MEDS Chinese Medicine (2024)
Clausius Scientific Press, Canada

DOI: 10.23977/medcm.2024.060415
ISSN 2616-1753 Vol. 6 Num. 4

Comprehensive Advances in the Pharmacological Research of Chinese Herbal Medicine: Eucommia Ulmoides

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Keywords: Eucommia ulmoides; pharmacological effects; osteoporosis; antitumor; antihypertensive

Abstract: Eucommia ulmoides, a plant of the Euphorbiaceae family, has been widely used as a traditional Chinese medicine in the medical field. The author reviewed relevant literature from the past two decades, focusing on the pharmacological effects of Eucommia ulmoides in the areas of anti-osteoarthritis, osteoporosis, antihypertensive, hypoglycemic, antioxidant, and antitumor activities. Significant advances have been observed in the pharmacological research related to osteoporosis, osteoarthritis, and antitumor effects. However, further exploration is needed in the areas of anti-obesity, immune modulation, and sedative-hypnotic effects. Therefore, this article aims to lay the groundwork for the development of new drugs from Eucommia ulmoides by elucidating its molecular mechanisms that promote health.

Chinese herbal medicine Eucommia ulmoides (Du Zhong) was first recorded in the Shen Nong Ben Cao Jing (Shen Nong's Classic of Materia Medica). It is the dried bark of the Eucommia ulmoides Oliv. tree, belonging to the family Eucommiaceae. Du Zhong is known for its properties of tonifying the liver and kidneys, strengthening tendons and bones, and stabilizing pregnancy. It is commonly used to treat conditions such as liver and kidney deficiency, lower back and knee soreness, weakness of tendons and bones, dizziness, and pregnancy-related bleeding or fetal restlessness[1].Traditional Chinese medicine research has demonstrated that Du Zhong possesses effects such as strengthening the kidneys and lumbar region, dispelling wind and dampness, and stabilizing pregnancy. It is widely used in treating symptoms like cold pain in the waist and knees, muscular weakness, pregnancy bleeding, and fetal instability. In recent years, with the advancement of research by domestic and international scholars on the chemical constituents, pharmacological activities, and clinical applications of Du Zhong, over 100 active chemical components have been identified. These discoveries provide strong theoretical support for its clinical and pharmacological applications. This article, based on recent literature, reviews the pharmacological effects of Du Zhong, focusing on its roles in osteoporosis, osteoarthritis, blood pressure reduction, lipid-lowering, blood glucose

regulation, anti-tumor activities, and antioxidant properties.

1. Treatment of Osteoporosis and Osteoarthritis

1.1 Osteoporosis (OP)

Osteoporosis (OP) is a metabolic bone disease characterized by decreased bone mass and disruption of bone microarchitecture, leading to increased bone fragility and susceptibility to fractures[2]. OP not only reduces patients' quality of life but can also pose a serious threat to their survival in severe cases, imposing a significant burden on society. Due to the relatively mild side effects of herbal medicines, they have gained attention from researchers and high recognition from patients worldwide. Studies have shown that three flavonoid components in Eucommia ulmoides—kaempferol, quercetin, and rutin—exhibit anti-osteoporotic effects[3]. Tan et al.[4] isolated 5-hydroxymethylfurfural from the cortex of Eucommia ulmoides and subsequently confirmed its role as an enhancer of osteoblast generation.

In experiments using osteoporotic rat models, administration of Du Zhong Jian Gu Fang (a bone-strengthening formula containing Eucommia ulmoides) through intragastric treatment increased bone mineral density in rats. The results suggest that Du Zhong Jian Gu Fang can act on the Wnt/β-catenin signaling pathway to treat OP [5].Clinical applications of Du Zhong Yao Tong Wan (a lumbar pain formula) and Quan Du Zhong capsules have shown that these formulations can increase bone density, regulate blood calcium and phosphorus levels, and affect bone metabolism, thereby exerting therapeutic effects on OP[6].

