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Natural Compounds from *Eucommia ulmoides* and Their Medicinal Properties

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Abstract *Eucommia ulmoides*, a traditional medicinal plant, has been widely recognized for its therapeutic applications in Chinese medicine. This study focuses on analyzing the natural compounds found in *Eucommia ulmoides* and their medicinal properties and identifies the major phytochemical classes through various extraction and analytical techniques, followed by a quantitative and qualitative analysis. The pharmacological effects of these bioactive compounds were explored, with an emphasis on their antioxidant, anti-inflammatory, cardiovascular benefits,and immunomodulatory effects. Additionally, this study investigates biosynthetic pathways and genetic engineering approaches to enhance the production of beneficial compounds. Case studies are presented to demonstrate the therapeutic use of *Eucommia ulmoides* in hypertension, diabetic,arthritis, and neuroprotection. This study compares traditional applications with modern pharmacological advancements, addressing safety concerns, industrial applications, and market potential. The findings suggest that *Eucommia ulmoides* holds significant promise for future medicinal applications, offering a bridge between traditional knowledge and modern science.
Keywords *Eucommia ulmoides*; Phytochemicals; Bioactive compounds; Medicinal properties; Pharmacological effects

1 Introduction

Eucommia ulmoides Oliv., commonly known as Dù-zhòng in Chinese, is a unique species within the Eucommiaceae family (Xie et al., 2023). This plant has been a cornerstone of traditional Chinese medicine for nearly two millennia, with its leaves, bark, seeds, and flowers being utilized to treat a variety of ailments across China, Japan, and Korea (He et al., 2014). The plant is renowned for its therapeutic properties, which include antihypertensive, antihyperglycemic, and antioxidative effects, among others (Niu et al., 2016). The traditional use of *E. ulmoides* spans a wide range of applications, from treating hypertension and diabetes to enhancing sexual function ,improved gastrointestinal function and combating osteoporosis.

Natural compounds have long been a focal point in medicinal research due to their diverse biological activities and potential therapeutic benefits. The phytochemical constituents of *E. ulmoides*, such as lignans, iridoids, flavonoids, and phenolics, have been extensively studied for their pharmacological properties (Zhu and Sun, 2018). These compounds exhibit a broad spectrum of bioactivities, including anti-inflammatory, antioxidant, and neuroprotective effects, making them valuable candidates for drug development and therapeutic applications (Wang et al., 2019). The exploration of these natural compounds not only enhances our understanding of traditional medicinal practices but also paves the way for the development of novel pharmaceuticals.

This study systematically investigates the natural compounds present in *E. ulmoides* and evaluate their medicinal properties; isolates and identifies the bioactive constituents of *E. ulmoides*, assesses their pharmacological activities, and explores their potential applications in modern medicine. By providing a comprehensive analysis of the phytochemical and pharmacological profiles of *E. ulmoides*, this study seeks to bridge the gap between traditional knowledge and contemporary scientific research, ultimately contributing to the development of new therapeutic agents derived from natural sources.

2 Phytochemical Composition of *Eucommia ulmoides*

2.1 Major classes of compounds identified

Eucommia ulmoides, a traditional Chinese medicinal plant, contains a diverse array of bioactive compounds. The major classes of compounds identified in *E. ulmoides* include iridoids, lignans, flavonoids, phenylpropanoids, phenolics, steroids, and terpenoids (Figure 1) (He et al., 2014; Zhu and Sun, 2018; Wang et al., 2019; Zhao et al., 2022). Specifically, iridoid glycosides such as geniposidic acid, aucubin, and scyphiphin D are prominent (Niu et al., 2016). Additionally, lignans like pinoresinol-di-O-β-D-glucopyranoside and various flavonoid glycosides have been isolated.

