PIOTROWSKA, Julia, WITKOWSKA, Antonina Teresa, DOMAŃSKA, Adrianna, ŁUBIŃSKA-KOWALSKA, Aleksandra, ŻAK-GONTARZ, Agata, MINDA, Aleksandra, WITKOWSKA, Adrianna, ZAPALSKA, Barbara Anna, JANIKOWSKA, Justyna, DŁUGOSZ, Krzysztof Julian and WENDLAND, Monika. Effects of berberine administration on insulin resistance, lipid profile and general health - Narrative Review. Journal of Education, Health and Sport. 2025;82:60324. eISSN 2391-8306.
https://doi.org/10.12775/JEHS.2025.82.60324
https://apcz.umk.pl/JEHS/article/view/60324

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).
Punkty Ministerialne 40 punktów. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).
The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 15.04.2025. Revised: 25.04.2025. Accepted: 01.06.2025. Published: 03.06.2025.

Effects of berberine administration on insulin resistance, lipid profile and general health- Narrative Review

Julia Piotrowska, Adrianna Witkowska, Adrianna Domańska, Aleksandra Łubińska-Kowalska,

Agata Żak-Gontarz, Aleksandra Minda, Antonina Teresa Witkowska, Barbara Anna Zapalska,

Justyna Janikowska, Krzysztof Długosz, Monika Wendland

Julia Piotrowska e-mail: juliapiotrowska848@gmail.com Faculty of Medicine University of Warmia and Mazury, Aleja Warszawska 30, 11-082 Olsztyn, Poland ORCID: 0009-0006-3261-018X

Adrianna Witkowska e-mail: ada.dywity@gmail.com Faculty of Medicine University of Warmia and Mazury, Aleja Warszawska 30, 11-082 Olsztyn, Poland ORCID: 0009-0008-7314-8045

Adrianna Domańska e-mail: adrianna.domanska21@gmail.com Faculty of Medicine University of Warmia and Mazury, Aleja Warszawska 30, 11-082 Olsztyn, Poland ORCID: 0009-0002-2720-2641

Aleksandra Łubińska-Kowalska mail: aleksandra.lubinska0@gmail.com Faculty of Medicine University of Warmia and Mazury, Aleja Warszawska 30, 11-082 Olsztyn, Poland ORCID: 0009-0007-2699-5965

Agata Żak-Gontarz e-mail: agata.janina.zak@gmail.com Stefan Cardinal Wyszyński Provincial Specialist Hospital SPZOZ in Lublin, Aleja Kraśnicka 100, 20-718 Lublin, Poland; ORCID: 0009-0003-6533-9048

Aleksandra Minda e-mail: aleksandra.m99@wp.pl Infant Jesus Clinical Hospital Williama Heerleina Lindleya 4, 02-005 Warsaw, Poland; ORCID: 0009-0004-8862-712X

Antonina Teresa Witkowska e-mail: toniateresa99@gmail.com Praga Hospital of the Transfiguration of the Lord Aleja Solidarności 67 03-401 Warsaw, Poland ORCID: 0009-0007-9954-1462

Barbara Anna Zapalska e-mail: bzapalska17@gmail.com Independent Public Central Clinical Hospital of University Clinical Center of Medical University of Warsaw ul. Banacha 1A 02-097 Warszawa, Poland; ORCID 0009-0004-6417-877X

Justyna Janikowska e-mail: justyna.janikowska@gmail.com National Medical Institute of the Ministry of the Interior and Administration in Warsaw PIM MSWiA ul. Wołoska 137 02-507 Warsaw, Poland; ORCID: 0009-0001-8277-0855

Krzysztof Długosz e-mail: krzysztofjdlugosz@gmail.com University clinical hospital in Olsztyn, Warmia-Masuria, Poland; ORCID: 0009-0000-8134-6115

Monika Wendland e-mail: monika.z.wendland@gmail.com Mazovian "Bródnowski" Hospital Ludwika Kondratowicza 8, 03-242 Warszawa; ORCID: 0009-0009-6894-8846

ABSTRACT

Introduction and purpose: Berberine is a bioactive substance of natural origin that can be found in various plants. It has been used in natural medicine for ages. Recent studies have shown its potency in improving insulin resistance, lipid profile, carbohydrate metabolism and overall health. It also shows promise for aiding in weight management. This review aims to summarise current evidence and research on effects mentioned above based on various studies and their findings.

Materials and Methodology: A comprehensive literature search was conducted using different databases such as PubMed, Medline, Cochrane Library, Clinical Key, Springer, MDPI, Google Scholar. Studies that evaluated effects mentioned above were included. Extraction of the data was focused on key findings, dosage of berberine, duration of supplementation, study, dosing and characteristics of examined populations.

Results: Evidence found suggests that berberine significantly improves insulin sensitivity. It does so by modulation of molecular pathways. Including activation of AMP-activated protein kinase(AMPK) and

improvement in expression of insulin receptor. In addition berberine exhibits beneficial influence on blood pressure, lipid profile and inflammatory markers. However the differences in population characteristics and study designs can have significant importance and can't be overlooked.

