MiniReview

Benefits of Puerarin in Attenuating Various Diseases

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Abstract

Puerarin, an isoflavone derivative isolated from the traditional Chinese medicine Pueraria lobata, has garnered significant attention from researchers due to its potential health benefits. In recent years, there have been many studies on puerarin, but there are few reviews on puerarin. This article aims to introduce the pharmacological effects of puerarin, points out the shortcomings of existing research, and puts forward future research directions.

Keywords: puerarin, cardiovascular disease, benefits


1 INTRODUCTION

Pueraria is a kind of natural medicine and food plant. Moreover, Pueraria lobata holds the highest medicinal value, initially documented in Shen Nong’s Herbal Classic and Compendium of Materia Medica. The primary component of Pueraria lobata possessing medicinal value is puerarin, a bioactive isoflavone glycoside. Recently, puerarin has been shown in studies to have a strong effect on a variety of cancers, cardiovascular disease (CVD), liver diseases, obesity, neurodegenerative diseases, and renal diseases. Various diseases may benefit from either singular medication or a combination of medications.

Puerarin (7’, 4’-dihydroxy-8-C-glucosyl isoflavone, C21H22O9, Figure 1), appears as white needle-like crystals. Puerarin is slightly soluble in water, with its solubility is only 6.24g/L at room temperature (25°C), and readily dissolves in substances like methanol and ethanol, etc. With modern medical development, the medicinal functions and pharmacological effects of puerarin have been gradually confirmed. At present, puerarin has found widespread application in the clinical treatment of conditions such as hypertension, coronary heart disease, diabetes, gastric cancer, intestinal cancer, and other diseases. It has been formulated into tablets,
capsules, granules, injections, emulsions, and pellets. However, the underlying mechanisms of puerarin in disease regulation remain unknown. Here, we summarize the functions of puerarin and discuss its underlying mechanisms in various diseases, which will serve as a theoretical foundation for future research.

2 PUERARIN AND CVD

CVD has become the leading cause of death due to disease in the world, and the number of patients is increasing annually, imposing a substantial medical burden on society. It is very important to search for new prevention and treatment methods. Studies have reported that puerarin could improve various CVDs.

2.1 Hypertension

Hypertension is a prevalent chronic condition classified as a metabolic disease. Sustained high blood pressure can damage multiple target organs such as the heart, kidney, and brain. Additionally, it contributes to metabolic dysfunction and significantly increases the risk of CVDs. Its complex etiology and pathology lead to high disability and mortality rates, posing a serious threat to people’s health due to complications. Multiple studies have demonstrated the vasodilatory and antihypertensive effects of puerarin. Yan et al.\(^1\) declared that puerarin can alleviate myocardial remodeling in spontaneously hypertensive rats, lower reactive oxygen species (ROS) levels, restore Matrix metalloproteinase (MMP) levels, and reduce Ca\(^{2+}\) overload. Puerarin may decrease TRPC6 expression and inhibit NFATc3 nuclear translocation by reducing CaN activity. Puerarin, as a TRPV4 agonist, caused endothelium-dependent vasodilation in mouse mesenteric arteries, lowering blood pressure in high-salt-induced hypertensive mice, according to Zhou et al.\(^3\). Through a patch clamp experiment, puerarin stimulated TRPV4-mediated cation currents and induced relaxation in mouse mesenteric arteries by engaging the TRPV4-small-conductance Ca\(^{2+}\)-activated K\(^+\) channel (SKCa) / intermediate-conductance K\(^+\) channel (SKi). Ca\(^{2+}\)-activated K\(^+\) channel (IKCa) pathway can reduce systolic blood pressure in hypertensive mice. Tan et al.\(^3\) found that puerarin may be utilized as a new antihypertensive drug, and its suppression of the NF-κB/JNK and ERK1/2 pathways may be one of the underlying mechanisms. Puerarin enhances acetylcholine- and insulin-mediated vasorelaxation and insulin-stimulated Akt/NO signaling to suppress the NF-κB inflammatory pathway, thereby inhibiting the insulin-activating PI3K/eNOS pathway by resulting in the phosphorylation of the insulin receptor substrate (IRS) 1 at serine residues when vascular insulin signaling is impaired. Li et al.\(^4\) investigated that puerarin has a positive effect on the circulatory system in rats with hypertension brought on by Ang II. This effect may be partly attributed to its antioxidant properties and an increase in phosphorylated eNOS. Puerarin could enhance endothelium-dependent relaxation and correct the Ang II-induced alterations in the protein expression of the certain molecules. Shi et al.\(^5\) found that puerarin is a potential antihypertensive agent, causing a reduction in rats’ heart rates while increasing NO and cGMP levels. The mechanism through which puerarin lowers blood pressure involves eNOS as a primary target. High doses of puerarin increased the phosphorylated eNOS protein while reducing the levels of AT1 and Cav1.

