MAZUREK, Aleksandra, PAWLICKI, Mateusz, STACHYRAK, Karol, MIKA, Dawid, MAZUR, Bartosz, TUREK, Kamila, LAMBACH, Maciej, GREGUŁA, Anna, KŁOS, Aleksandra and WILANOWSKA, Wiktoria. Berberine in the treatment of type 2 diabetes - literature review. Journal of Education, Health and Sport. 2024;67:49000. eISSN 2391-8306.
https://dx.doi.org/10.12775/JEHS.2024.67.49000
https://apcz.umk.pl/JEHS/article/view/49000

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 2024;
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The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 27.02.2024. Revised: 05.05.2024. Accepted: 08.05.2024. Published: 13.05.2024.

Berberine in the treatment of type 2 diabetes - literature review

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Abstract

Introduction and purpose :

Type 2 diabetes is currently a serious problem worldwide. Each year, the number of individuals with carbohydrate metabolism disorders is increasing. This is due to an unhealthy lifestyle, lack of physical activity, and a diet rich in highly processed foods. Currently, the treatment of type 2 diabetes is based on the use of oral antidiabetic medications, with the first choice often being a derivative of biguanides, such as metformin. Berberine has been used in China for many years as a hypoglycemic agent, and its efficacy is compared to metformin preparations. This paper focuses on the benefits of using berberine in patients with prediabetes or type 2 diabetes and compares the effects of berberine preparations to classical medications used in diabetes treatment.

Material and methods :

The literaue was reviewed in PubMed and Google Scholar scientific database in 2013-2023 using the following keywords : berberine, diabetes mellitus type 2, hyperlipidemia, hyperglicemia

Conclusions :

The studies included in this manuscript have shown that berberine is a promising agent for adjunctive treatment in type 2 diabetes. It exhibits a range of positive effects such as lowering blood glucose levels, improving lipid profile, with no serious adverse effects reported. However, further research is needed to confirm these findings and develop an effective treatment plan.

Keywords: Berberine; diabetes type 2; hyperglicemia; hyperlipidemia

Berberine in the treatment of type 2 diabetes – literature review

Type 2 diabetes represents one of the most serious health challenges in contemporary society, evolving into a global health issue with increasing prevalence. It is anticipated that by the year 2054, approximately 783 million individuals will be afflicted with this condition. (1) Type 2 diabetes is a chronic metabolic disorder characterized by disturbances in glucose metabolism. This condition arises from abnormal insulin secretion and cellular insulin resistance, leading to excessive accumulation of glucose in the bloodstream. (2) Characteristic symptoms include polyuria, excessive thirst, fatigue and increased appetite (3). In recent years, there has been a significant increase in the incidence of type 2 diabetes, which is associated with unhealthy lifestyles, lack of physical activity, excessive body weight, and the aging of populations (1). Berberine is a plant-derived alkaloid exhibiting both biological and pharmacological activities. Presently, it is gaining significant popularity due to its promising anticancer effects, cholesterol-lowering properties in the blood, and hypoglycemic action (4). As part of these efforts, attempts are being made to incorporate berberine into the treatment of patients diagnosed with type 2 diabetes, prediabetes, and insulin resistance.

Results

Typically, oral hypoglycemic drugs are used in the treatment of type 2 diabetes, with metformin, a derivative of biguanides, being the first-line agent of choice. (3) It demonstrates glucose-lowering effects in the blood, reduces insulin resistance in cells, and improves lipid profile in patients with hypercholesterolemia, thus contributing to a decreased risk of cardiovascular events. (5) (6)

The bioavailability and mechanism of action of berberine

Berberine has been used in China for many years as a hypoglycemic drug, with its effectiveness comparable to metformin. Berberine is commonly administered orally in the form of sulfates and chlorides. Studies (7,8) (8) have shown that the bioavailability of berberine preparations after oral administration is low due to poor absorption in the gastrointestinal tract and the first-pass effect in the liver and intestine. It is metabolized in the liver by cytochrome P450, mainly by CYP2D6, and its metabolites are excreted in urine, feces, and bile (9) (10) (11) (12). Berberine lowers blood glucose levels by increasing the expression

of insulin receptors, elevating the levels of glucagon-like peptide-1 (GLP-1), which in turn stimulates insulin secretion from pancreatic beta cells, and participating in the activation of adenosine monophosphate-activated protein kinase (AMPK), leading to increased glucose uptake from the blood (13) (14).