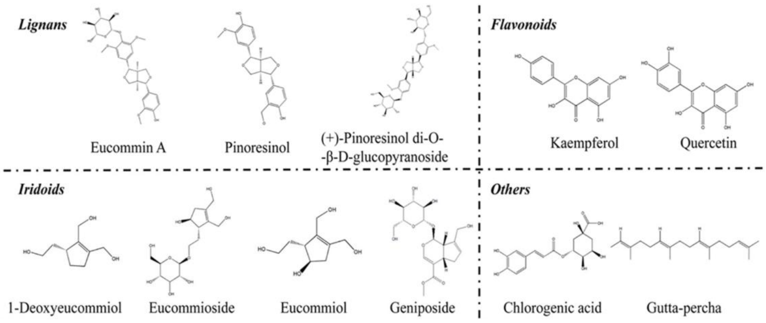

Figure 1 The main active chemical compounds in *E. ulmoides* (Adopted from Zhao et al., 2022)

2.2 Methods of extraction and analysis

The extraction and analysis of compounds from *E. ulmoides* involve several advanced techniques. Ultra-performance liquid chromatography (UPLC) coupled with electrospray ionization-tandem mass spectrometry (ESI-MS) is commonly used for both qualitative and quantitative analysis (Chai et al., 2012). High-performance liquid chromatography (HPLC) combined with diode-array detection (DAD) and quadrupole time-of-flight mass spectrometry (Q-TOF-MS/MS) is also employed to profile glycosides and other compounds. Supercritical CO2 fluid extraction is another method used to isolate phytosterols and iridoids from *E. ulmoides* seeds (Tang et al., 2021).

2.3 Quantitative and qualitative analysis of compounds

Quantitative and qualitative analyses of *E. ulmoides* compounds have revealed significant variations depending on the plant part and processing method. For instance, UPLC-UV has been used to quantify ten compounds, including iridoids, phenylpropanoids, and flavonoids, in different medicinal parts of *E. ulmoides*. The seed meal of *E. ulmoides* has been analyzed to identify and quantify six iridoid compounds, revealing their stability under various conditions (Figure 2) (Ma et al., 2022). Additionally, HPLC-MS/MS has been validated for pharmacokinetic studies of specific compounds like pinoresinol-di-β-D-glucopyranoside in rat plasma (Wang et al., 2012).

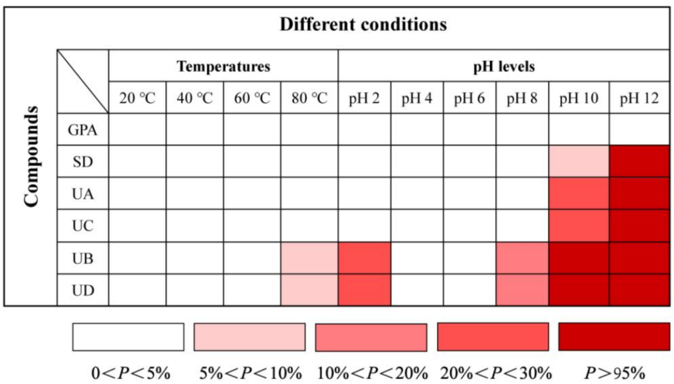

Figure 2 Illustration of stability degree for the tested compounds under the conditions of different temperatures and pH levels (Adopted from Ma et al., 2022)

Image caption: *P*: Degradation degree; GPA: geniposidic acid (monomer); SD: scyphiphin D (dimer); UA: ulmoidoside A (trimer); UB: ulmoidoside B (trimer); UC: ulmoidoside C (tetramer); UD: ulmoidoside D (tetramer) (Adapted from Ma et al., 2022)

The study of Ma et al. (2022) demonstrates the stability of six iridoid compounds under varying temperature and pH conditions. The compounds remain relatively stable at lower temperatures (20 °C to 60 °C), showing minimal degradation. However, as the pH becomes more alkaline (pH 10 and 12), the degradation significantly increases, particularly for the trimer and tetramer compounds. This suggests that higher pH levels have a profound impact on the stability of these iridoids, making them less stable in basic environments while maintaining better stability at neutral and acidic pH. Temperature does not appear to significantly affect degradation under these conditions.