2.2 Myocardial Infarction and Myocardial Ischemia-Reperfusion

Myocardial infarction is one of the leading causes of death in patients with coronary heart disease all over the world. Early treatment of acute myocardial infarction restores blood supply to the ischemic myocardium and reduces the risk of death. When the interrupted myocardial blood supply is restored within a certain time frame, however, it causes more severe damage to the original ischemic myocardium; this is known as myocardial ischemia / reperfusion injury (MIRI). The pathophysiology of MIRI is linked to oxidative stress, intracellular calcium overload, energy metabolism disorder, apoptosis, endoplasmic reticulum stress, autophagy, pyroptosis, necroptosis, and ferroptosis. These mechanisms interact, exacerbating their effects either directly or indirectly. While apoptosis and autophagy historically received more attention, necroptosis and ferroptosis also hold significant roles. Several studies have shown that puerarin decreased apoptosis, ferroptosis, and inflammation. Guo et al.\(^6\) declared that puerarin effectively decreased the myocardial infarct area and raised the left ventricular developed pressure in diabetic rats with myocardial I/R. It also lowered oxidative stress, inflammation, and NF-κB protein expression. Additionally, puerarin increased nitric oxide generation, expression of phosphorylated endothelial nitric oxide synthase protein, and decreased the caspase-3 activity. It also activated the levels of VEGFA and Ang I protein expression. Puerarin could help diminish diabetic rats with myocardial I/R injury by upregulating VEGFA/Ang I and suppressing apoptosis. Ding et al.\(^7\) declared that puerarin possesses therapeutic potential for treating acute myocardial infarction. Pretreatment with puerarin significantly reduced infarct size in I/R mice, as well as the activities of myeloperoxidase and cardiac enzymes such as CK-MB, AST, and LDH. Puerarin inhibited ferroptosis and inflammation by reducing MDA and 4-HNE.
synthesis, increasing PTGS2 mRNA expression, and decreasing PTGS2 protein expression while increasing GPX4 protein expression. Zhao et al.\textsuperscript{[8]} found that in the mouse MI-RI model, puerarin effectively reduced myocardial infarct size and LDH release. This reduction correlated with decreased levels of COX2, galectin-3, and cleaved PARP-1 protein, alongside a decrease in LDH release. Puerarin may lessen myocardial damage by encouraging protein SUMOylation through an ER/ERK/SUMO2-dependent pathway. Han et al.\textsuperscript{[9]} suggested that puerarin significantly protected cardiomyocytes damaged by H/R. Through controlling autophagy-related genes and suppressing cardiomyocyte autophagy, puerarin increased cardiomyocyte survival, inhibited cardiomyocyte apoptosis, and decreased LDH, MDA levels, and myocardial damage. Aside from improving myocardial fibers, puerarin also has a cardioprotective impact by affecting the sodium-potassium pump and calcium ion channels. This, in turn, controls the PI3K/Akt, NF-κB, and caspases signaling pathways, minimizing cardiovascular damage brought on by inflammation, oxidative stress, and apoptosis. Wang et al.\textsuperscript{[10]} declared that puerarin could alleviate structural damage and dysfunction in the heart, significantly reducing myocardial infarct size, serum CK-MB activity, and apoptotic cell death. Puerarin protected against MI/R injury most likely through the SIRT1/NF-κB pathway which could reduce inflammatory responses.