1.2 Treatment of Osteoarthritis (OA)

The therapeutic effects of Eucommia ulmoides on osteoarthritis (OA) are also noteworthy. Zhou Chengyan et al.[7] found that the water extract of Eucommia ulmoides could inhibit the exudation of inflammatory substances caused by inflammatory stimuli, with the anti-inflammatory effect in the high-dose group comparable to that of aspirin. Another study investigated the effects of aucubin, a compound from Eucommia ulmoides, on the proliferation and apoptosis of OA chondrocytes. The results showed that the aucubin-treated group significantly promoted the proliferation of OA chondrocytes and inhibited their apoptosis compared to the control group[8].Sun et al.[9] used an MTT assay to assess the appropriate concentrations of Eucommia ulmoides polysaccharides (EUP). Rabbits were divided into a sham operation group, an OA group, and an EUP group. The results demonstrated that EUP at concentrations of 50 μg/mL or 100 μg/mL promoted macrophage proliferation. One potential mechanism for delaying OA progression could be related to the polarization state of macrophages, providing theoretical and experimental support for future studies on the mechanisms and pharmacological effects of EUP. Additionally, in clinical applications, it was observed that combining compound Du Zhong Jian Gu granules with glucosamine sulfate capsules effectively improved OA symptoms in patients[10].

2. Effects on Blood Pressure, Lipid Levels, and Blood Glucose

2.1 Blood Pressure-Lowering Effect

In recent years, Eucommia ulmoides has gained significant attention from researchers due to its efficient antihypertensive effects and lack of toxic side effects. It has been confirmed that compounds such as caffeic acid, geniposidic acid, and rutin in Eucommia ulmoides contribute to its blood pressure-lowering properties[11].

A study using water extracts of male flowers from Eucommia ulmoides to treat spontaneously hypertensive rats showed that the extract achieved antihypertensive effects by regulating angiotensin-converting enzyme 2 (ACE2) in a dose-dependent manner[12].

2.2 Lipid-Lowering Effect

Over the past two decades, blood lipid levels among the Chinese population have shown a continuous upward trend, and hyperlipidemia (HLP) has become one of the major risk factors for cardiovascular diseases. Consequently, finding safe and effective treatments has been a research priority.

Studies have shown that the total flavonoids in Eucommia ulmoides leaves can significantly reduce serum levels of total cholesterol, triglycerides, lipoproteins, apolipoprotein B, and low-density lipoprotein cholesterol in hyperlipidemic rats, while significantly increasing high-density lipoprotein cholesterol and apolipoprotein A levels, thus achieving excellent lipid-lowering effects[13]. Additionally, chlorogenic acid from Eucommia ulmoides can effectively reduce liver lipid levels and blood lipid concentrations, showing significant regulation of lipid metabolism[14].

2.3 Blood Glucose-Lowering Effect

China has a high prevalence of diabetes, and in recent years, traditional Chinese medicine (TCM) approaches for the treatment and prevention of diabetes have become increasingly popular.In one study, researchers investigated the hypoglycemic effects of Eucommia ulmoides on diabetic mice induced by streptozotocin. Blood glucose levels were monitored, and fasting serum insulin (FNS) levels were measured using radioimmunoassay. The insulin sensitivity index (ISI) was then calculated. The results showed that water extracts of Eucommia ulmoides significantly reduced blood glucose levels and improved insulin sensitivity in the mice[15].Similarly, Liu Guorong et al.[16] found in their experimental study that Eucommia ulmoides polysaccharides also exhibited excellent hypoglycemic effects in diabetic mice.

3. Antitumor and Antioxidant Effects

3.1 Antitumor Effects

The promotion of tumor cell apoptosis by natural small-molecule compounds forms the foundation for antitumor drug development. In recent years, with deeper insights into tumor biology and pharmacology, the mechanisms and effects of natural small-molecule compounds in cancer treatment have gained significant attention. Qian Wendan et al.[17] found that pentacyclic triterpenoids in Eucommia ulmoides exhibit significant antitumor activity. The mechanism involves inhibiting lysosome formation in tumor cells and inducing mitochondrial fragmentation. Additionally, other studies revealed that aucubin has a dose-dependent inhibitory effect on the proliferation of non-small cell lung cancer cells. It achieves this by arresting the cell cycle of A549 human alveolar basal epithelial cells at the G0/G1 phase, thereby promoting apoptosis[18]. These findings highlight the exploratory potential of Eucommia ulmoides in inhibiting tumor cell growth.

