AMP-ATP-AMPK activation, which is a result of inhibiting the mitochondrial electron transport chain complex I. By increasing the stability and expression of low-density lipoprotein receptor (LDLR) mRNA, BR can reduce hepatic gluconeogenesis and lipid accumulation. In addition to having anti-oxidant and anti-fibrotic properties through activating the PI3K/Akt/NRF-2/HO-1 cascade and inhibiting TGF- β /Fibronectin/Vimentin/ α -SMA/NF- κ B signaling, BR demonstrated protective qualities against diabetic nephropathy. By blocking the action of α -glucosidase, BR also contributes to a decrease in intestinal glucose absorption.(1)



3. Berberine on glucose metabolism in animals

Berberine has been demonstrated to lower blood sugar, improve insulin sensitivity, and lessen weight gain in mouse models of type 2 diabetes that are dietary and hereditary. Berberine reduced fasting insulin, PBG, body weight, and the homeostasis model of assessment-insulin resistance (HOMA-IR) in obese rats fed a high-fat diet. Berberine administration markedly reduced fast-beta glucose (FBG) and increased insulin tolerance in rats with type 2 diabetes caused by a high-fat diet and low doses of streptozotocin (STZ). Berberine enhanced glucose tolerance and decreased body weight in leptin receptor-deficient db/db mice(3,4,5) In alloxan-induced type 1 diabetic rats, berberine also restored the injured pancreas(6).

The first-line treatment for type 2 diabetic mellitus (T2DM) is now metformin, which has been used for decades to regulate blood sugar. Since it was discovered that metformin lowers the risk of cancer and activates AMP-activated protein kinase (AMPK), it has attracted a lot of attention. Berberine, a drug made from the root of the berberis vulgaris L. plant, was another remedy for diarrhea. The benefits of berberine in regulating inflammation, cancer growth, and glucose and lipid balance have been demonstrated by recent studies conducted in both experimental and clinical settings.

Metformin decreases the hepatic production of glucose and increases the absorption of glucose in muscle and adipose tissue, which improves hyperglycemia and hyperlipidemia and reduces non-alcoholic fat liver disease (16). By shielding β -islets from glucotoxicity and lipotoxicity and enhancing insulin sensitivity in peripheral tissues, metformin can help restore insulin secretion (10, 11). The initial target of metformin that has been discovered is 5'-AMP activated protein kinase (AMPK), while some effects are thought to be mediated by AMPK-independent pathways (12, 13).

In 1986, berberine's effects on type 2 diabetes were first reported (14). A three-month study by Yin et al. compared the effectiveness of metformin and berberine in treating 36 individuals with Type 2 Diabetes Mellitus (T2DM). Random assignment was used to allocate subjects to receive metformin or berberine. The hypoglycemic effects of berberine were comparable to those of metformin, according to the results. Hemoglobin A1c (HbA1c), fasting glucose, and postprandial glucose levels dropped by 7.5%, 6.9%, and 11.1%, respectively, during the experiment. Zhang et al.'s independent clinical examination supported these conclusions (15, 16).

Berberine has been shown in an analysis incorporating data from 21 clinical trials to have therapeutic advantages for Type 2 Diabetes different treatment options (17). Studies have indicated that berberine functions similarly to metformin by regulating several effectors, including AMPK, MAPK, PKC, PPAR α , and PPAR γ (16, 18). Notably, berberine can increase the uptake of glucose in muscle, liver, and adipose tissue by activating AMPK. It can also inhibit gluconeogenesis in the liver by downregulating important gluconeogenic enzymes like glucose-6-phosphatase and phosphoenolpyruvate carboxyl kinase (19).

Conclusion :

Diabetes mellitus is a metabolic disease that results in hyperglycemia, which can cause a number of long-term problems as well as death. Insulin-resistant type 2 diabetes is treated with antidiabetic medications, which carry a significant risk. As a result, research has been done on using natural substances, such as berberine, as substitute antidiabetic medications. The isoquinoline alkaloid molecule berberine functions as an anti-hyperglycemia agent by enhancing the body's control over the metabolism of fat and glucose. Berberine has the ability to suppress mitochondrial activity and trigger the AMPK pathway, which in turn interacts with multiple other metabolic pathways pertaining to the breakdown of fat or glucose. In addition to its ability to prevent diabetes, berberine also functions as an anti-inflammatory and antioxidant by lowering the production of reactive oxygen species.

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