The content of bioactive compounds can vary significantly based on the habitat and processing methods. For example, stir-frying with salt-water enhances the extraction of chlorogenic acid, while carbonizing leads to a significant loss of major components. Principal component analysis (PCA) has been used to classify different parts of *E. ulmoides* based on their chemical compositions, highlighting the distinct profiles of bark, leaves, and male flowers (Yan et al., 2018).

The phytochemical composition of *E. ulmoides* is rich and varied, with advanced analytical methods enabling detailed qualitative and quantitative assessments. These findings support the plant's extensive use in traditional medicine and its potential for further pharmacological and commercial applications.

3 Bioactive Compounds and Their Pharmacological Effects

3.1 Antioxidant properties

E. ulmoides exhibits significant antioxidant properties, primarily attributed to its rich content of bioactive compounds such as flavonoids, iridoids, and phenols. Studies have shown that dietary supplementation with *E. ulmoides* leaf extracts (ELE) enhances antioxidant capacity in various models. For instance, in weaned piglets, ELE supplementation increased serum and liver total antioxidant capacity (T-AOC) and alkaline phosphatase (AKP) levels, indicating improved antioxidant status (Ding et al., 2020). Additionally, the leaves of *E. ulmoides* contain compounds like quercetin and kaempferol, which have demonstrated potent soluble epoxide hydrolase (sEH) inhibitory activity, contributing to their antioxidant effects. The antioxidant properties of *E. ulmoides* are further supported by its ability to upregulate the expression of antioxidant genes such as CAT and SOD in genetically improved farmed tilapia (GIFT), enhancing their resistance to oxidative stress (Huang et al., 2022).

3.2 Anti-inflammatory and analgesic effects

E. ulmoides has been traditionally used for its anti-inflammatory and analgesic properties. Modern pharmacological research has identified several bioactive compounds responsible for these effects. For example, the male flowers of *E. ulmoides* contain asperuloside, which has been shown to delay muscle aging by improving mitochondrial function and reducing inflammation through the DAF-16 mediated pathway (Chen et al., 2023). Furthermore, extracts from *E. ulmoides* leaves have demonstrated significant anti-inflammatory activity by inhibiting the nuclear factor kappa B (NF-κB) pathway, reducing the production of pro-inflammatory mediators such as nitric oxide (NO), tumor necrosis factor (TNF)-α, and interleukins (IL-1β, IL-6) in lipopolysaccharide (LPS)-stimulated RAW 264.7 cells (Wang et al., 2019). These findings are corroborated by another study where compounds isolated from *E. ulmoides* leaves, including quercetin and kaempferol, exhibited potent NF-κB inhibitory effects, further validating their anti-inflammatory potential (Bai et al., 2015).

3.3 Cardiovascular and metabolic health benefits

E. ulmoides has been extensively studied for its cardiovascular and metabolic health benefits. The bark extract of *E. ulmoides* has been shown to reduce blood pressure and inflammation in high-salt diet and N(omega)-nitro-L-arginine methyl ester (L-NAME) induced hypertensive mice (Figure 3). This effect is partly mediated by the regulation of gut microbiota, particularly the enrichment of the Parabacteroides strain, which exerts anti-hypertensive effects by reducing inflammatory cytokines such as IL-17A (Yan et al., 2022). Additionally, *E. ulmoides* has been reported to possess antihyperglycemic and antihyperlipidemic activities, making it beneficial for managing diabetes and obesity (Huang et al., 2021). The leaves of *E. ulmoides* also contain bioactive compounds that improve lipid metabolism and immune function, as evidenced by their positive effects on milk quality and biochemical properties in dairy cows (Teng et al., 2021). These multifaceted benefits highlight the potential of *E. ulmoides* as a therapeutic agent for cardiovascular and metabolic health.

