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Therapeutic Potential of Berberine in Hypertension: A Narrative Review

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Abstract

Hypertension is one of the most prevalent chronic diseases worldwide and a leading contributor to cardiovascular morbidity and mortality. Despite the availability of effective antihypertensive drugs, blood pressure control remains suboptimal in many patients, prompting growing interest in complementary and plant-derived therapies. Berberine, a natural isoquinoline alkaloid isolated from plants such as *Coptis chinensis* and *Berberis* species, has been used in traditional medicine for centuries and is now receiving increased scientific attention for its cardiovascular benefits. Experimental and clinical studies suggest that berberine may reduce blood pressure through multiple mechanisms, including improvement of endothelial function, activation of AMP-activated protein kinase (AMPK), modulation of the renin–angiotensin–aldosterone system (RAAS), and anti-inflammatory and antioxidant effects. This review summarizes and explains the current evidence on berberine and hypertension, with in-text citations and references presented according to APA style.

Keywords: Berberine, Hypertension, Blood pressure, Endothelial dysfunction, AMPK, Complementary medicine

Introduction

Hypertension, often referred to as the "silent killer," affects more than one billion individuals globally and substantially increases the risk of stroke, myocardial infarction, heart failure, and chronic kidney disease (World Health Organization [WHO], 2023). Although lifestyle modification and pharmacological therapies are effective, long-term blood pressure control is frequently limited by adverse drug effects, polypharmacy, cost, and poor adherence (Mills et al., 2020).

These limitations have encouraged exploration of complementary approaches, including bioactive compounds derived from medicinal plants. Berberine is one such compound that has gained attention due to its wide range of metabolic and cardiovascular effects. Traditionally prescribed for gastrointestinal infections, berberine has more recently been shown to influence glucose metabolism, lipid homeostasis, inflammation, and vascular function—processes that are closely linked to hypertension (Cicero & Baggioni, 2016). Understanding how berberine affects blood pressure regulation may help clarify its potential role as an adjunct therapy for hypertension.

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Chemical Characteristics and Pharmacokinetics of Berberine

Berberine is a quaternary ammonium isoquinoline alkaloid with the molecular formula C20H18NO4+. It is characterized by low oral bioavailability, largely due to poor intestinal absorption, P-glycoprotein–mediated efflux, and extensive first-pass metabolism in the liver (Liu et al., 2016). Despite this limitation, berberine and its active metabolites accumulate in target organs such as the liver, kidneys, heart, and blood vessels, allowing it to exert systemic effects (Tan et al., 2011).

To overcome poor bioavailability, recent studies have explored novel delivery systems, including nanoparticles, lipid-based carriers, and structural derivatives, which may enhance the antihypertensive efficacy of berberine (Zhang et al., 2020).

Pathophysiology of Hypertension: Relevance to Berberine

Hypertension is a complex, multifactorial condition involving genetic predisposition and environmental influences. Key pathophysiological mechanisms include endothelial dysfunction, overactivation of the RAAS, increased sympathetic nervous system activity, oxidative stress, chronic low-grade inflammation, and vascular remodeling (Carretero & Oparil, 2000).Importantly, many of these pathways are modulated by berberine. This multi-target profile distinguishes berberine from conventional antihypertensive drugs, which typically act on a single pathway, and provides a mechanistic basis for its potential benefit in blood pressure regulation.

Mechanisms of Antihypertensive Action of Berberine

Berberine lowers blood pressure through several interrelated mechanisms, targeting both vascular function and systemic regulatory pathways.

Improvement of Endothelial Function

Endothelial dysfunction, characterized by reduced nitric oxide (NO) availability, is a hallmark of hypertension. Berberine has been shown to enhance endothelial nitric oxide synthase (eNOS) activity, leading to increased NO production and improved vasodilation (Lan et al., 2015). In addition, berberine protects endothelial cells from oxidative stress–induced injury, thereby restoring normal vascular tone (Wang et al., 2017).

Activation of AMP-Activated Protein Kinase (AMPK)

AMPK plays a central role in energy metabolism and vascular homeostasis. Berberine is a potent activator of AMPK, and this activation has been linked to improved endothelial function, reduced vascular smooth muscle contraction, and inhibition of abnormal cell proliferation (Zhang et al., 2011). These effects collectively contribute to reduced peripheral vascular resistance and lower blood pressure.

Modulation of the Renin–Angiotensin–Aldosterone System

The RAAS is a critical regulator of blood pressure and fluid balance. Overactivation of this system promotes vasoconstriction and sodium retention. Experimental evidence suggests that berberine suppresses angiotensin-converting enzyme expression and attenuates angiotensin II–mediated vasoconstriction, resulting in antihypertensive effects (Li et al., 2014).