2.3 Cardiac Hypertrophy
Cardiac hypertrophy is the abnormal thickening or enlargement of the myocardium resulting from changes in cardiomyocyte size and other myocardium components such as extracellular matrix. According to research findings, puerarin could enhance mitochondrial function and decrease the mRNA expression of genes associated with heart hypertrophy. Sun et al.\textsuperscript{[11]} demonstrated that puerarin works well to increase cardiomyocyte viability and improve mitochondrial function. It reduces cellular inflammation by preventing NLRP3-caspase-1-GSDMD-mediated pyroptosis in RAW264.7 cells and H9C2 cells. During dilated cardiomyopathy, puerarin successfully controlled the pyroptosis signaling pathway, and this control was linked to the P2X7 receptor. Wang et al.\textsuperscript{[12]} suggested that pre-treatment with puerarin could potentially serve as a therapeutic approach for controlling and preventing ISO-induced myocardial hypertrophy (MH) in the future. The protective effects of puerarin against MH are evidenced by significantly decreased levels of mRNA and protein expression related to MH biomarkers such as atrial and brain natriuretic peptides. Puerarin effectively inhibited p65 phosphorylation and suppressed the activation of the Wnt signaling pathway, thereby mitigating the symptoms of MH induced by ISO. Ye et al.\textsuperscript{[13]} declared that puerarin inhibited MH in the TAC model, controlling the lncRNAs / mRNAs co-expression network to have positive effects on cardiac hypertrophy. Puerarin reduced cardiac hypertrophy by controlling the AMPK, mTOR, and Nrf2 pathways. Hou et al.\textsuperscript{[14]} stated that puerarin may improve heart function in cardiac hypertrophy patients. Nuclear respiratory factor 1, estrogen-related receptor, and mitochondrial transcription factor A were all highly upregulated in hearts after puerarin administration. Puerarin decreased Ang II’s ability to cause the accumulation of NEFAs and the deletion of ATP and mitochondrial membrane potential. Through the stimulation of the PPARGC1A pathway and control of energy metabolism, puerarin inhibits heart hypertrophy in AACC-treated OVX rats. Zhao et al.\textsuperscript{[15]} suggested that puerarin significantly helped Nrf2 nuclear accumulation, reduced Keap1 levels in the heart, and increased downstream proteins in combination to substantially diminish ventricular hypertrophy. Zhang et al.\textsuperscript{[16]} declared that puerarin reduced heart hypertrophy and elevated expression of miR-15b and miR-195 in primary cardiomyocytes. Puerarin could decrease the rate of protein synthesis. It also decreased the mRNA expression of heart hypertrophic genes and the amount of cell surface area. Liu et al.\textsuperscript{[17]} suggested that puerarin dramatically increased the rate of phosphorylation of AMPK, which further decreased the expression of the mTOR target proteins S6 ribosomal protein and 4E-binding protein 1.

2.4 Atherosclerosis
Coronary heart disease, cerebral infarction, and peripheral vascular disease are all primarily brought on by atherosclerosis. Atherosclerosis is the term used to describe the yellow, atheromatous look of the lipids that build up in the lining of the arteries. Puerarin decreased the P264X7R expression which was enhanced by high concentrations of free fatty acids (FFA) in RAW2.4 macrophages. It prevented the high FFA-induced mRNA expression of calcium ion current, ERK phosphorylation, TNFα, and iNOS. These results showed that puerarin inhibited P2X4R-mediated inflammation to prevent the inflammatory reaction linked to high plasma FFA levels\textsuperscript{[18]}. Puerarin reduced atherosclerotic lesions in ApoE−/− mice by inhibiting monocyte adhesion both in vitro and in vivo; its protective effect is mediated by activation of the ERK5/KLF2 signaling pathway\textsuperscript{[19]}. Puerarin inhibited the expression of tissue factors in HUVECs by stimulating the PI3K/Akt/endothelial nitric oxide synthase signaling pathway and preventing the activation of ERK1/2 and NF-κB. These findings suggest that puerarin has anticoagulant properties and may represent a promising new therapeutic option for the treatment of coronary thrombosis\textsuperscript{[20]}. The capacity of puerarin to control the NF-κB signaling pathway may be connected to puerarin’s inhibitory action on atherosclerosis\textsuperscript{[21]}.  

