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BERBERINE IN METABOLIC DISORDERS: THE "NATURE'S OZEMPIC" PHENOMENON - A NARRATIVE REVIEW

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ABSTRACT

Background: Metabolic disorders, particularly type 2 diabetes and obesity, represent one of the greatest public health challenges of the 21st century. In response to the limitations and side effects of conventional pharmacotherapy, many patients are seeking natural alternatives. Berberine, a traditional medicinal plant compound, has become increasingly popular on social media under the label "Nature's Ozempic."
Objective: This narrative review provides a comprehensive synthesis of berberine in metabolic disorders. It examines its molecular mechanisms, clinical evidence, safety profile, pharmacological interactions, and the public health consequences of its rapid rise on social media.
Methods: A targeted literature search was conducted in PubMed, Scopus, Web of Science, and Google Scholar. Priority was given to randomised controlled trials, meta-analyses, mechanistic studies, and recent publications analysing social media trends. The articles published between 2009 and 2026 were primarily included.
Main Findings: Berberine acts through multiple pathways, most notably AMPK activation, modulation of the gut microbiota, and anti-inflammatory effects. Clinical studies show mild but consistent improvements in glycemic control, insulin sensitivity, and lipid parameters, particularly in patients with type 2 diabetes or metabolic syndrome. Its impact on body weight and visceral fat is generally limited. Short-term safety is acceptable, with mainly mild gastrointestinal side effects, although potential interactions with cytochrome P450 enzymes and P-glycoprotein have been documented.
Conclusions: Berberine may serve as a useful adjunctive option in selected patients, but it cannot replace standard therapies such as metformin or statins. Its growing popularity on social media has encouraged widespread self-medication, raising concerns about safety and unrealistic expectations. Larger, longer-term, and more diverse studies are needed to define its true clinical value and long-term safety.

KEYWORDS

Berberine, Metabolic Syndrome, Nutraceuticals, Social Media, "Nature's Ozempic"

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1. Introduction

Metabolic disorders constitute a growing global public health challenge. Over recent decades, non-communicable diseases have surpassed infectious diseases as the leading threat to longevity, primarily due to rapid urbanization and the increase in sedentary lifestyles. Obesity has reached unprecedented levels worldwide, with more than one billion individuals now classified as clinically obese (World Health Organization [WHO], 2024a). The global burden of type 2 diabetes mellitus (T2DM) has also greatly increased; it is currently estimated that approximately 800 million adults have T2DM (WHO 2024b). Dyslipidemia, hypertension, and impaired glucose metabolism are common components of metabolic syndrome, which in turn contribute substantially to the global health care and socio-economic burdens. While conventional pharmacotherapy remains the cornerstone of metabolic disease management, increasing attention has been directed towards nutraceuticals and plant-derived bioactive compounds. This shift is partly driven by a desire for "natural" therapies and concerns regarding the adverse-effect profiles of some synthetic drugs. Social media and other forms of digital communication have also markedly influenced awareness and interest in nutraceuticals and dietary supplements (Gauch & Smollich, 2025). Berberine, an isoquinoline alkaloid with a long history of use in traditional Chinese medicine, exemplifies this larger movement toward natural products. On platforms such as TikTok and Instagram, berberine has been labeled "Nature's Ozempic," contributing to its popularity as a weight-management supplement. The dissemination of potentially oversimplified or inaccurate health information and encouragement of self-medication through social media platforms could have negative effects (Gauch & Smollich, 2025). Scientific interest in berberine has increased

because its reported effects appear to involve multiple pathways relevant to metabolic regulation, including glucose metabolism, lipid homeostasis, inflammation, and gut microbiota-related mechanisms. Clinical evidence suggests that berberine may improve glycemic parameters, although the magnitude of effect varies depending on baseline metabolic status. (Xie et al., 2022). Despite the promising clinical data for berberine, there is a significant gap between viral popularity and pharmacologic safety. Without appropriate professional oversight, the growing use of berberine increases the potential for clinically relevant drug-drug interaction. Therefore, a critical synthesis of current evidence is needed, particularly in the context of widespread public interest and online health misinformation**.**

The aim of this narrative review is to summarize current evidence on berberine in metabolic disorders, with a focus on proposed molecular mechanisms, clinical findings, safety considerations, and public health implications. It also discusses how social-media-driven trends may influence patterns of berberine use, self-medication practices, and risk communication in metabolic health.