Additionally, studies have shown that berberine inhibits adipogenesis by blocking PPARγ, C/EBPα, and SREBP-1c, thereby reducing cholesterol and triglyceride levels and contributing to weight loss. Furthermore, it also attenuates oxidative stress in cells, which plays a role in the pathogenesis of metabolic diseases (13) (15) (10) (16). Moreover, berberine demonstrates preventive action against kidney damage due to hyperglycemia (17)(18) (19) (20).

The action of berberine in the treatment of carbohydrate metabolism disorders.

It is considered that dysfunction of pancreatic beta cells plays a crucial role in the pathogenesis of type 2 diabetes, which in turn is impaired by oxidative stress and inflammatory processes.

The effectiveness of berberine supplementation in combination with metformin was investigated compared to the classical metformin intake regimen in patients with type 2 diabetes. Patients were divided into two groups of 20 individuals each, where one group received metformin alone and the other received metformin along with the tested supplement containing berberine, hesperidin, and chromium picolinate at a dose of 250 mg, which they took for 12 weeks. After this period, a significant decrease in fasting blood glucose levels and glycated hemoglobin concentrations was observed in patients receiving the additional supplement compared to the control group receiving only metformin, where such reductions were not recorded. No significant changes were observed in lipid profile, C-peptide levels, or HOMA-IR index in either group, which have been reported in other studies using berberine preparations but at higher doses. Importantly, no adverse effects were observed after the administration of the berberine-containing supplement (21).

In a meta-analysis conducted by Yaping Liang et al., based on 208 collected studies, it was confirmed that the inclusion of berberine in the treatment of patients with type 2 diabetes resulted in a reduction in fasting plasma glucose (FPG), postprandial glucose (PPG), and glycated hemoglobin (HbA1c) levels. This effect was most pronounced when berberine was used in combination with standard hypoglycemic drugs. The data are as follows: FPG (WMD = -0.54 mmol/l, 95% CI: -0.77 to -0.30), PPG (WMD = -0.94 mmol/l, 95% CI: -1.27 to -0.61), and HbA1c (WMD = -0.54 mmol/l, 95% CI: -0.93 to -0.15). However, the meta-analysis

showed that the inclusion of berberine supplementation in the treatment with standard hypoglycemic drugs did not yield favorable effects in patient groups over 60 years of age, patients taking more than 2 g of berberine per day, and those undergoing treatment for longer than 90 days. (18) (22)

In a randomized clinical trial involving a group of 34 individuals with confirmed prediabetes, a berberine preparation was administered at a dose of 500 mg three times daily for 12 weeks. After this period, it was observed that berberine reduced glycemic control indices in the treated group, with this reduction being clinically and statistically significant ($p<10^{-5}$). In the treated group, fasting plasma glucose (FPG) decreased from 6.75 ± 0.23 mmol/l to 5.33 ± 0.28 mmol/l, fasting insulin (FI) decreased from 9.81 ± 0.36 to 7.88 ± 0.52 mmol/l, 2-hour oral glucose tolerance test (2h-OGTT) decreased from 10.44 ± 0.52 to 8.12 ± 0.40 mmol/l, glycated hemoglobin (HbA1c) decreased from 6.40% ± 0.20 to 5.43% ± 0.21%, and homeostatic model assessment-insulin resistance (HOMA-IR) decreased from 3.61 ± 0.31 to 2.41 ± 0.14.

Additionally, individuals participating in this study did not report any serious adverse effects after using the berberine preparation, only mildly intensified gastrointestinal discomfort. (23)

One of the fundamental mechanisms in the pathogenesis of type 2 diabetes is hyperlipidemia and obesity, which over time leads to vascular atherosclerosis and an increased incidence of cardiovascular complications. Therefore, in patients with metabolic disease, efforts are made to reduce body weight and improve lipid profile. (24) (25) In a study conducted in China, the effects of metformin and berberine in the treatment of metabolic diseases including diabetes were compared. It was found that berberine exhibited weaker hypoglycemic effects compared to metformin. However, both berberine and metformin significantly contributed to reducing levels of total cholesterol, low-density lipoprotein cholesterol, and triglycerides. Furthermore, the impact of both substances on the levels of proinflammatory cytokines present in the serum, liver, and arteries, including TNFα, IL-6, IL-1β, and NF-κB, was assessed. It was observed that both berberine and metformin led to a significant reduction in the levels of these cytokines. (26)