2.5 Diabetic Cardiomyopathy (DCM)
Diabetes has many consequences, one of which is DCM. One of the potential causes of DCM is inflammation\textsuperscript{[22]}. The present investigation supports that puerarin-V ameliorates cardiac function, and mitochondrial respiratory
function, reduces oxidative stress, decreases cardiac inflammation, and ameliorates localized death in DCM rats\cite{23}. Sonodynamic therapy utilizes an ultrasonic sulfur hexafluoride microbubble contrast agent, which is enriched with geranylglycerol, to augment targeted drug administration and pharmacodynamics for the treatment of DCM. Puerarin microbubbles (PMBs) significantly improved HUVEC migration, according to a test on wound healing. When compared to the DCM model group, histological and physiological changes in the treated group demonstrated a significant therapeutic effect of PMBs\cite{24}. The pathophysiology of DCM, including that brought on by high glucose and high lipid (HGHL), is heavily dependent on inflammation. Puerarin has been demonstrated to reduce the HGHL-induced hypertrophy, apoptosis, and cardiomyocyte inflammation\cite{25}.

3 PUIERARIN AND CANCER

An increasing amount of research shows that puerarin prevents the development, survival, and metastasis of several tumor cell types.

3.1 Lung Cancer

Lung cancer is the primary cause of death due to cancer globally and non-small cell lung cancer (NSCLC) accounts for more than 85% of those cases\cite{26}. Only 26% of patients diagnosed with NSCLC survive for more than 5 years\cite{27}, thus, it is necessary to find more effective therapeutic modalities for NSCLC. Currently, it is found that puerarin may slow down the development of NSCLC cells and trigger apoptosis, according to several researches\cite{28}. The underlying mechanisms might involve downregulating DTL upregulating miR-490\cite{29} and regulating the miR-342/CCND1 axis\cite{30}. Moreover, a recent study revealed that PRN-5FU NMs, which included both puerarin (PRN) and 5-fluorouracil, significantly increased the amount of apoptosis in human lung cell lines HEL-299 and A549\cite{31}. A different study revealed that puerarin 6”-O-xyloside (PXY) can inhibit lung cancer stem-like cells (LCSLCs) characteristics, suggesting that it might be a suitable drug for treating lung cancer by eradicating LCSLCs\cite{32}. Furthermore, previous research has shown that puerarin can enhance the anticancer effects of macropheage populations by shifting them back to the M1 subgroup\cite{33}. These research results give us fresh perspectives on how puerarin can be used in combination with other medications to treat malignancies.

3.2 Ovarian Cancer (OC)

OC is the second most common cause of gynecologic cancer death among women worldwide. For decades, OC survival rates have only slightly changed in both developing and developed countries. In an animal model, deregulated WNT/β-catenin has been linked to the emergence of murine malignancies that resemble human endometrioid OC\cite{34}. Recent fundamental research found that puerarin increased the apoptosis of platinum-resistant OC cells, the downregulation of SIRT1 and subsequent suppression of WNT/β-catenin signaling are two factors that contribute to this process\cite{35}, but the mechanisms needed further investigation. In addition, according to the newest study, puerarin therapy drastically reduced OC cell viability, proliferation, and cell apoptosis. It also increased the expression of tumor suppressor genes in vitro and in vivo\cite{36}. These findings might offer clues for novel OC treatments.