Conclusions: Berberine appears to be an effective alternative for conventional treatments in managing blood glucose levels, improving lipid profile and overall health by showing lots of beneficial properties. Yet to come to such conclusions further large-scale, long- term, randomised, controlled clinical trials are needed.

INTRODUCTION

Berberine ($C_{20}H_{18}NO_4$) is a natural alkaloid, more specifically and isoquinolone alkaloid that to the protoberberine alkaloids [1] that is under the spotlight for its potential effects on health.

It is found in many plants such as: Berberis vulgaris (barberry), Berberis aristata (tree turmeric) and Coptis chinensis (Chinese goldthread). It has been used for ages in traditional medicine to treat wide variety of health conditions such as diabetes, gastrointestinal issues and also cardiovascular diseases especially in China, India, Iran and other countries. [1], [2]. When it comes to pharmacological effects berberine appears to have large therapeutic potential.

1. PHARMACOLOGICAL EFFECTS

1.1 Berberine exhibits antidiabetic effect, which might be useful in managing type 2 diabetes. It improves insulin sensitivity and reduces blood glucose levels by activating AMP- activated protein (AMPK) [3] By doing so berberine helps managing carbohydrate metabolism more effectively, making it a potential alternative for conventional pharmacological treatments[4, 17, 18, 23]. Insulin secretory agents are widely utilized for managing type 2 diabetes, though conventional options like sulfonylureas and glinides often lead to hypoglycemia as a side effect. Recent studies have identified berberine as a promising alternative due to its ability to inhibit voltage-gated potassium channels in pancreatic β cell membranes, effectively stimulating insulin secretion without triggering hypoglycemia. This occurs because berberine's glucose-lowering properties are specifically activated under hyperglycemic conditions or when glucose levels are high. [24]

1.2 When it comes to its lipid lowering effects it does so by promoting excretion of cholesterol and inhibition of its production in the liver which in effect results in reduced low-density lipoprotein (LDL) cholesterol and triglycerides while simultaneously increasing high-density lipoprotein (HDL) levels. [1] [23] It does so by stimulating AMP- activated protein kinase (AMPK). This enhances fatty acid oxidation and limit cholesterol synthesis. Also by increasing LDL receptors in liver cells. On top of that

it promotes cholesterol to bile acids covertion by upregulating the CYP7A1 enzyme. On the other hand by downregulating NPC1L1 transporter in the intestines it reduces dietary cholesterol uptake. It is also important to note that this effects were mostly studied on mice[7]. Some studies suggest that combining berberine with statins could be cost efficient strategy for managing cholesterol [29, 34]

1.3 Anti- Inflammatory and Antioxidant Properties: Berberine exhibits strong anti-inflammatory and antioxidant effects. It reduces oxidative stress, inflammation and pro inflammatory markers. It does so by inhibition of NADPH Oxidase (NOX). This enzyme is responsible for producing reactive oxygen species (ROS). By reducing ROS production, berberine decreases oxidative stress. It also does so by stalling the expression of cyclooxygenase 2 (COX-2) and prostaglandin E2 [25]. This alkaloid also exhibits anti-inflammatory effect by inhibiting activation of the nuclear factor-kappa B (NF-KB) -a transcription factor involved in the inflammatory response [6]

1.4 It also has antibacterial and antipyretic effects [1] Berberine has antimicrobial properties against bacteria, viruses, fungi and protozoa. This makes it possible agent in treatment of range of infections[8].

1.5 Berberine, an alkaloid, has demonstrated the ability to suppress the growth of various cancer cell types. Recent findings indicate that berberine enhances the effectiveness and safety of chemoradiotherapy treatments [21]. Research has revealed its anticancer properties across multiple cancer types, including breast, lung, stomach, liver, colon, ovarian, cervical, and prostate cancers. By inhibiting cancer cell growth and triggering apoptosis, berberine shows promise as a potential therapeutic option in oncology. [9, 19, 20, 22, 31]

1.6 Berberine improves cardiovascular health not only by its antioxidant and lipid regulating properties. It also improves endothelial function: it increases the production of nitric oxide (NO) and reduces the expression of endothelin-1 (ET-1). NO is a vasodilator that has protective properties against atherosclerosis while ET-1 is a vasoconstrictor that has negative impact on vascular function. [10, 11, 33]

1.7 Berberine was also shown to be beneficial for gut microbiota leading to an increase in beneficial bacteria and decrease in harmful ones. This influence was shown to have cardioprotective effects along with beneficial effect on metabolic health. [11]

1.8 Berberine was linked to hepatoprotective effects as well. It was shown to be effective particularly in treatment of non- alcoholic fatty liver (NAFLD). It improves liver function markers and reduces liver fat accumulation. [13]

1.9 Berberine has proven effective in addressing hormonal imbalances by lowering testosterone levels

and free androgen index (FAI), boosting sex hormone-binding globulin (SHBG), and alleviating symptoms associated with androgen excess, such as hirsutism and acne. This makes it an excellent candidate for supplementation in women with polycystic ovary syndrome (PCOS). Additionally, berberine enhances the effectiveness of commonly prescribed treatments for PCOS, including metformin and oral contraceptives [28, 5].

These qualities position berberine as a promising option for a diverse range of patients [12, 13].