Similar results were observed in a 2023 study involving a group of 49 overweight individuals with impaired fasting glucose (IFG), which examined the effect of berberine phospholipid supplementation on glycemic profile. The study included 28 women and 21 men who were randomly assigned to either the placebo group (n=25) or the group receiving berberine

preparation at a dose of 550 mg twice daily (n=24). Results were observed after 30 and 60 days of supplementation. After 60 days, a significant decrease in glucose, total cholesterol, low-density lipoprotein cholesterol, triglycerides, HOMA index, Apo A, and Apo B was observed compared to the placebo group. Additionally, no negative side effects or toxic effects on the liver or kidneys were reported in the supplementation group. (27)

In another study conducted on groups of mice with diet-induced hyperglycemia, significant effects of berberine on increasing insulin secretion and consequently lowering blood glucose levels were observed. However, in the group of mice with hyperglycemia induced by global or pancreatic islet β-cell-specific Kcnh6 knockout there was no improvement in the glycemic profile. In the same study, conducted on a group of 15 healthy men, the impact of berberine on insulin secretion in humans was assessed. A single 1g dose of berberine tablets or placebo was administered, and blood samples were collected. After 160 minutes, an approximately 40% increase in insulin secretion and an increase in C-peptide levels were observed in the group receiving berberine preparations compared to the placebo group. However, this increase was observed only in a state of hyperglycemia, and berberine did not affect fasting glucose levels. (28)

The impact of berberine on diabetic nephropathy

In the course of type 2 diabetes mellitus and with the duration of the disease, organ complications arise due to hyperglycemia. One of the severe complications is diabetic kidney disease (DKD), occurring in up to 40% of patients with type 2 diabetes (29). It is caused by damage to podocytes in the renal glomeruli, manifesting as proteinuria in patients. In 2022, in China, guidelines for the treatment of diabetic nephropathy were released by the Chinese Medical Association, emphasizing the beneficial effects of herbs and natural active compounds (NACs), including berberine (30).

In one study conducted on animals with high-fat diet-induced hyperlipidemia, a berberine preparation was administered at a dose of 150 mg/kg·d dissolved in 0.5% carboxymethyl cellulose for 12 weeks to evaluate the kidney status and compare it to a control group that did not receive berberine. It was found that berberine treatment significantly reduced collagen deposition in the interstitial tubules of rats ($p<0.05$) and also decreased tubular atrophy and inflammatory infiltration compared to the group not receiving berberine.

Additionally, the levels of E-cadherin and α-SMA were assessed using immunofluorescence and Western Blot techniques, and the expression of the NLRP3 inflammasome was examined using Western Blot and RT-PCR methods. In the berberine-treated group, an increase in E-cadherin expression, a decrease in α-SMA expression, and a reduction in the expression of NLRP3, ASC, caspase-1, and IL-1β were observed. The use of berberine leads to inhibition of interstitial fibrosis in the kidneys and increases the expression of nephrin and podocin (29) (20).

Conclusions

Type 2 diabetes presents a significant challenge in contemporary times, leading to numerous and serious side effects. Therefore, it is crucial to implement appropriate and, above all, effective treatment in patients with as few adverse effects as possible. Berberine emerges as a promising remedy due to its demonstrated positive effects such as glucose level reduction, improved insulin sensitivity, lipid profile enhancement, and nephroprotective action, with a lack of serious or burdensome side effects associated with its use. Nevertheless, further studies on larger patient cohorts are necessary to confirm these reports and develop an effective treatment plan incorporating berberine supplementation.

Author's contribution

Conceptualization, Aleksandra Mazurek,Aleksandra Kłos and Mateusz Pawlicki methodology, Bartosz Mazur; software, Dawid Mika; check, Kamila Turek, Aleksandra Kłos and Maciej Lambach; formal analysis, Anna Greguła and Wiktoria Wilanowska; investigation, Kamila Turek and Maciej Lambach; resources, Aleksandra Mazurek; data curation, Anna Greguła; writing - rough preparation, Aleksandra Mazurek; writing - review and editing, Maciej Lambach, Kamila Turek; visualization, Aleksandra Mazurek ; supervision, Mateusz Pawlicki; project administration, Dawid Mika; receiving funding, Karol Stachyrak

All authors have read and agreed with the published version of the manuscript.