3.3 Bladder Cancer

Bladder cancer is one of the most common types of cancer around the world. The findings on bladder cancer have started to surface in recent years\cite{37}. Based on several previous studies, puerarin inhibited cell viability and proliferation and encouraged cell apoptosis in T24 cells, also, deactivated the NF-κB signaling pathway via upregulation of miR-16\cite{38}. The suppression of SIRT1/p53 signaling pathway is thought to be a potential mechanism\cite{39}. Recently, a study indicated that puerarin controls the circ_0020394/miR-328-3p/NRBP1 axis to inhibit cell viability, migration, invasion, and glycolysis while promoting apoptosis in bladder cancer\cite{40}. More research into additional uses for puerarin will be promising in the future.

4 PUERARIN AND RENAL DISEASES

Puerarin, a drug that inhibits autophagy activation, has been shown to protect renal tubular epithelial cells from damage caused by calcium oxalate crystals. The study found that puerarin significantly attenuated CaOx crystal-induced autophagy and cytotoxicity by altering SIRT1 expression. The protective effect was related to the SIRT1/AKT/p38 signaling pathway, suggesting potential therapeutic targets for treating nephrolithiasis\cite{41}. End-stage renal disease (ESRD) is primarily caused by diabetic nephropathy (DN), a microvascular complication affecting diabetic patients. DN morbidity and mortality have increased in developing nations. Chronic inflammation and fibrosis are common pathways for DN development in ESRD. puerarin, an active ingredient in kudzu vine root, reduces apoptosis and prevents cadmium-induced damage. Standard puerarin (SP), discovered in the 1990s, has been shown to reduce inflammatory factors, alleviate diabetes-related symptoms, and lower TNF-α levels in fat rats. It can also reduce blood glucose and lipid levels, mitigate renal damage, and inhibit INF-γ and TGF-β1 expression. SP can also relieve renal tissue damage in diabetic rats by up-regulating miRNA-140-5p\cite{42}.

Puerarin has also been studied for its effect on calcium signaling in renal cells. The study found that puerarin-induced calcium rises in MDCK renal tubular cells, which were reduced by removing extracellular Ca\cite{43}. Treatment with endoplasmic reticulum Ca pump inhibitors or phospholipase C inhibitors partially inhibited puerarin-
induced calcium rises. Puerarin, a drug that inhibits autophagy activation, protects renal tubular epithelial cells from calcium oxalate crystal damage. It alters SIRT1 expression, reducing autophagy and cytotoxicity. Puerarin also reduces apoptosis and prevents cadmium-induced damage in the kudzu vine root. It also targets the miR-342-3p/TGF-β/SMAD axis[46].

5 PUERARIN AND LIVER DISEASES

Alcoholic liver disease (ALD) is a growing global health concern, with steatosis and steatohepatitis as early pathogenesis. Puerarin, an isoflavone derived from Pueraria lobata, was found to have cardioprotective, neuroprotective, anti-inflammatory, and antioxidant properties, which improved the ALD effect. A study using the NIAAA model and ethanol-induced AML-12 cells explored puerarin’s protective effect on ALD, showing it attenuated EtOH-induced liver injury and inhibited levels of SREBP-1c, TNF-α, IL-6, and IL-1β. Puerarin might suppress liver lipid accumulation and inflammation by regulating MMP8, making it a promising clinical candidate for ALD treatment[47].

Nonalcoholic fatty liver disease (NAFLD) is a global public health issue with a prevalence rate of 25.24% among adults. Puerarin, a natural antioxidant, has been reported to lower serum lipids, but its specific mechanism of action is not well understood due to its complexity[48]. A study evaluating the preventive effects of two doses of puerarin on high-fat and high-fructose diet-induced NAFLD in rats found that puerarin ameliorated lipid levels in the serum and liver, reduced the expression of hepatic lipid accumulation in NAFLD rats, increased levels of antioxidant markers, decreased the content of inflammatory factors, and improved liver function[49]. Liu et al. [50] declared that Puerariae Lobatae radix flavonoids (PLF) and puerarin have anti-alcoholic liver injury effects in zebrafish. They alleviate hepatic steatosis and regulate alcohol and lipid metabolism. The study suggests that puerarin may be the main active component of PLF. The underlying mechanism involves the regulation of the AMPKα-ACC signaling pathway. These findings provide insights into potential therapeutic compounds for the treatment of ALD.