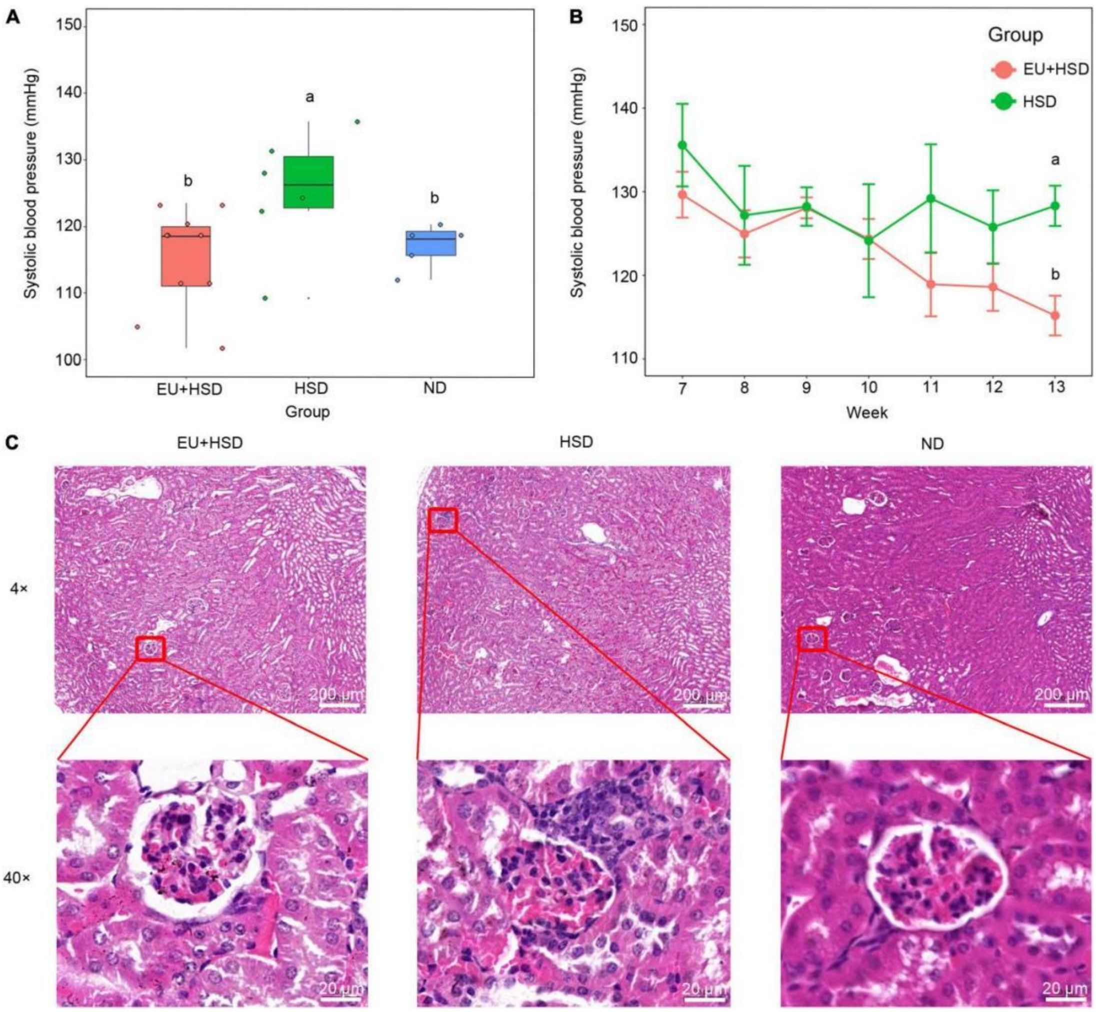

Figure 3 Anti-hypertensive effect of EU. Blood pressure (A) in the EU + HSD, HSD, and ND groups in week 13 and (B) in the EU + HSD and HSD groups from weeks 7 to 13. (C) HE staining of kidney tissues in the EU + HSD, HSD, and ND groups (Adopted from Yan et al., 2022)

The study of Yan et al. (2022) illustrates the anti-hypertensive effects of EU supplementation on systolic blood pressure over time in different groups. The EU + HSD group exhibits a significant reduction in blood pressure compared to the HSD-only group, especially by week 13. Histological analysis of kidney tissues (C) shows that the EU + HSD group has healthier kidney structures compared to the damage seen in the HSD group. These findings suggest that EU may have protective effects against hypertension and kidney damage, particularly in the context of a high-salt diet.

