

# Metabolic Syndrome and Berberine: A Framework of Situation

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## ABSTRACT

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## Introduction

The metabolic syndrome is a cluster of risk factors associated with an increased risk of heart disease, type 2 diabetes, and stroke [1]. Metabolic syndrome is characterized by obesity, insulin resistance, and dyslipidemia. The complexity of metabolic syndrome has posed various obstacles in the management of this multifaceted health problem. Although the prevalence of metabolic syndrome has been continuously increasing for years, current pharmacological treatments have failed to provide adequate and effective treatment [2]. Obesity is defined as a persistent state of positive energy balance with excess fat buildup in the adipose tissues [3]. Following the discovery of functional brown adipose tissue (BAT) in adult humans using a combination of imaging techniques [4], there has been a growing interest in treating obesity and diabetes by activating and recruiting BAT, due to BAT's unique function in dissipating chemical energy in the form of non-shivering thermogenesis. As a result, activating BAT and converting fat-accumulating white adipose tissue (WAT) into energy-dissipating BAT could be a viable and effective strategy [5].

Berberine (BBR) is a natural product of quaternary ammonium salt from the group of isoquinoline alkaloids (2,3-methylenedioxy-9,10 dimethoxyprotoberberine chloride;  $C_{20}H_{18}NO_4^+$ ). BBR can be extracted from a wide range of plants, including *Coptis chinensis* (Goldthread), *Hydrastis canadensis* (Goldenseal), *Berberis aquifolium* (Oregon grape), *Berberis aristata*

(Tree Turmeric), *Berberis vulgaris* (Barberry), and *Arcangelisia flava* [6]. BBR was recently discovered to have anti-obesity properties via controlling BAT thermogenesis and suppressing adipogenesis [7]. BBR has also been shown to have therapeutic effects in the treatment of insulin resistance and dyslipidemia in earlier investigations [8]. Excess weight and physical inactivity cause insulin resistance, which is a major risk factor for metabolic syndrome [9]. BBR has been shown to affect glucose metabolism control, specifically decreasing insulin resistance and lowering blood glucose levels, making it a possible treatment for metabolic syndrome.

By modulating the expression of insulin receptor, insulin receptor substrate-1, and glucagon receptor substrate-1, BBR was reported to reduce insulin resistance in a high-fat diet-induced insulin resistance rat model [8]. BBR has also been considered as an appropriate hypoglycemic agent due to its influence on the AMPK signaling cascade and concomitant activation of glycolysis [10]. As demonstrated in the H9c2 myoblast cell line treated with insulin to create insulin resistance, BBR could alleviate the reduction in glucose consumption and uptake via stimulating AMPK activation [11]. BBR can prevent the onset of diabetic nephropathy, possibly by blocking the PI3K/Akt/AS160/GLUT1 signal pathway, which regulates high glucose-induced aberrant glomerular mesangial cell proliferation and the cell cycle, indicating that BBR could be used to treat diabetic nephropathy [12]. Furthermore, BBR inhibits

the expression of pro-inflammatory genes in the adipose tissue of obese mice, suggesting that BBR may modulate both the acute and low-grade inflammatory responses in obesity [13].

BBR therapy suppresses the development of insulin resistance and protects obese rats from gaining weight in comparison to untreated animals because it has a long-term role in the gastrointestinal tract and is engaged in the remodeling of the gut microbiota [14]. BBR also lowers obesity and alleviates systemic inflammation [15]. According to research on the gut microbiota, BBR dramatically alters its composition and selectively eliminates or promotes the growth of several intestinal microbes, BBR's anti-insulin resistance, anti-obesity, and anti-diabetes activities contribute to the lowering of systemic inflammation. Berberine is a natural substance that has been used for years to treat bacterial infections. Recent research has revealed BBR's tremendous promise in the treatment of metabolic syndrome due to its anti-obesity effect via BAT activation and the conversion of white to brown adipocytes. Moreover, BBR's insulin resistance and dyslipidemia modulation activity enables it to provide metabolic syndrome therapeutic treatment. BBR may be an effective treatment for metabolic syndrome, according to current *in vitro* and *in vivo* research. The total effect of BBR in metabolic syndrome was not studied comprehensively since preclinical models for metabolic syndrome are restricted. Once the effect of BBR has been established in animal models, clinical trials to determine its therapeutic effectiveness must be done.

## Disclosure Statement

The author declare that there are no conflicts of interest.

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