Funding statement

The study did not receive special funding

Informed Consent Statement

Not applicable

Acknowledgments

Not applicable

Conflict of Interest Statement

The authors report no conflict of interests

References :

1. Ahmad E, Lim S, Lamptey R, Webb DR, Davies MJ. Type 2 diabetes. The Lancet. 2022 Nov 19;400(10365):1803–20.
2. Antar SA, Ashour NA, Sharaky M, Khattab M, Ashour NA, Zaid RT, et al. Diabetes mellitus: Classification, mediators, and complications; A gate to identify potential targets for the development of new effective treatments. Biomedicine & Pharmacotherapy. 2023 Dec 1;168:115734.
3. Baska A, Leis K, Gałązka P. Berberine in the Treatment of Diabetes Mellitus: A Review. Endocr Metab Immune Disord Drug Targets [Internet]. 2021 Oct 23 [cited 2023 Dec 20];21(8):1379–86. Available from: https://pubmed.ncbi.nlm.nih.gov/33092516/
4. Och A, Podgórski R, Nowak R. toxins Biological Activity of Berberine-A Summary Update. [cited 2023 Dec 16]; Available from: https://pubmed.ncbi.nlm.nih.gov.
5. Rena G, Hardie DG, Pearson ER. The mechanisms of action of metformin. Diabetologia [Internet]. 2017 Sep 1 [cited 2024 Jan 6];60(9):1577. Available from: /pmc/articles/PMC5552828/
6. Kleibert M, Zygmunciak P, Łakomska K, Mila K, Zgliczyński W, Mrozikiewicz-Rakowska B. Insight into the Molecular Mechanism of Diabetic Kidney Disease and the Role of Metformin in Its Pathogenesis. Int J Mol Sci [Internet]. 2023 Sep 1 [cited 2024 Jan 6];24(17). Available from: /pmc/articles/PMC10487922/

7. Liu CS, Zheng YR, Zhang YF, Long XY. Research progress on berberine with a special focus on its oral bioavailability. Fitoterapia. 2016 Mar 1;109:274–82.
8. Feng X, Sureda A, Jafari S, Memariani Z, Tewari D, Annunziata G, et al. Berberine in Cardiovascular and Metabolic Diseases: From Mechanisms to Therapeutics. Theranostics [Internet]. 2019 [cited 2024 Feb 13];9(7):1923. Available from: /pmc/articles/PMC6485276/
9. Wang K, Feng X, Chai L, Cao S, Qiu F. The metabolism of berberine and its contribution to the pharmacological effects. Drug Metab Rev [Internet]. 2017 Apr 3 [cited 2024 Jan 5];49(2):139–57. Available from: https://pubmed.ncbi.nlm.nih.gov/28290706/
10. Xu X, Yi H, Wu J, Kuang T, Zhang J, Li Q, et al. Therapeutic effect of berberine on metabolic diseases: Both pharmacological data and clinical evidence. Biomedicine & Pharmacotherapy. 2021 Jan 1;133:110984.
11. Cheng M, Liu R, Wu Y, Gu P, Zheng L, Liu Y, et al. LC–MS/MS determination and urinary excretion study of seven alkaloids in healthy Chinese volunteers after oral administration of Shuanghua Baihe tablets. J Pharm Biomed Anal. 2016 Jan 25;118:89–95.
12. Zhang L, Wu X, Yang R, Chen F, Liao Y, Zhu Z, et al. Effects of Berberine on the Gastrointestinal Microbiota. Front Cell Infect Microbiol [Internet]. 2020 Feb 19 [cited 2024 Feb 13];10. Available from: /pmc/articles/PMC7933196/
13. Liu CS, Zheng YR, Zhang YF, Long XY. Research progress on berberine with a special focus on its oral bioavailability. Fitoterapia. 2016 Mar 1;109:274–82.
14. Yu Y, Liu L, Wang X, Liu X, Liu X, Xie L, et al. Modulation of glucagon-like peptide-1 release by berberine: In vivo and in vitro studies. Biochem Pharmacol. 2010 Apr 1;79(7):1000–6.
15. Pirillo A, Catapano AL. Berberine, a plant alkaloid with lipid-and glucose-lowering properties: From in vitro evidence to clinical studies. 2015 [cited 2023 Dec 27]; Available from: http://dx.doi.org/10.1016/j.atherosclerosis.2015.09.032
16. Och A, Podgórski R, Nowak R. Biological Activity of Berberine—A Summary Update. Toxins (Basel) [Internet]. 2020 Nov 1 [cited 2024 Jan 6];12(11). Available from: /pmc/articles/PMC7697704/