2. Methodology

This review provides a comprehensive overview of berberine's role in managing metabolic disorders, evaluating its therapeutic potential alongside the clinical and public health challenges associated with its increasing use. The literature search included PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar. Terms related to berberine ("berberine", "Berberis vulgaris") were combined with terms referring to metabolic disorders, including "type 2 diabetes", "obesity", "metabolic syndrome", "dyslipidemia", and "insulin resistance". Additional search terms included "AMPK", "gut microbiota", "drug interactions", "social media", and "Nature's Ozempic". Articles published between 2009 and 2026 were mainly considered. The review included randomized controlled trials, meta-analyses, and mechanistic studies with potential clinical relevance. Publications on social media trends and health misinformation related to berberine were also included when relevant to the aims of the review. Case reports, editorials, and conference abstracts were excluded. As this was a narrative review, no formal quality assessment or quantitative synthesis was performed. The aim was to provide a critical overview of the available evidence, with emphasis on the consistency of findings, the main limitations of current studies, and the gap between scientific evidence and social-media-driven use of berberine.

3. Main findings

3.1. Molecular Mechanisms of Action

Understanding how berberine works at the molecular level is important for interpreting its metabolic effects and for judging how far preclinical findings may translate into clinical benefit. The available data suggest that berberine acts through several overlapping pathways rather than a single dominant mechanism.

3.1.1 AMPK Activation

One of the most well-characterized mechanisms among those proposed is related to AMPK signaling. Given its central position in maintaining cellular energy balance, it provides a logical basis for berberine's reported impacts on glucose and lipid metabolism. Experimental studies have demonstrated that activation of AMPK results in metabolic changes relevant to insulin resistance, such as enhanced glucose uptake and changes in lipid metabolism (Tabeshpour et al., 2017). In obese mice, berberine increased the phosphorylation of AMPK and acetyl-CoA carboxylase in the liver and skeletal muscle and was also associated with higher expression of genes involved in fatty acid oxidation (Kim et al., 2009). Taken together, these findings suggest that AMPK activation may be an important component of berberine's metabolic activity, particularly in relation to lipid handling and energy balance. However, the extent of its contribution to the findings from human studies is unknown.

3.1.2 Inhibition of Hepatic Gluconeogenesis

Berberine has also been reported to reduce hepatic glucose production, which is clinically relevant because excessive gluconeogenesis contributes to fasting hyperglycemia in insulin resistance and type 2 diabetes mellitus (T2DM). This effect does not seem to depend exclusively on AMPK, as experimental work suggests that berberine may also interfere with glucagon-related signaling. In a preclinical model, berberine-induced mitochondrial dysfunction with AMP accumulation resulted in increased peripheral glucose uptake (Zhang et al., 2018). The same study linked AMP accumulation to reduced cyclic AMP levels, lower downstream protein kinase A signaling, attenuation of glucagon-driven gluconeogenesis, and increased acetylation followed by degradation of phosphoenolpyruvate carboxykinase 1 (PEPCK1), a key enzyme in hepatic gluconeogenesis (Zhang et al., 2018). It is important to emphasize that this glucagon-inhibitory effect

was described as independent of AMPK activation, indicating that berberine may influence glucose homeostasis through more than one mechanistic route. Additionally, a larger body of preclinical studies has demonstrated improved glucose management through reduced gluconeogenesis and improved glucose utilization in multiple pathways (Tabeshpour et al., 2017).