3.2 Antioxidant Effects

During normal metabolic processes, body cells generate free radicals and also produce antioxidants to neutralize them. However, when this dynamic balance is disrupted, oxidative reactions occur, which are linked to nearly all diseases. Yu Feng et al.[19] extracted chlorogenic acid from

Eucommia ulmoides leaves using ultrasound-assisted natural deep eutectic solvents (NADES). Subsequent research confirmed that chlorogenic acid extracted via NADES exhibits significant antioxidant activity, with free radical scavenging effects positively correlated with its concentration within a certain range. Oxidative stress can independently promote the onset and progression of liver fibrosis. It can also interact with other pathological processes such as inflammation, apoptosis, and autophagy, thereby influencing the occurrence and outcome of liver fibrosis[20].

4. Other Effects

4.1 Antibacterial and Antiviral Effects

Chlorogenic acid in Eucommia ulmoides has been found to possess diverse antibacterial properties. According to relevant studies[21], it exhibits bactericidal effects against Helicobacter pylori, Klebsiella pneumoniae, Staphylococcus aureus, and Staphylococcus epidermidis. Additionally, Eucommia ulmoides leaf extracts have been shown to effectively inhibit Aspergillus flavus and Aspergillus niger[22].

4.2 Sedative and Hypnotic Effects

Li et al.[23] discovered that alcohol extracted from Eucommia ulmoides male flowers using systematic solvent methods can significantly reduce spontaneous activities in mice, lower seizure incidence, and shorten sleep latency. Furthermore, water-soluble alkaloids extracted from male flowers of Eucommia ulmoides demonstrated notable sedative and hypnotic effects in experimental studies[24].

4.3 Immunomodulatory Effects

Research has shown that polysaccharides from Eucommia ulmoides leaves can enhance immune function by increasing the phagocytosis rate of peritoneal macrophages, the clearance capacity, and the serum hemolysin levels in mice. Additionally, it boosts the thymus and spleen indices. Medium and high doses significantly raise serum levels of interleukin-4 (IL-4), interleukin-2 (IL-2), and IgG, while high doses also increase IgM levels, thereby enhancing the immune capabilities of mice[25].

4.4 Anti-Obesity Effects

In Japan, researchers[27] fractionated Eucommia ulmoides green leaf extract (EGLE) into five components using high-porous polystyrene gel, isolating geniposidic acid, acteoside, and chlorogenic acid for anti-obesity studies. Using a high-fat diet to create a metabolic syndrome mouse model, they assessed the anti-obesity effects of these compounds. The results showed that acteoside significantly inhibited increases in body weight, white adipose tissue weight, plasma triglyceride levels, and free fatty acid levels in model mice. Furthermore, Hao et al.[28] found that Eucommia ulmoides chlorogenic acid could regulate cholesterol metabolism by inhibiting HMG-CoA reductase (HMGCR) in HepG2 cells, thus preventing obesity and dyslipidemia.

4.5 Tocolytic Effects

Studies indicate that Eucommia ulmoides leaf infusions can inhibit uterine contractions in isolated rat uteri and counteract oxytocin-induced uterine contractions, demonstrating effective tocolytic properties against oxytocin-induced miscarriages in pregnant mice[28]. Lin Na et al.[29] randomly assigned patients with a history of infertility, threatened miscarriage, fetal death, or habitual abortion

to three groups: a traditional Chinese medicine treatment group (Atractylodes and Eucommia ulmoides mixture), a Western medicine treatment group (dydrogesterone), and a combined treatment group. The combined treatment group had a significantly higher cure rate compared to the other two groups, indicating that the Atractylodes-Eucommia ulmoides mixture is highly effective for such patients.

5. Conclusion

As a traditional Chinese medicinal herb, Eucommia ulmoides has long been valued by researchers and practitioners alike. To date, over 130 chemical components have been identified in Eucommia ulmoides, and investigations into its chemical composition, pharmacological effects, and clinical applications are still ongoing. However, most of the existing studies have focused on its therapeutic potential in conditions such as osteoporosis, osteoarthritis, hypertension, and hyperlipidemia, while reports on its anti-obesity, immunomodulatory, and other effects remain relatively limited. In particular, recent findings suggest that Eucommia ulmoides may play a role in the treatment of certain neurological disorders, opening new avenues for research. This review of its pharmacological effects aims to provide a reference for further studies and clinical applications of Eucommia ulmoides. With continued exploration, there is great potential to advance the modernization of traditional Chinese medicine, contributing to its vibrant development in the contemporary era.

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