17. Liang Y, Xu X, Yin M, Zhang Y, Huang L, Chen R, et al. Effects of berberine on blood glucose in patients with type 2 diabetes mellitus: A systematic literature review and a meta-analysis. Endocr J. 2019;66(1).
18. Pirillo A, Catapano AL. Berberine, a plant alkaloid with lipid-and glucose-lowering properties: From in vitro evidence to clinical studies. 2015 [cited 2023 Dec 27]; Available from: http://dx.doi.org/10.1016/j.atherosclerosis.2015.09.032
19. Gong L, Wang R, Wang X, Liu J, Han Z, Li Q, et al. Research progress of natural active compounds on improving podocyte function to reduce proteinuria in diabetic kidney disease. Ren Fail. 2023 Dec 22;45(2).
20. Qin X, Jiang M, Zhao Y, Gong J, Su H, Yuan F, et al. Berberine protects against diabetic kidney disease via promoting PGC-1α-regulated mitochondrial energy homeostasis. Br J Pharmacol [Internet]. 2020 Aug 1 [cited 2024 Jan 9];177(16):3646. Available from: /pmc/articles/PMC7393204/
21. Sartore G, Ragazzi E, Antonello G, Cosma C, Lapolla A. Effect of a New Formulation of Nutraceuticals as an Add-On to Metformin Monotherapy for Patients with Type 2 Diabetes and Suboptimal Glycemic Control: A Randomized Controlled Trial. Nutrients [Internet]. 2021 Jul 1 [cited 2024 Jan 6];13(7). Available from: /pmc/articles/PMC8308828/
22. Rondanelli M, Riva A, Petrangolini G, Allegrini P, Giacosa A, Fazia T, et al. Berberine Phospholipid Is an Effective Insulin Sensitizer and Improves Metabolic and Hormonal Disorders in Women with Polycystic Ovary Syndrome: A One-Group Pretest–Post-Test Explanatory Study. Nutrients [Internet]. 2021 Oct 1 [cited 2024 Jan 6];13(10). Available from: /pmc/articles/PMC8538182/
23. Panigrahi A. Open Access BMC Endocrine Disorders. [cited 2023 Dec 27]; Available from: http://creativecommons.org/licenses/by/4.0/.TheCreativeCommonsPublicDomainDedicationwaiver
24. Tong X, Xu J, Lian F, Yu X, Zhao Y, Xu L, et al. Structural Alteration of Gut Microbiota during the Amelioration of Human Type 2 Diabetes with Hyperlipidemia by Metformin and a Traditional Chinese Herbal Formula: a Multicenter, Randomized, Open Label Clinical Trial. mBio [Internet]. 2018 May 1 [cited 2024 Jan 16];9(3). Available from: /pmc/articles/PMC5964358/

25. Ilyas Z, Perna S, Al-thawadi S, Alalwan TA, Riva A, Petrangolini G, et al. The effect of Berberine on weight loss in order to prevent obesity: A systematic review. Biomedicine & Pharmacotherapy. 2020 Jul 1;127:110137.
26. Guo HH, Shen HR, Wang LL, Luo ZG, Zhang JL, Zhang HJ, et al. Berberine is a potential alternative for metformin with good regulatory effect on lipids in treating metabolic diseases. Biomedicine & Pharmacotherapy. 2023 Jul 1;163:114754.
27. Rondanelli M, Gasparri C, Petrangolini G, Allegrini P, Avenoso D, Fazia T, et al. Berberine phospholipid exerts a positive effect on the glycemic profile of overweight subjects with impaired fasting blood glucose (IFG): a randomized double-blind placebo-controlled clinical trial. Eur Rev Med Pharmacol Sci [Internet]. 2023 Jul 1 [cited 2024 Jan 6];27(14):6718–27. Available from: https://pubmed.ncbi.nlm.nih.gov/37522683/
28. Zhao MM, Lu J, Li S, Wang H, Cao X, Li Q, et al. Berberine is an insulin secretagogue targeting the KCNH6 potassium channel. Nat Commun [Internet]. 2021 Dec 1 [cited 2024 Jan 6];12(1). Available from: /pmc/articles/PMC8460738/
29. Tuttle KR, Agarwal R, Alpers CE, Bakris GL, Brosius FC, Kolkhof P, et al. Molecular mechanisms and therapeutic targets for diabetic kidney disease. Kidney Int. 2022 Aug 1;102(2):248–60.
30. Gong L, Wang R, Wang X, Liu J, Han Z, Li Q, et al. Research progress of natural active compounds on improving podocyte function to reduce proteinuria in diabetic kidney disease. Ren Fail [Internet]. 2023 Dec 22 [cited 2024 Jan 9];45(2):2290930. Available from: https://www.tandfonline.com/doi/abs/10.1080/0886022X.2023.2290930