3.1.3 Modulation of LDL Receptor Expression and Complementary Lipid-Lowering Mechanisms

The influence on lipid metabolism may be one of berberine's more clinically recognizable actions. A distinct mechanism involves upregulation of hepatic low-density lipoprotein receptor (LDLR) expression, which enhances the clearance of circulating LDL cholesterol (Tabeshpour et al., 2017). This mechanism differs from that of statins. Whereas statins mainly reduce intracellular cholesterol synthesis by inhibiting HMG-CoA reductase, berberine seems to increase LDLR expression at the post-transcriptional level (Tabeshpour et al., 2017). This suggests that berberine may act through a pathway complementary to standard lipid-lowering therapy rather than simply mimicking it.

At the same time, LDLR upregulation does not fully explain all lipid-related effects of berberine. In a study comparing LDLR wild-type and LDLR-deficient mice, it was found that cholesterol lowering occurred in LDLR-competent animals fed a high-fat/high-cholesterol diet, whereas LDLR-deficient mice still showed reduced triglyceride levels without a similar cholesterol-lowering effect. This pattern supports a practical interpretation that LDLR contributes mainly to cholesterol reduction, while triglyceride lowering may involve additional pathways. The same study reported increased hepatic *Trib1* mRNA expression together with reduced expression of several lipogenic genes, pointing to a possible LDLR-independent mechanism for triglyceride reduction (Singh & Liu, 2019).

3.1.4 Regulation of Adipogenesis and Anti-Inflammatory Effects

Berberine's influence on metabolic health extends to the regulation of adipose tissue biology and the attenuation of chronic low-grade inflammation. Experimental studies imply that berberine may suppress adipogenic processes in obesity models, and this effect has been associated with reduced expression of peroxisome proliferator-activated receptor gamma (PPAR-γ), a factor regulating fat cell maturation (Hu and Davies, 2010). This is further supported by an observed increase in GATA-3 expression and the inhibition of CCAAT/enhancer-binding protein alpha (C/EBPα), both of which are critical determinants in adipocyte differentiation (Hu and Davies, 2010; Kong et al., 2025). These transcriptional changes may limit excessive adipose tissue expansion. Closely linked to this effect is berberine's capacity to reduce inflammatory activity within fat depots, including reduced macrophage infiltration and decreased signaling of pro-inflammatory mediators such as tumour necrosis factor-α (TNF-α) and interleukin-6 (IL-6), together with attenuation of oxidative stress (Kong et al., 2025; Tabeshpour et al., 2017). Taken together, the suppression of adipogenesis and the modulation of inflammatory and oxidative pathways represent complementary components of berberine's metabolic activity, potentially improving insulin resistance and tissue injury related to metabolic syndrome.

3.1.5 Gut Microbiota Regulation and GLP-1 Pathway Modulation

The interaction between berberine and the gut microbiota represents a bidirectional paradigm that is central to its systemic metabolic effects. While the intestinal microflora considerably influences the alkaloid's metabolism and bioavailability, berberine itself acts as a potent modulator of microbial composition and function (Wang et al., 2022). Bacterial conversion of berberine to dihydroberberine, a derivative characterized by superior intestinal absorption, could provide one explanation for how berberine can cause substantial metabolic impacts despite low oral bioavailability (Cheng et al., 2022). Berberine-related microbial changes have also been associated with improved intestinal barrier function, reduced metabolic endotoxemia, and altered production of microbial metabolites such as short-chain fatty acids and bile acids, ultimately contributing to better insulin sensitivity and metabolic homeostasis (Wang et al., 2022; Cheng et al., 2025).

Crucially, berberine's effects on the gut microbiota also engage the glucagon-like peptide-1 (GLP-1) pathway, the primary target of the popular "Ozempic-like" drugs. It is indicated that berberine promotes endogenous GLP-1 secretion from intestinal L-cells by optimizing the gut environment (Wu et al., 2023). In addition, berberine has been demonstrated to directly stimulate GLP-1 release by activating bitter taste receptors (TAS2Rs) expressed throughout the gastrointestinal tract. This process initiates a phospholipase C (PLC)-dependent signaling cascade, resulting in acute incretin discharge (Yu et al., 2015). These mechanisms may contribute to some of berberine's glucose-lowering effects observed in preclinical models. However, their clinical translation appears limited, resulting in only modest effects on appetite and body weight compared with synthetic GLP-1 receptor agonists (see Sections 3.2.2 and 4.1).