3.4 Anti-osteoporosis

E. ulmoides inhibits osteoclast differentiation, promotes osteoblast differentiation, reduces calcium loss, and causes estrogenic-like effects (Figure 4) (Yang et al., 2022). “Compendium of Materia Medica (Bencao Gangmu in Chinese)” recorded that the EB benefited qi and strengthened muscles and bones (Xie et al., 2022). The crude extract of EB increases the secretion of alkaline phosphatase (ALP), upregulates type I collagen (Col1) α mRNA and protein expression, and thereby promotes the proliferation and differentiation of osteoblasts (Guan et al., 2014). Flavonoids extracted from EB, including astragaloside, scutellarin and total lignans, promote the proliferation and differentiation of MC3T3-E1 subclone 14 osteoblasts, downregulate the protein expression of RANKL, upregulate the protein expression of OPG and Osx, and restore the OPG/RANKL ratio, thereby exerting an anti-osteoporotic effect (Zhang et al., 2014). Salted EB granules can reduce the loss of calcium and phosphorus in the urine of rats with ovariectomy (OVX)-induced OP; increase the mRNA and protein expression of OPG, RANKL, and RANK; promote bone formation; and increase bone mineral density (BMD) (Yang et al., 2023).

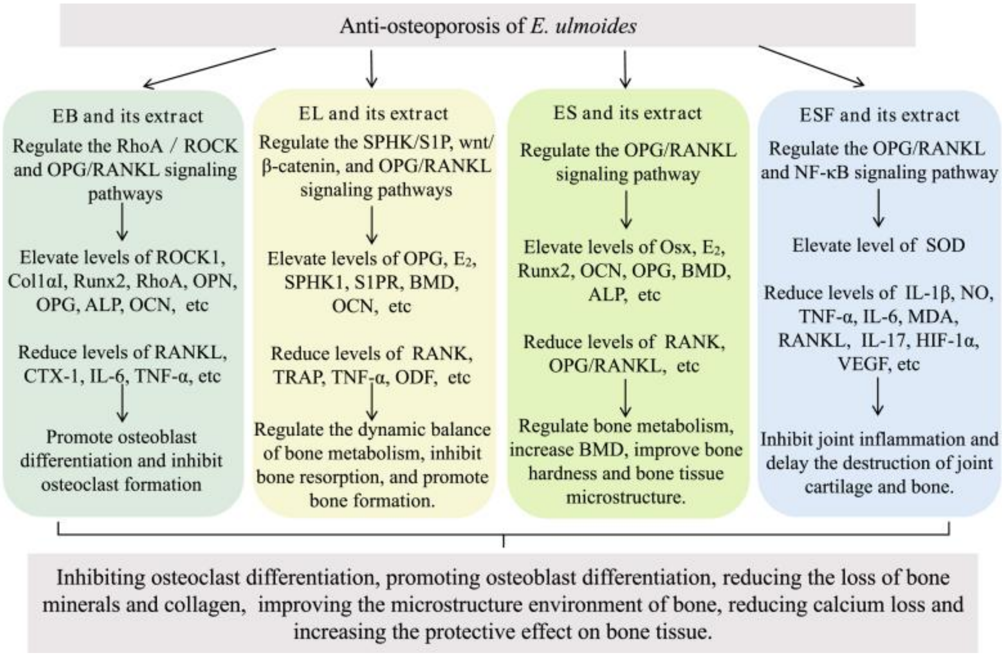

Figure 4 Anti-osteoporosis of effect of EU (Adopted from Peng et al., 2024)