Purpose of this article is to summarize effects berberine has on insulin sensitivity, lipid profile and overall health and to examine its potential to become an alternative for more conventional medications especially in patients who do not require urgent treatment.

Current understanding of berberine's effects on insulin sensitivity: Numerous studies have investigated impact of berberine on insulin sensitivity. It has been well documented that berberine activates AMPK, which plays crucial role in regulating glucose metabolism. Clinical trials and animal studies have proven this making it a potential agent for managing type 2 diabetes. In animal models berberine treatment resulted in reductions in infract volume and showed neuroprotective effects. It also had anti-inflammatory effects by reducing pro-inflammatory cytokines such as TNF-alfa, IL-1B and IL/6 and downregulating the TLR4/NF-KB signaling pathways while also increasing antioxidant levels. [14] Additional rigorously designed clinical trials are necessary to validate this results and safety in human subjects.

Materials and Methodology

A comprehensive literature search was conducted in order to find relevant studies on the effects of berberine on insulin sensitivity, lipid profile and overall health. The search was performed with the use of the academic databases mentioned below:PubMed, Medline, Cochrane Library, Clinical Key, Springer, MDPI, Google Scholar. The search included key words such as *berberine; insulin sensitivity; lipid profile; overall health; type 2 diabetes; dyslipidemia; metabolic syndrome; cardiovascular* in different combinations. The search was limited to articles published within years 2000-2025.

Inclusion criteria: Studies were included in this review if they met the following criteria

1. Population: Human subjects or animal models relevant to the topic of this review
2. Intervention: Studies that investigate the effects of berberine supplementation
3. Outcomes: Studies that shows effects on insulin sensitivity, lipid profile or overall health outcomes

4. Study Design: Randomized controlled trials, cohort studies and systemic reviews
5. Language: Articles published in English

Exclusion criteria: studies were excluded from the review if they met any of the following criteria:

1. Population: studies that involved in vitro experiments or cell culture models
2. Intervention: Studies that didn't focus on berberine specifically
3. Outcomes: Articles that did not report on insulin sensitivity, lipid profile or overall health results
4. Study Design: Editorials, letters to the editorials
5. Language: articles published in languages other than English

Data was extracted from the selected articles using a standarized extraction form. It focused on study characteristics, population characteristics, intervention details and outcomes. A narrative synthesis of the collected data was conducted summarizing the effects of berberine on insulin sensitivity, lipid profile and overall health. Eventually 34 articles were taken into account.

RESULTS

The analysis of studies demonstrates the efficacy of berberine in managing blood glucose levels, lipid profiles, and overall health. In this section we will briefly walk through results of some of the studies.

Insulin Sensitivity: A double-blind, randomized, placebo-controlled study involving 34 participants with prediabetes demonstrated notable improvements in glycemic control after 12 weeks of berberine therapy. Fasting Plasma Glucose (FPG) levels dropped from [6.75 ± 0.23 mmol/L] to [5.33 ± 0.28 mmol/L], fasting insulin (FI) levels decreased from [9.81 ± 0.36 mmol/L] to [7.88 ± 0.52 mmol/L], and 2-hour oral glucose tolerance test (2 h-OGTT) results improved from [10.44 ± 0.52 mmol/L] to [8.12 ± 0.40 mmol/L]. Hemoglobin A1C (HbA1c) declined from [$6.40\% \pm 0.20$] to [$5.43\% \pm 0.21$], and Homeostatic Model Assessment Insulin Resistance (HOMA-IR) values were reduced from [3.61 ± 0.31] to [2.41 ± 0.14]. These improvements were both statistically and clinically significant ($p < 10^{-5}$), with no reports of serious adverse effects or harm to liver and kidney function [12].

A study featured in *Nutrients* examined the absorption kinetics of berberine and its potential role in glycemic regulation. It compared plasma levels of berberine after administering either [500 mg] of berberine (B500) or [100 mg] and [200 mg] of dihydroberberine (D100 and D200). In a double-blind, crossover study involving five participants, D100 and D200 were found to reach higher peak plasma

concentrations (CMax). For example, the CMax of D100 was [3.76 ± 1.4 ng/mL], significantly surpassing that of B500 at [0.4 ± 0.17 ng/mL] ($p = 0.005$), while the CMax of D200 reached [12.0 ± 10.1 ng/mL] ($p = 0.005$). The area under the curve (AUC) supported these findings, with D100 achieving [284.4 ± 115.9 ng/mL × 120 min] compared to B500's [42.3 ± 17.6 ng/mL × 120 min] ($p = 0.04$). However, no significant changes in glucose ($p = 0.97$) or insulin ($p = 0.24$) levels were observed, likely due to the short study duration and the participants' insulin sensitivity [15].