3.2 Clinical Evidence in Metabolic Disorders

3.2.1 Type 2 Diabetes and Insulin Resistance

Berberine has improved several core glycemic parameters among patients with type 2 diabetes mellitus, most notably fasting plasma glucose, glycated hemoglobin, and postprandial glucose levels. These effects tend to be more pronounced in individuals with higher baseline glycemic values, which aligns well with the molecular pathways involving AMPK and gluconeogenesis inhibition discussed in section 3.1 (Xie et al., 2022; Kong et al., 2025). At the same time, clinical data did not demonstrate an increased risk of hypoglycemia or overall adverse events (Xie et al., 2022).

The clinical significance of berberine may extend beyond reducing glycemic levels. Improvements have also been reported in fasting insulin levels, HOMA-IR index, and body mass index, suggesting a possible beneficial effect on insulin resistance, particularly when berberine is used in combination with standard antidiabetic therapy (Guo et al., 2021). The results were similar for subjects with metabolic syndrome, who had lower fasting glucose levels and better glucose-related secondary outcomes after receiving berberine. However, these findings should be interpreted with caution due to differences in the subject populations, lack of complete safety data, and limited availability of long-term treatment duration and efficacy data (Liu et al., 2025).

3.2.2 Obesity and Weight Management

In the clinical context of overweight and obesity, berberine has been investigated primarily for its capacity to modulate main anthropometric markers, including total body mass, body mass index (BMI), waist circumference, and the accumulation of visceral adipose tissue. The majority of clinical observations in this domain represent the translation of the molecular inhibition of adipogenesis discussed in Section 3.1 into observable phenotypic outcomes. While weight loss and reduction in central fat distribution were found in several trials, this effect appears to be more pronounced in subjects with concomitant metabolic disturbances (Kong et al., 2025).

However, despite evidence from different study groups indicating the potential benefits of berberine for managing body weight, it is clear that there are limitations to the efficacy of the compound. For example, a randomized controlled trial conducted using 150 adults with obesity and metabolic dysfunction-associated steatotic liver disease demonstrated no significant reduction in visceral adipose tissue area or liver fat content after six months of berberine supplementation at doses of 1 gram per day. The compound was, however, well tolerated and produced favorable changes in some metabolic markers (Lei et al., 2026). This is particularly relevant in the current clinical context, where berberine is sometimes informally compared with semaglutide and other GLP-1 receptor agonists. However, the available evidence does not support an equivalent effect on weight reduction. Large randomized trials have shown that semaglutide produces clinically meaningful weight loss, and outcome studies have further demonstrated benefits extending beyond short-term changes in surrogate metabolic markers (Lincoff et al., 2023; Wilding et al., 2021). On the other hand, berberine appears to have a minor and less consistent effect on body weight and adiposity-related outcomes.

Taken together, berberine seems to provide limited but potentially useful support for weight management. Its effects are more reliable for selected metabolic and anthropometric parameters than for substantial changes in overall body composition (Shi et al., 2025).

3.2.3 Dyslipidemia and Cardiovascular Risk

Clinical studies have primarily examined the impact of berberine on lipid parameters associated with cardiometabolic risk, with particular focus on triglycerides, LDL cholesterol, and total cholesterol. In patients with metabolic syndrome, the most consistent benefit has been a clear reduction in triglyceride concentrations, accompanied by moderate decreases in LDL cholesterol and total cholesterol. Effects on HDL cholesterol have been smaller and more variable (Liu et al., 2025). This lipid-modifying pattern is very similar to what is seen with the use of berberine in patients with type 2 diabetes. Pooling results from meta-analysis shows reduced levels of triglycerides, total cholesterol, and LDL cholesterol in many cases accompanied by increased levels of HDL cholesterol (Guo et al., 2021). These findings suggest that the lipid effects of berberine may extend across different groups of patients with cardiometabolic disturbances, although the magnitude of benefit appears variable between studies. Recent randomized data also demonstrate that berberine may improve selected cardiovascular risk markers, including LDL cholesterol, apolipoprotein B, and high-sensitivity C-reactive protein (Lei et al., 2026).