4 Biosynthesis and Structure Modification

4.1 Biosynthetic pathways

The biosynthetic pathways of natural compounds in *E. ulmoides* are complex and involve various enzymes and metabolic routes. For instance, the biosynthesis of glycosides, such as aucubin and geniposide, is facilitated by uridine diphosphate glycosyltransferases (UGTs), which catalyze the transfer of glycosyl groups from uridine-5′-diphosphate-glucose (UDPG) to specific substrates (Ouyang et al., 2021). Additionally, the methylerythritol-phosphate (MEP) pathway is predominantly responsible for the synthesis of isoprenyl diphosphate, a precursor in the rubber biosynthesis process in *E. ulmoides*. The dynamic changes in metabolite accumulation during leaf growth and development also highlight the importance of flavonoid and phenylpropanoid biosynthetic pathways, which are regulated by transcription factors such as MYB and bHLH (Li et al., 2019).

4.2 Genetic engineering

Genetic engineering has the potential to enhance the production of valuable compounds in *E. ulmoides*. The identification and characterization of 91 putative *EuUGT* genes across the complete genome of *E. ulmoides* provide a foundation for genetic manipulation aimed at optimizing glycoside biosynthesis. The high-quality de novo assembly of the *E. ulmoides* haploid genome, which includes 26,001 predicted protein-coding genes, offers new insights into genome structure and evolution, facilitating targeted genetic engineering efforts (Li et al., 2020). These advancements can lead to improved industrial and medicinal applications of *E. ulmoides* through the enhancement of specific biosynthetic pathways.

4.3 Structure-activity relationship

The structure-activity relationship (SAR) of compounds derived from *Eucommia ulmoides* is crucial for understanding their pharmacological properties. For example, the SAR of flavonoids isolated from *E. ulmoides* leaves has been studied in relation to their soluble epoxide hydrolase (sEH) inhibitory activity and anti-inflammatory properties. Compounds such as quercetin and kaempferol exhibited significant sEH inhibitory activity, with IC50 values of (22.5 ± 0.9) and (31.3 ± 2.6) μM, respectively (Bai et al., 2015). Additionally, the estrogenic properties of six compounds from *E. ulmoides* were found to vary significantly in their selectivity for estrogen receptor subtypes α and β, indicating diverse phytoestrogen activities (Wang et al., 2011). These findings underscore the importance of detailed SAR studies to elucidate the mechanisms of action and potential therapeutic applications of *E. ulmoides* compounds.

5 Case Studies

5.1 Therapeutic use in hypertension

E. ulmoides has shown significant potential in the treatment of hypertension. A study demonstrated that *E. ulmoides* bark extract can reduce blood pressure and inflammation by regulating the gut microbiota. Specifically, the extract was found to enrich the *Parabacteroides* strain, which has anti-hypertensive effects by reducing levels of inflammatory cytokines such as renal IL-17A (Yan et al., 2022). Another study highlighted the use of *E. ulmoides* in combination with *Tribulus terrestris*, showing that this drug pair can regulate ferroptosis by mediating the neurovascular-related ligand-receptor interaction pathway, which is beneficial for treating hypertension and preventing ischemic stroke (Figure 5) (Zhang et al., 2022). These findings suggest that *E. ulmoides* can be an effective natural remedy for managing hypertension through multiple mechanisms, including gut microbiota modulation and neurovascular protection.