Lipid Profile: A meta-analysis of 18 studies (n = 1788 participants) revealed that berberine effectively improved lipid parameters over treatment durations ranging from [4 to 24 weeks]. Berberine reduced LDL cholesterol by [−0.46 mmol/L] (95% CI: −0.62 to −0.30), total cholesterol by [−0.48 mmol/L] (95% CI: −0.63 to −0.33), and triglycerides by [−0.34 mmol/L] (95% CI: −0.46 to −0.23). Apolipoprotein B levels also declined by [−0.25 g/L] (95% CI: −0.40 to −0.11). HDL cholesterol showed modest increases of [0.06 mmol/L] (95% CI: 0.00 to 0.11), with the effect more pronounced in women ([0.11 mmol/L]) compared to men ([−0.07 mmol/L]). Mild gastrointestinal adverse events were reported in 12 studies (2–23%), but no serious adverse effects were documented. [16]

Blood pressure: Berberine also demonstrated improvements in systolic blood pressure, reducing it by [−5.46 mmHg] (95% CI: −8.17 to −2.76, $p < 0.001$), and fasting blood glucose levels, which decreased by [−7.74 mg/dL] (95% CI: −10.79 to −4.70, $p < 0.001$). These effects contribute to its role in reducing cardiovascular risk factors [32]

Additional Observations: A 2025 systematic review highlighted berberine's neuroprotective benefits in animal models of ischemic stroke. Significant reductions in infarct volume were observed at doses ranging from [10 mg/kg] to [300 mg/kg] ($p < 0.05$). Berberine reduced levels of pro-inflammatory cytokines like TNF-α, IL-1β, and IL-6, and downregulated the TLR4/NF-κB signaling pathway. Antioxidant effects included decreased malondialdehyde and increased superoxide dismutase and glutathione levels ($p < 0.05$). Additional benefits included enhanced neurogenesis and synaptic plasticity, marked by increased expression of BDNF, TrkB, and synaptic proteins SYP and PSD95, and reduced apoptotic markers such as cleaved caspase-3 ($p < 0.05$). [14]

DISCUSSION

We summarised berberine beneficial effects in the table below (Table 1):

Benefit	Mechanism	Application
Insulin Sensitivity	Activation of AMPK; modulation of	Type 2 diabetes, prediabetes

	insulin receptor	
Lipid Regulation	Promotes cholesterol excretion; inhibits hepatic synthesis	Dyslipidemia, cardiovascular health
Anti-inflammatory	Reduces pro-inflammatory cytokines; modulates NF-κB pathway	Chronic inflammation, metabolic syndrome
Antioxidant Effects	Neutralizes ROS; enhances antioxidant enzymes	Oxidative stress-related disorders
Hepatoprotection	Reduces liver fat accumulation; improves liver function markers	Fatty liver disease, NAFLD
Gut Microbiota Modulation	Increases beneficial bacteria; decreases harmful ones	Metabolic and cardiovascular health
Hormonal Regulation	Reduces androgen levels; improves hormonal balance	PCOS, hirsutism, acne

Table 1. Berberine beneficial effects [3, 17, 23, 25]

Taken all the beneficial properties into account can berberine become a substitute for more conventional treatments?

For example berberine has been shown to lower HbA1c levels similarly to metformin, while offering additional benefits in lipid regulation and anti-inflammatory properties[30].

In terms of lipid-lowering effects, berberine achieves reductions in LDL cholesterol and triglycerides comparable to statins, although through a different mechanism-enhancing cholesterol excretion and inhibiting its synthesis in the liver. While statins remain the first-line treatment for dyslipidemia, berberine may serve as an alternative for patients who are statin-intolerant or as an adjunct therapy for those with persistently elevated lipid levels despite statin use. Berberine's therapeutic potential extends to specific patient populations. For instance:

- **Prediabetic individuals**: Berberine's ability to improve insulin sensitivity and delay progression to type 2 diabetes makes it a valuable option for individuals in the prediabetes stage.

- **Patients with metabolic syndrome**: Given its effects on glucose metabolism, lipid profiles, and inflammation, berberine could be especially beneficial for those with coexisting conditions like hypertension, dyslipidemia, and abdominal obesity.
- **Women with PCOS**: Berberine's role in regulating hormonal imbalances, reducing androgen levels, and improving insulin sensitivity positions it as a promising supplement for women with polycystic ovary syndrome.
- **Cardiovascular risk patients**: Its lipid-lowering, endothelial function-enhancing, and anti-inflammatory properties may benefit those with a high risk of cardiovascular events.

We made a summarised comparison in the table below (Table 2) to show potential benefits of substituting conventional medications with berberine:

Category	Berberine	Conventional Medications
Insulin Sensitivity	Activates AMPK, improves glucose metabolism, reduces HbA1c and fasting plasma glucose.	Metformin activates AMPK but lacks lipid-regulating and anti-inflammatory effects.
Lipid Regulation	Lowers LDL and triglycerides, promotes HDL production by inhibiting hepatic cholesterol synthesis.	Statins lower LDL by inhibiting HMG-CoA reductase but have minimal impact on HDL levels.
Hypoglycemia Risk	Glucose-lowering effects are activated under hyperglycemic conditions, minimizing hypoglycemia.	Sulfonylureas and glinides stimulate insulin release, increasing hypoglycemia risk.
Anti-inflammatory Effects	Reduces pro-inflammatory cytokines and oxidative stress; modulates NF-κB and	Limited or no direct anti-inflammatory effects in most conventional treatments.

	antioxidant pathways.	
Broader Benefits	Offers hepatoprotection, gut microbiota modulation, and hormonal regulation (e.g., PCOS).	Conventional drugs typically target specific conditions without broader health benefits.
Patient Suitability	Useful for prediabetic patients, metabolic syndrome, PCOS, and statin-intolerant individuals.	Often not tailored for overlapping metabolic conditions or statin intolerance.
Adverse Effects	Favorable safety profile with fewer gastrointestinal side effects compared to metformin.	Statins may cause muscle pain; metformin may cause gastrointestinal upset; others vary.
Combination Potential	Promising adjunct therapy with statins or metformin, enhancing efficacy and reducing doses.	Often used alone or with limited compatibility for natural supplements.