6 PUERARIN AND OBESITY

Puerarin has anti-inflammatory and lipid-lowering effects in obese mice. It regulates macrophages and TNF-α in adipose tissue, leading to reduced fat accumulation, improved lipid metabolism, and decreased inflammation. Puerarin shows potential as a treatment for obesity and its related complications by modulating ATM-induced inflammation through the TNF-α/NF-κB pathway[51]. Wang et al. [52] demonstrated that puerarin has a beneficial effect on body weight, insulin levels, and glucose homeostasis in mice fed a high-fat diet. This effect is associated with an increase in the abundance of Akkermansia muciniphila in the gut microbiota. The study suggests that puerarin may be useful in preventing obesity and improving intestinal integrity through its regulatory effects on the gut microbiota and gut epithelial cells. Xu et al. [53] found that puerarin has the potential to therapeutically improve hepatic glucose and lipid homeostasis. The study demonstrated that puerarin can prevent hepatic insulin resistance and steatosis both in vitro and in vivo. The protective effects of puerarin are mediated through the regulation of the AMPK pathway. Puerarin improves hepatic insulin sensitivity by modulating the AMPK/Akt pathway and reduces hepatic steatosis by inhibiting the expression of lipogenic genes via the AMPK/ACC pathway.

7 PUERARIN AND OTHERS

7.1 Osteoporosis

Osteoporosis is a systemic metabolic bone disease characterized by bone microstructure degradation and a loss in bone mass and bone quality. Many studies have confirmed that puerarin could promote the proliferation of bone marrow mesenchymal stem cells and differentiate into osteoblasts, which plays an important role in balancing bone metabolism and maintaining the stability of bone structure[54]. Puerarin therapy altered the endogenous metabolic profiles of ovariectomized rats, eliciting antiosteoporosis and anti-hyperlipidemic benefits from a new serum metabolomics viewpoint. The key metabolic aspects of metabolic profiles after puerarin administration in ovariectomized rats were phospholipid metabolism represented by LysOPE and S1P, and PUFA production represented by n-3 and n-6 PUFAs. Puerarin reduces osteoclastogenesis by reducing intracellular ROS levels through the inhibition of NOX1 and the enhancement of antioxidant enzymes such as HO-1, which in turn inhibits the activation of the MAPK and NF-B signaling pathways[55]. Puerarin can be combined with various composite scaffolds, and remarkable results have been achieved in animal experiments. It not only provides a scientific basis for the treatment of osteoporosis and bone defect-related diseases, but also broads the medicinal value and clinical application of puerarin.

7.2 Puerarin and Alzheimer’s Disease

Puerarin has good anti-Alzheimer’s disease potential, wherein puerarin plays an anti- Alzheimer’s disease role by maintaining brain synaptic plasticity[56]. Liu et al. [57] found that puerarin has the potential to penetrate the blood-brain barrier and has high stability in molecular docking and kinetic simulation with acetylcholinesterase (AChE), cyclooxygenase-2, and caspase-3, which play a central role in the occurrence and development of Alzheimer’s disease. This component can inhibit AChE activity in vivo, restore the activity of antioxidant defense substances to normal levels, reduce the expression of inflammatory factors and apoptosis genes in the brain,
and down-regulate the expression of cyclooxygenase-2, and caspase-3, indicating that this component can prevent and alleviate Alzheimer’s disease.