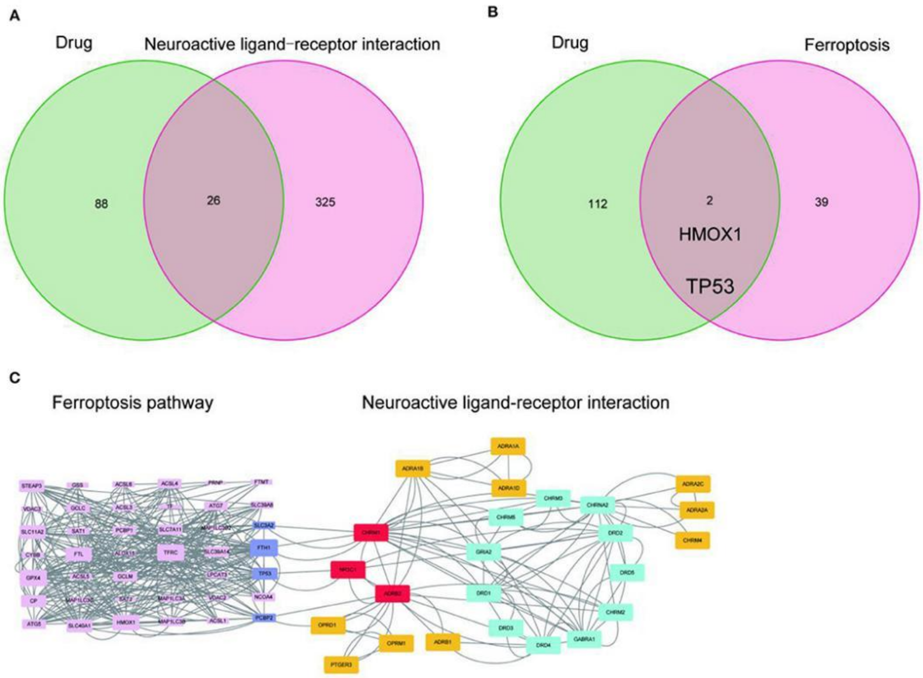

Figure 5 Network analysis of the active compounds of EUO-TT L. mediating the neuroactive ligand-receptor interaction pathway regulating ferroptosis. Intersection analysis of drug-neuroactive ligand-receptor interaction pathway (A); Intersection analysis of drug-ferroptosis pathway (B); PPI network of neuroactive ligand-receptor interaction pathway - ferroptosis pathway (C) (Adopted from Zhang et al., 2022)

The study of Zhang et al. (2022) analysis illustrates how the active compounds of EUO-TT L. intersect with neuroactive ligand-receptor interaction and ferroptosis pathways. The Venn diagrams highlight overlapping genes, particularly *HMOX1* and *TP53*, which are central to both pathways. The protein-protein interaction (PPI) network further connects the ferroptosis and neuroactive ligand-receptor interaction pathways, indicating a complex interaction between neuroactive signaling and cell death mechanisms. This suggests that targeting these interactions may provide a therapeutic approach for conditions related to neurodegeneration or oxidative stress-related diseases.

5.2 Treatment of arthritis

Eucommia ulmoides has been traditionally used in Chinese medicine to treat rheumatoid arthritis (RA). Recent research has provided scientific backing for its efficacy. An experimental study using a collagen-induced arthritis (CIA) rat model found that a 70% ethanol extract of *E. ulmoides* significantly ameliorated arthritis symptoms (Figure 6). The extract reduced foot swelling, decreased the arthritis index, and improved pathological conditions in joint tissues. Mechanistically, the extract suppressed the proliferation of synoviocytes, reduced the number of Th17-positive cells, and downregulated serum IL-17 expression. It also increased anti-inflammatory effects by upregulating IL-10 and inhibited key pro-inflammatory cytokines such as TNFα and IL-1β (Figure 7). Additionally, the extract showed potential in preventing bone destruction by downregulating RANKL mRNA and upregulating OPG mRNA (Figure 8) (Wang et al., 2016). These results support the traditional use of *E. ulmoides* in treating RA and highlight its potential as a natural therapeutic agent for arthritis.