4. Discussion

4.1. Comparison with Conventional Therapies

The broad metabolic effects of berberine naturally raise an important clinical question: how does it compare with established pharmacotherapy?

In type 2 diabetes, metformin remains the first-line treatment, while statins continue to be the cornerstone of dyslipidemia management due to their proven cardiovascular benefit. The available clinical evidence indicates that berberine may improve glycemic control and selected lipid parameters, but these effects remain modest when compared with standard pharmacological treatment (Xie et al., 2022; Dong et al., 2013). Although lipid improvements have been reported, its lipid-lowering potency remains clearly weaker than that of moderate- or high-intensity statin therapy (Dong et al., 2013). A similar comparison can be made in relation to obesity treatment. Even though berberine is sometimes discussed in the context of weight management, the available evidence does not support an effect comparable to that of semaglutide (see Section 3.2.2).

These differences are clinically important. Established drugs are supported not only by favorable effects on surrogate metabolic markers but also by robust evidence for long-term risk reduction. In contrast, the current evidence base for berberine remains largely limited to short-term changes in glycemic and lipid parameters. Even so, berberine may be helpful for individuals who cannot tolerate sufficient statin doses or who prefer "natural" options (Evbayekha et al., 2023). Among lipid-lowering nutraceuticals, it ranks among the more effective agents, typically achieving LDL cholesterol reductions of 15–20% (Cheung et al., 2023).

In summary, berberine does not replace guideline-directed medical therapy, but it can be a reasonable adjunctive option in carefully selected patients, especially those intolerant to standard pharmacotherapy or seeking additional natural support.

4.2 Clinical Safety and Pharmacological Interactions

Although berberine is often presented as a nutraceutical, it has clear pharmacological effects. For that reason, evaluating its safety should involve more than checking basic tolerability and should also consider the potential for drug-drug interactions. Randomized trials in patients with metabolic disorders suggest that berberine is reasonably safe in the short term. Reported adverse effects are usually mild and mainly gastrointestinal, typically abdominal discomfort, bloating, constipation, or diarrhoea, and only rarely lead to stopping treatment (Imenshahidi & Hosseinzadeh, 2019). There is also no convincing evidence of hepatotoxicity. The current database classifies berberine as unlikely to cause clinically apparent liver injury (National Institute of Diabetes and Digestive and Kidney Diseases, 2020). However, most available studies are relatively short, so the long-term safety evidence base is still limited.

From a clinical perspective, the more important issue may be pharmacokinetic interactions. Berberine can inhibit several major cytochrome P450 enzymes, including CYP2D6, CYP2C9, and CYP3A4, and this has been associated with increased exposure to probe substrates (Guo et al., 2012). This is particularly relevant for cardiometabolic patients, who commonly take multiple drugs that are metabolized through these pathways. In addition, berberine appears to influence P-glycoprotein activity and undergoes extensive intestinal first-pass metabolism, which could potentially alter the absorption of other co-administered medicines (Kwon et al., 2020). In summary, berberine seems to be reasonably well tolerated over the short to medium term and is not correlated with clinically significant liver injury. However, its inhibitory effects on drug-metabolizing enzymes and transporters warrant caution in patients exposed to polypharmacy. Larger studies with longer follow-up, together with real-world pharmacovigilance data, are still needed to define its safety profile more confidently in routine clinical practice.

4.3 Public Health Implications of Social Media Trends: the "Nature's Ozempic" Phenomenon

The growing popularity of berberine under the label "Nature's Ozempic" has developed within a digital environment in which health information is increasingly shaped by platform algorithms, short-form video formats, and engagement-driven visibility. This has created an opportunity for many users to access a first level of guidance from platforms like TikTok and Instagram regarding weight loss, glucose levels, and overall metabolic health.