Table 2. Potential benefits of substituting conventional medications with berberine [33]

Despite these promising applications, it is important to note that variations in study protocols, including dosage, treatment duration, and population characteristics, make it challenging to draw universal conclusions. Standardized, large-scale clinical trials are warranted to confirm berberine's efficacy and safety across diverse patient groups. Additionally, research into synergistic therapies combining berberine with established medications such as metformin or statins could pave the way for optimized treatment strategies. For now we don't recommend substituting conventional medications with berberine but results of many studies looks promising and it can definitely be used as beneficial supplement.

In the world of supplements we have many well-known and documented beneficial ones like curcumin or resveratrol. Berberine seems to be less known but it does not seem to be less effective. Below there is comparative table (Table3) highlighting the differences and similarities between berberine, curcumin, and resveratrol:

Table 3. Differences and similarities between berberine, curcumin, and resveratrol [31]

Category	Berberine	Curcumin	Resveratrol
Source	Alkaloid derived from plants like Berberis species.	Polyphenol derived from turmeric (Curcuma longa).	Polyphenol found in grape skins, red wine, and berries.
Primary Benefits	Improves insulin sensitivity, lipid profile, and metabolic health; anti-inflammatory and antioxidant effects.	Anti-inflammatory, antioxidant, supports musculoskeletal, cardiovascular, and immune health.	Anti-aging, antioxidant, supports cardiovascular and brain health, and aids in longevity.
Mechanism of Action	Activates AMPK, modulates insulin receptors, reduces oxidative stress, and regulates lipid metabolism.	Modulates NF-κB, COX-2, and other inflammatory pathways; neutralizes reactive oxygen species.	Activates SIRT1, modulates inflammatory pathways, and enhances mitochondrial function.
Metabolic Health	Effective in managing type 2 diabetes, dyslipidemia, and metabolic syndrome.	Limited direct effects on glucose metabolism but supports systemic health.	Supports glucose metabolism and insulin sensitivity; aids in weight management.
Anti-inflammatory Effects	Reduces pro-inflammatory cytokines and oxidative stress.	Strong anti-inflammatory effects, particularly in chronic inflammation and arthritis.	Reduces inflammation and oxidative stress; supports vascular health.
Gut Health	Modulates gut microbiota, increasing	Supports gut health indirectly through anti-	Limited direct effects on gut health but

	beneficial bacteria and reducing harmful ones.	inflammatory and antioxidant properties.	supports systemic inflammation reduction.
Hepatoprotection	Protects liver health, reduces fat accumulation, and improves liver function markers.	May protect liver health by reducing inflammation and oxidative stress.	Limited evidence of direct hepatoprotective effects; supports overall cellular health.
Cancer Research	Shows potential in inhibiting cancer cell proliferation and inducing apoptosis.	Demonstrates anti-cancer properties by targeting multiple signaling pathways.	Exhibits anti-cancer effects by modulating cell cycle and promoting apoptosis.
Safety Profile	Generally well-tolerated; mild gastrointestinal side effects reported in some cases.	Safe at recommended doses; high doses may cause gastrointestinal discomfort.	Safe at recommended doses; potential interactions with medications like blood thinners.
Applications	Type 2 diabetes, metabolic syndrome, PCOS, cardiovascular health, and liver health.	Arthritis, cardiovascular health, immune support, and chronic inflammation management.	Cardiovascular health, neuroprotection, anti-aging, and longevity support.

While curcumin and resveratrol have already gained widespread recognition for their remarkable benefits, berberine remains a hidden gem in the world of natural supplements. Its potential to improve metabolic health, regulate lipids, and offer broader therapeutic effects is undeniable. With robust scientific evidence backing its efficacy, berberine deserves to be in the spotlight alongside other well-known supplements. Greater awareness of its multifaceted benefits could pave the way for more widespread adoption, unlocking its potential to transform health management for diverse patient populations.

SUMMARY

Introduction and purpose

Berberine, a natural isoquinolone alkaloid, demonstrates significant potential in improving metabolic health. Current evidence suggests that berberine enhances insulin sensitivity through AMPK activation and modulation of insulin receptor expression. It also exhibits lipid-lowering effects by promoting cholesterol excretion and inhibiting hepatic cholesterol synthesis, leading to reduced LDL and triglyceride levels alongside elevated HDL cholesterol.