7.3 Puerarin and Bowel Disease

Jeon et al.\cite{56} used a mouse model of DSS-induced colitis. Puerarin treatment reduced colon shortening, pathological damage to the colon, and myeloperoxidase activity. Puerarin significantly reduced inflammation by inhibiting NF-κB and pro-inflammatory mediator secretion. Furthermore, puerarin demonstrated anti-oxidative effects by modulating the expression of the NF-E2 p45-related factor 2 (Nrf2) pathway and antioxidant enzymes. Puerarin inhibited intestinal epithelial barrier dysfunction by increasing tight junction protein expression. These findings indicate that puerarin has anti-inflammatory and anti-oxidative properties in a mouse model of colitis. Puerarin was found to be effective in reversing abdominal pain and diarrhea in rats with irritable bowel syndrome. The therapeutic effect was achieved by regulating the richness of the gut microbiota in order to maintain the intestinal micro-ecology’s stability. Furthermore, the suppressed expression of corticotropin-releasing hormone receptor 1 may be related to the activity of the hypothalamic-pituitary-adrenal axis. At the same time, intestinal function was improved by increasing colonic epithelial cell proliferation by upregulating p-ERK/ERK expression and repairing the colonic mucus barrier by upregulating occludin expression\cite{57}. All of these findings indicate that puerarin may have excellent therapeutic effects on irritable bowel syndrome.

8 CONCLUSION

Puerarin is an isoflavone component extracted from Pueraria lobata root, which has rich sources, mature extraction technology, extensive pharmacological effects and many clinical applications. At present, the research on puerarin in cardiovascular and cerebrovascular, hypertension, tumor, DN and other aspects of body protection is more in-depth and detailed (Figure 2). With the development of science and technology and the advancement of the professional field, it is possible to develop drugs that are truly suitable for patients when strengthening the clinical research of puerarin, so as to solve the clinical practical problems.

Except for gastrointestinal symptoms, headache, dizziness, and leukocytopenia, puerarin caused few adverse reactions in clinical trials\cite{58}. However, puerarin has the potential to cause hemolysis. Puerarin-induced hemolysis was concentration and time-dependent when human erythrocytes were incubated in saline containing more than 2mM puerarin for more than 2h\cite{59}. Puerarin can cause low blood pressure in healthy people, resulting in dizziness, fainting, and other unpleasant symptoms. Furthermore, puerarin may interact with certain medications, resulting in decreased efficacy or exacerbation of adverse reactions. Puerarin, for example, can reduce the efficacy of some drugs by activating the CYP450 enzyme and decreasing the concentration of some drugs\cite{60}. As a result, while using puerarin, keep an eye out for drug interactions and adjust the medication regimen as needed.

Puerarin-related formulations such as emulsions, pellets, cyclodextrin inclusion complexes, solid dispersions, dispersions, liposomes, and nanoparticles have been increasingly used in basic research and clinical applications in recent years, in addition to conventional formulations such as

![Figure 2. The effect of puerarin.](https://doi.org/10.53964/jmpp.2024002)
capsules, granules, soft capsules, and injections. Because puerarin is slightly soluble in water, we can study the targeted therapy of other pathways, signals, and targets in the future based on the specific mechanism of pharmacological action of puerarin, to develop corresponding targeted preparations for clinical treatment that are more comprehensive, rapid, and effective. Furthermore, additional research on puerarin’s other pharmacological activities can serve as a reference for the rational development and clinical application of puerarin.

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Conflicts of Interest
The authors declared no conflict of interest.

Author Contribution
Wang Z and Gu J contributed equally to this work. Zhang L conceptualized and reviewed the manuscript. Wang Z, Zhou Y, Zhu L, Hu W, and Cui C drafted the manuscript. Gu J, Zhang Q, and Sun J did the manuscript revision work and proofread the article. All authors contributed to the manuscript and approved the final version.

Abbreviation List
AChE, Acetylcholinesterase
ALD, Alcoholic liver disease
CVD, Cardiovascular disease
DCM, Diabetic cardiomyopathy
DN, Diabetic nephropathy
ESRD, End-stage renal disease
FFA, Free fatty acids
HGHL, High glucose and high lipid
LCSLCs, Inhibit lung cancer stem-like cells
MMP, Matrix metalloproteinase
MH, Myocardial hypertrophy
MIRI, Myocardial ischemia/reperfusion injury
NAFLD, Nonalcoholic fatty liver disease
NSCLC, Non-small cell lung cancer
OC, Ovarian cancer
PLF, Puerariae Lobatae radix flavonoids
PMBs, Puerarin microbubbles
ROS, reactive oxygen species
SP, Standard puerarin

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