Research on health misinformation has consistently shown that social media tends to amplify content that is simplified, emotionally appealing, or transformation-oriented rather than clinically nuanced (Suarez-Lledo & Alvarez-Galvez, 2021). In a recent analysis of 500 posts, misinformation was more common on TikTok than on Instagram, and weight-loss messaging was among the most affected categories (Diyab et al., 2025). Notably, the posts that received the greatest amount of engagement were not necessarily the ones that

were the most credible. Additionally, there is a similar trend of misinformation related to semaglutide on social media. Many of the posts highlighted the dramatic "before-and-after" results of individuals who used the drug while omitting discussion of the side effects, approved indications, or regulatory constraints (Propfe & Seifert, 2026). When berberine is promoted as "Nature's Ozempic," a comparable simplification may occur: a pharmacologically active compound is framed through comparison with an established prescription therapy, and a dietary supplement may be perceived as a therapeutic alternative. This shift is increasingly relevant in clinical practice. Patients may initiate berberine after exposure to online content, often reassured by the idea that "natural" automatically means "safe". As discussed in earlier sections, however, berberine has measurable effects on glucose and lipid metabolism and can interact with other medications.

Therefore, the primary public health issue surrounding this trend is not just the distribution of incorrect information but the potential behavior changes that could result in patients taking steps to manage their own metabolic conditions outside of professional medical supervision. Digital platforms reward clarity, speed, and strong narratives, whereas metabolic medicine depends on nuance, conditional interpretation, and balanced communication of benefit and risk. As long as these two different logics exist in parallel to one another, compounds such as berberine will continue to be distributed as both supplements and as simplified representations of health-related concepts in a digitally mediated health environment.

Addressing this phenomenon requires more than correcting isolated inaccurate statements. It involves strengthening digital health literacy, improving the visibility of evidence-based content, and recognizing that metabolic disease management increasingly unfolds within environments shaped by technological design as much as by clinical guidelines.

4.4 Limitations of Current Evidence

Although some research has demonstrated promising results for berberine, there are limitations in the existing body of research due to a variety of both methodological and interpretive issues. A major limitation is that most of the studies have been conducted for a relatively short period of time and have used a wide range of different doses, varying interventions, different combinations of background therapies, and different study populations, which will make it difficult to compare the findings from these studies to one another and reduce confidence in the consistency of the evidence base as a whole (Guo et al., 2021).

Additionally, a significant proportion of the literature focuses on surrogate metabolic outcomes rather than directly establishing a durable clinical benefit and/or a long-term reduction in cardiovascular disease risk through measurement of changes in glycemic and lipid parameters. Therefore, although changes in glycemic and lipid parameters are generally of clinical relevance, the apparent efficacy of berberine should be viewed with an appropriate degree of caution.

Finally, while the potential benefits of berberine may be greater than suggested by the availability of published literature, the current literature is narrow in terms of scope compared to the growing interest in this agent. The recent meta-analyses of purified berberine trials indicate that the number of trials using this agent remains small and the quality of secondary evidence varies, which limits the strength and applicability of the existing conclusions regarding the clinical use of berberine (Shi et al., 2025; Liu et al., 2025).

In summary, additional large-scale, long-duration, and methodologically consistent studies need to be completed before the role of berberine in daily clinical practice can be definitively established.

Conclusions

Berberine is a compound with a broad range of biological activities, showing potential in improving metabolic parameters, enhancing insulin sensitivity, and modulating lipid profiles. It can serve as a valuable supportive role (adjunct) to existing therapies; however, it must not be viewed as a direct replacement for standard pharmacological treatments such as metformin or statins. A pressing concern remains the surge of social media trends, such as "Nature's Ozempic", which encourage unsupervised self-medication based on unrealistic expectations. This phenomenon not only fosters misinformation but also heightens the risk of adverse drug-drug interactions and may dangerously delay the initiation of necessary conventional medical care.

In summary, the promising, yet still developing, evidence regarding berberine's efficacy should serve as a catalyst for more rigorous, large-scale, and long-term clinical trials. Such research is essential to fully define berberine's true value and safety profile within modern medicine, ensuring that its diverse potential is harnessed responsibly under expert supervision.

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