Beyond its metabolic benefits, berberine shows anti-inflammatory and antioxidant properties, aiding in the reduction of oxidative stress and pro-inflammatory markers. It has additional therapeutic effects, including improved endothelial function, hepatoprotection, and gut microbiota modulation, further contributing to overall health. While these findings highlight its potential as an alternative to conventional treatments, differences in study populations, supplementation protocols, and durations indicate a need for further large-scale, long-term randomized controlled trials to fully establish its efficacy and safety. [26]

Metabolic health plays a pivotal role in overall well-being, influencing energy production, fat metabolism, insulin functionality, and cellular balance. Among the natural compounds drawing attention for their therapeutic potential, berberine-a bioactive alkaloid extracted from plants like Berberis species-has emerged as a topic of significant research interest. Historically used in traditional medicine for its anti-microbial and anti-diabetic properties, berberine has gained recent scientific traction for its role in improving metabolic functions and addressing systemic health issues. The purpose of this discussion is to explore the mechanisms, known benefits, and potential of berberine in metabolic regulation, alongside an evaluation of its broader health-related applications.

In a world increasingly burdened by metabolic syndromes, including obesity, type 2 diabetes, and cardiovascular complications, alternative or complementary therapeutic solutions are of growing importance. While pharmacological drugs dominate treatment protocols, natural substances like berberine offer promise due to their multifaceted properties, lower toxicity, and long-standing historical usage. Could berberine potentially be an alternative to statins, metformin or well known anti-inflammatory supplements like curcumin?

Brief description of the state of knowledge:

Berberine demonstrates extensive benefits in regulating key metabolic functions. One of its most well-documented effects lies in enhancing insulin sensitivity. This is achieved through the activation of AMP-activated protein kinase (AMPK), a critical energy sensor in the body. By activating AMPK, berberine

promotes glucose uptake in cells and aids in the modulation of insulin receptor expression. The result is improved cellular glucose metabolism and a reduction in insulin resistance, which are crucial for managing conditions like type 2 diabetes.

Beyond glucose regulation, berberine exhibits a profound impact on lipid metabolism. Studies indicate its ability to lower low-density lipoprotein (LDL) cholesterol and triglycerides while promoting high-density lipoprotein (HDL) cholesterol. It achieves this lipid-lowering effect by inhibiting hepatic cholesterol synthesis and enhancing cholesterol excretion. These properties position berberine as a promising candidate for addressing dyslipidemia and reducing the risk of cardiovascular events.

Anti-Inflammatory and Antioxidant Effects

Chronic inflammation and oxidative stress are central to the pathogenesis of metabolic syndromes. Berberine exerts anti-inflammatory effects by suppressing pro-inflammatory cytokines and modulating pathways involved in inflammation. Simultaneously, its antioxidant properties help in neutralizing reactive oxygen species, thereby reducing oxidative stress and mitigating cellular damage.

Additional Therapeutic Roles

The benefits of berberine extend beyond metabolic health. Emerging studies suggest its role in improving endothelial function, which is essential for maintaining vascular health. Berberine has been observed to protect liver health through its hepatoprotective effects, potentially aiding in conditions like fatty liver disease. Additionally, its ability to modulate gut microbiota highlights another layer of health benefits, as gut health is increasingly recognized as a key player in overall systemic health.

While these findings underscore berberine's potential as an alternative or complement to conventional treatments, further large-scale, long-term randomized controlled trials are essential to establish its safety and efficacy. Future research should explore synergistic therapies combining berberine with established medications and focus on identifying patient subgroups- such as those with PCOS or metabolic syndrome- who may benefit most from its use

Conclusions

Berberine, rooted in traditional medicine, emerges as a potent candidate for improving metabolic health and providing broader health benefits. Its mechanisms, from AMPK activation to anti-inflammatory and lipid-modulating effects, reveal a compound that operates on multiple levels to address complex health challenges. Beyond metabolic functions, its antioxidant, hepatoprotective, and gut-modulating roles further establish its therapeutic versatility.

While current findings are promising, the translation of berberine's benefits into clinical practice requires careful consideration. Differences in supplementation protocols, population diversity, and the need for long-term safety assessments call for more rigorous studies. However, as a natural compound with a favorable safety profile and multifaceted benefits, berberine holds significant potential in transforming the landscape of alternative and integrative medicine. Its role as a complement to established treatments offers hope for addressing the growing global burden of metabolic disorders and related conditions.

Disclosure:

Authors' contribution:

Conceptualization: Julia Piotrowska, Adrianna Domańska; Methodology: Julia Piotrowska Adrianna Witkowska; Software: Aleksandra Łubińska- Kowalska, Agata Żak- Gontarz; Formal analysis: Aleksandra Minda, Agata Żak- Gontarz; Investigation resources: Julia Piotrowska, Monika Wendland, Krzysztof Długosz; Data curation: Justyna Janikowska, Antonina Teresa Witkowska; writing-rough preparation: Julia Piotrowska, Barbara Anna Zapalska; writing-review and editing: Julia Piotrowska, Adrianna Domańska, Antonina Teresa Witkowska; Visualization: Aleksandra Łubińska- Kowalska, Barbara Anna Zapalska, Krzysztof Długosz; Supervision: Aleksandra Minda, Justyna Janikowska, Adrianna Witkowsa; Project administration: Julia Piotrowska, Monika Wendland

Supplementary Materials: they have not been provided

Funding: This review received no specific grant from any funding agency in the public, commercial or not- for- profit sectors.