Anti-Inflammatory and Antioxidant Effects

Chronic inflammation and oxidative stress contribute to the initiation and progression of hypertension. Berberine has been shown to inhibit pro-inflammatory cytokines, such as tumor necrosis factor-α and interleukin-6, while reducing reactive oxygen species production (Zhu et al., 2018). By limiting inflammation and oxidative damage, berberine helps preserve vascular elasticity and function.

Effects on Vascular Smooth Muscle Cells

Berberine directly relaxes vascular smooth muscle cells by inhibiting calcium influx and regulating ion channel activity, leading to vasodilation (Ko et al., 2000). Additionally, it suppresses vascular remodeling, a structural change associated with long-standing hypertension and arterial stiffness.

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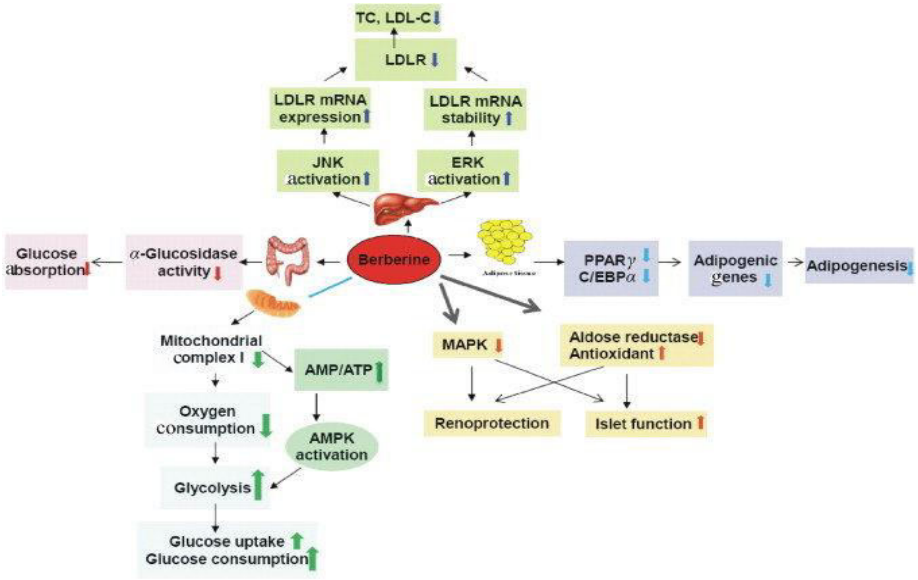

Fig. 1: Berberine lowers blood pressure by improving endothelial function and nitric oxide availability, activating AMP-activated protein kinase (AMPK), inhibiting the renin–angiotensin–aldosterone system (RAAS), and reducing inflammation and oxidative stress, leading to decreased peripheral vascular resistance

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Evidence from Preclinical Studies

Numerous animal studies support the antihypertensive effects of berberine. In spontaneously hypertensive rats, berberine administration significantly reduced systolic and diastolic blood pressure and improved endothelial function (Zhang et al., 2011). Similar findings have been reported in angiotensin II–induced hypertensive models, where berberine attenuated oxidative stress and vascular remodeling (Wang et al., 2017). These preclinical findings provide strong mechanistic support for the blood pressure–lowering potential of berberine.

Clinical Evidence

Clinical data on berberine and hypertension remain limited but encouraging. Small clinical trials have reported modest reductions in systolic and diastolic blood pressure, particularly in patients with metabolic syndrome or type 2 diabetes (Cicero et al., 2012). In several studies, berberine was used as an adjunct to standard therapy and was associated with improved blood pressure control and metabolic parameters. However, variability in study design, dosage, and duration limits the generalizability of these findings. Larger, well-designed randomized controlled trials are required to confirm berberine's antihypertensive efficacy in diverse patient populations.

Safety and Drug Interactions

Berberine is generally well tolerated, with gastrointestinal symptoms such as constipation, diarrhea, and abdominal discomfort being the most commonly reported adverse effects (Liu et al., 2016). Berberine may interact with cytochrome P450 enzymes and drug transporters, potentially altering the pharmacokinetics of antihypertensive and cardiovascular drugs. Therefore, caution is advised when berberine is used alongside conventional medications.

Limitations and Future Perspectives

Despite promising evidence, several limitations remain. These include poor oral bioavailability, limited high-quality clinical trials, and insufficient long-term safety data. Future research should focus on optimizing berberine formulations, establishing dose–response relationships, and conducting large-scale randomized controlled trials to better define its role in hypertension management.

Conclusion

Berberine is a biologically active natural compound with multiple mechanisms relevant to blood pressure regulation. By improving endothelial function, activating AMPK,

modulating RAAS activity, and reducing inflammation and oxidative stress, berberine demonstrates clear antihypertensive potential. While it cannot replace conventional antihypertensive drugs, berberine may serve as a useful complementary therapy, particularly in patients with metabolic comorbidities. Further rigorous clinical research is essential before its widespread clinical application.

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