Institutional Review Board Statement: not applicable. This narrative review did not involve any new studies with human/animal participants performed by the authors. Therefore it was not subjected to Institutional Review Board approval.

Informed Consent Statement: not applicable for the reasons stated above

Data Availability Statement: The data supporting the findings of this study are available within the article. Data are also available in the databases such as PubMed, Google Scholar, Clinical Key.

Acknowledgements: The authors have no acknowledgements to declare

Conflict of Interest Statement: The authors declare no conflict of interest.

Declaration of the use of generative AI and AI-assisted technologies in the writing process: In preparing this work, the author(s) used ChatGPT for the purpose of translation and interpunction correction. After

using this tool/service, the author(s) have reviewed and edited the content as needed and accept full responsibility for the substantive content of the publication.

PEER REVIEW:

No. Name Surname Email Affiliation/Address Country Validated

1. Anna Cukrowska e-mail: ankacuk@gmail.com Maria Skłodowska-Curie County Hospital ul. Duboisa 68, 07-300 Ostrów Mazowiecka, Poland

2. Michał Bielecki e-mail: michbiel@gmail.com The Independent Group of Public Ambulatory Care Institutions Warsaw-Mokotów, Madalińskiego 13, 02-513 Warsaw, Poland

3. Szymon Wolak e-mail: wolakszymon96@gmail.com Henryk Klimontowicz Specialist Hospital ul. Węgierska 21, 38-300 Gorlice, Poland

4. Alicja Wolak e-mail: wolakalicja98@gmail.com Henryk Klimontowicz Specialist Hospital ul. Węgierska 21, 38-300 Gorlice, Poland

5. Kamila Żelazny e-mail: kam.witkowska@gmail.com Rafał Czerwiakowski County Hospital ZOZ in Bielsk Podlaski ul. Kleszczelowska 1, 17-100 Bielsk Podlaski, Poland

References:

1. Gao Y, Wang F, Song Y, et al. The status of and trends in the pharmacology of berberine: a bibliometric review [1985–2018]. Chin Med. 2020;15(1):7. doi:10.1186/s13020-020-0288-z.

2. Khashayar A, Bahari Z, Elliyeh M, et al. Therapeutic effects of berberine in metabolic diseases and diabetes mellitus. Rev Bras Farmacogn. 2021;31:272–281. doi:10.1007/s43450-021-00159-0.

3. Jin Y, Liu S, Ma Q, et al. Berberine enhances the AMPK activation and autophagy and mitigates high glucose-induced apoptosis of mouse podocytes. Eur J Pharmacol. 2017;794:106–114. doi:10.1016/j.ejphar.2016.11.037.

4. Utami AR, Maksum IP, Deawati Y. Berberine and its study as an antidiabetic compound. Biology. 2023;12(7):973. doi:10.3390/biology12070973.

5. Ionescu OM, Frincu F, Mehedintu A, et al. Berberine: A promising therapeutic approach to polycystic ovary syndrome in infertile/pregnant women. Life (Basel). 2023;13(1):125. doi:10.3390/life13010125.

6. An N, Zhang G, Li Y, et al. Promising antioxidative effect of berberine in cardiovascular diseases. Front Pharmacol. 2022;13:837391. doi:10.3389/fphar.2022.837391.

7. Ilyas Z, Perna S, Al-thawadi S, et al. The effect of berberine on weight loss in order to prevent obesity: A systematic review. Biomed Pharmacother. 2020;127:110137. doi:10.1016/j.biopha.2020.110137.

8. Jin Y, Khadka DB, Cho WJ. Pharmacological effects of berberine and its derivatives: A patent update. Expert Opin Ther Pat. 2016;26(2):229–243. doi:10.1517/13543776.2016.1118060.

9. Song D, Hao J, Fan D. Biological properties and clinical applications of berberine. Front Med. 2020;14(5):564–582. doi:10.1007/s11684-019-0724-6.

10. Lau CW, Yao XQ, Chen ZY, et al. Cardiovascular actions of berberine. Cardiovasc Drug Rev. 2001;19(3):234–244. doi:10.1111/j.1527-3466.2001.tb00068.x.

11. Bagade A, Tumbigeremutt V, Pallavi G. Cardiovascular effects of berberine: A review of the literature. J Restor Med. 2017;6:100. doi:10.14200/jrm.2017.6.0100.

12. Panigrahi A, Mohanty S. Efficacy and safety of HIMABERB® berberine on glycemic control in patients with prediabetes: Double-blind, placebo-controlled, and randomized pilot trial. BMC Endocr Disord. 2023;23(1):190. doi:10.1186/s12902-023-01442-y.

13. Chang X, Wang Z, Zhang J, et al. Lipid profiling of the therapeutic effects of berberine in patients with nonalcoholic fatty liver disease. J Transl Med. 2016;14(1):266. doi:10.1186/s12967-016-0982-x.

14. Laein GD, Boumeri E, Ghanbari S, et al. Neuroprotective effects of berberine in preclinical models of ischemic stroke: A systematic review. BMC Pharmacol Toxicol. 2025;26:40. doi:10.1186/s40360-025-00843-0.

15. Moon JM, Ratliff KM, Hagele AM, et al. Absorption kinetics of berberine and dihydroberberine and their impact on glycemia: A randomized, controlled, crossover pilot trial. Nutrients. 2022;14(1):124. doi:10.3390/nu14010124.

16. Blais JE, Huang X, Zhao JV. Overall and sex-specific effect of berberine for the treatment of dyslipidemia in adults: A systematic review and meta-analysis of randomized placebo-controlled trials. Drugs. 2023;83:403–427. doi:10.1007/s40265-023-01841-4.

17. Mazurek A, Pawlicki M, Stachyrak K, et al. Berberine in the treatment of type 2 diabetes: Literature review. J Educ Health Sport. 2024;67:49000. doi:10.12775/JEHS.2024.67.49000.

18. Ochyra Ł, Łopuszyńska A, Pawlicki M, et al. Berberine in the treatment of polycystic ovary syndrome. J Educ Health Sport. 2022;12(4):309–314. doi:10.12775/JEHS.2022.12.04.024.

19. Rozwadowska P, Bator P, Razik M, et al. Anticancer properties of berberine: Analysis of the latest reports. J Educ Health Sport. 2024;61:73–86. doi:10.12775/JEHS.2024.61.005.

20. Xiong RG, Huang SY, Wu SX, et al. Anticancer effects and mechanisms of berberine from medicinal herbs: An updated review. Molecules. 2022;27(14):4523. doi:10.3390/molecules27144523.

21. Kou Y, Tong B, Wu W, et al. Berberine improves chemo-sensitivity to cisplatin by enhancing cell apoptosis and repressing PI3K/AKT/mTOR signaling pathway in gastric cancer. Front Pharmacol. 2020;11:616251. doi:10.3389/fphar.2020.616251.

22. Wang J, Yang S, Cai X, et al. Berberine inhibits EGFR signaling and enhances the antitumor effects of EGFR inhibitors in gastric cancer. Oncotarget. 2016;7(46):76076–76086. doi:10.18632/oncotarget.12589.

23. Ye Y, Liu X, Wu N, et al. Efficacy and safety of berberine alone for several metabolic disorders: A systematic review and meta-analysis of randomized clinical trials. Front Pharmacol. 2021;12:653887. doi:10.3389/fphar.2021.653887.

24. Xie W, Su F, Wang G, et al. Glucose-lowering effect of berberine on type 2 diabetes: A systematic review and meta-analysis. Front Pharmacol. 2022;13:1015045. doi:10.3389/fphar.2022.1015045.

25. Och A, Och M, Nowak R, et al. Berberine, a herbal metabolite in the metabolic syndrome: The risk factors, course, and consequences of the disease. Molecules. 2022;27(4):1351. doi:10.3390/molecules27041351.

26. Li Z, Wang Y, Xu Q, et al. Berberine and health outcomes: An umbrella review. Phytother Res. 2023;37(5):2051–2066. doi:10.1002/ptr.7806.

27. Guo HH, Shen HR, Wang LL, et al. Berberine is a potential alternative for metformin with good regulatory effect on lipids in treating metabolic diseases. Biomed Pharmacother. 2023;163:114754. doi:10.1016/j.biopha.2023.114754.

28. Jurgiel J, Graniak A, Opyd P, et al. The role of berberine in polycystic ovary syndrome: A summary of knowledge. Ginekol Pol. 2024;95(4):276–284. doi:10.5603/gpl.95138.

29. Xia Y, Leung K, Zhao JV. Cost-effectiveness analysis of statins, berberine, and their combined use for primary prevention of cardiovascular disease. medRxiv. 2025; doi:10.1101/2025.02.20.25322455.

30. McCubrey JA, Lertpiriyapong K, Steelman LS, et al. Effects of resveratrol, curcumin, berberine, and other nutraceuticals on aging, cancer development, cancer stem cells, and microRNAs. Aging (Albany NY). 2017;9(6):1477–1536. doi:10.18632/aging.101250.

31. Guo HH, Shen HR, Wang LL, et al. Berberine is a potential alternative for metformin with good regulatory effect on lipids in treating metabolic diseases. Biomed Pharmacother. 2023;163:114754. doi:10.1016/j.biopha.2023.114754.

32. McCubrey JA, Lertpiriyapong K, Steelman LS, et al. Effects of resveratrol, curcumin, berberine, and other nutraceuticals on aging, cancer development, cancer stem cells, and microRNAs. Aging (Albany NY). 2017;9(6):1477–1536. doi:10.18632/aging.101250.

33. Zamani M, Zarei M, Nikbaf-Shandiz M. The effects of berberine supplementation on cardiovascular risk factors in adults: A systematic review and dose-response meta-analysis. Front Nutr. 2022;9:1013055. doi:10.3389/fnut.2022.1013055.

34. Lan J, Zhao Y, Dong F, et al. Meta-analysis of the effect and safety of berberine in the treatment of type 2 diabetes mellitus, hyperlipemia, and hypertension. J Ethnopharmacol. 2015;161:69–81. doi:10.1016/j.jep.2014.09.049.