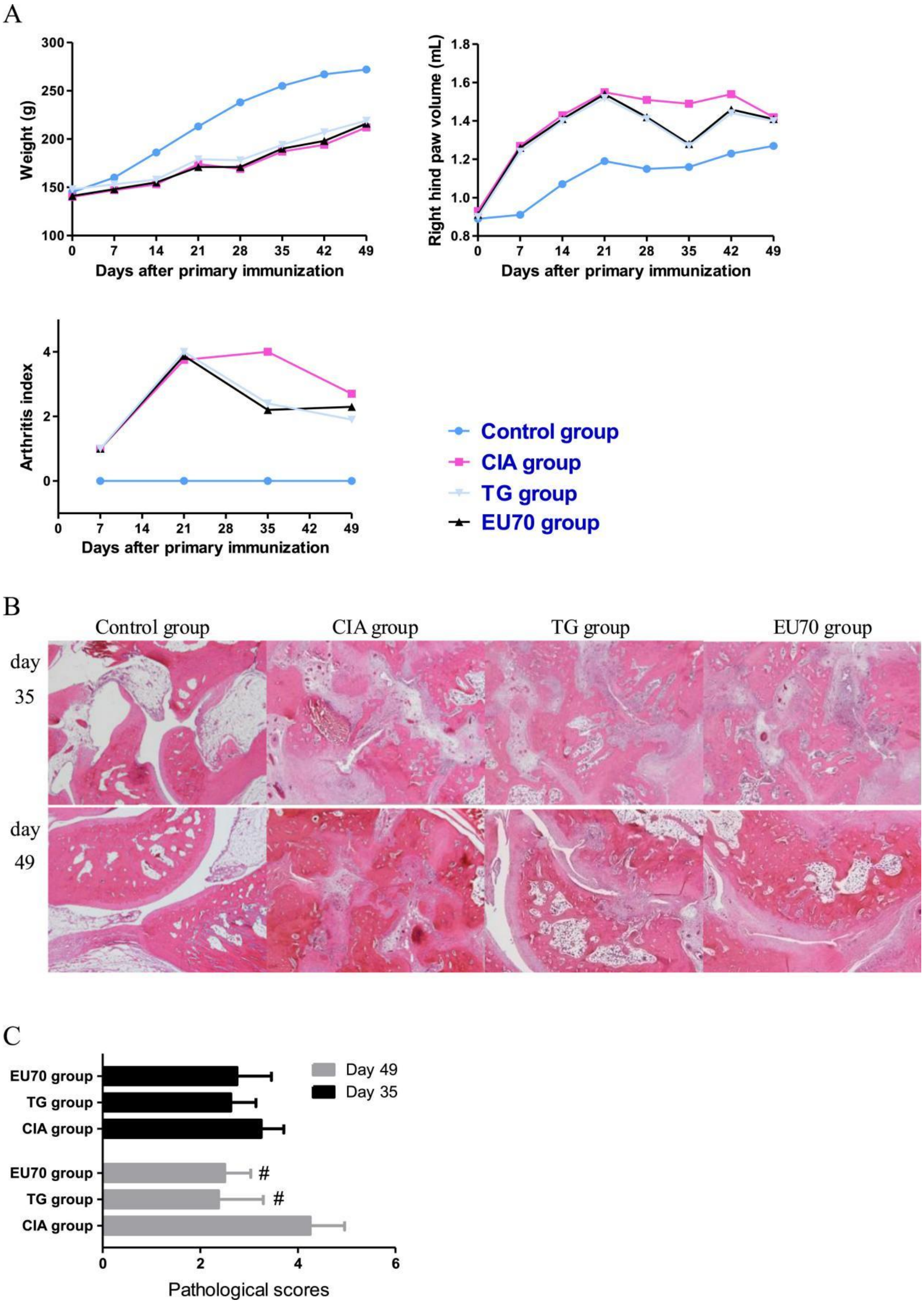

Figure 6 EU70 alleviates the symptoms of RA *in vivo* and improves the pathological state of inflammation. A. Equal numbers of male and female rats were used to develop the CIA model with a first and booster immunization. After the first subcutaneous injection of the CII/CFA emulsion (5 mg/mL) in the tail and right hind paw, the rats' body weights, right hind paw volume, and arthritis indexes were recorded on different study days. B. Pathological sections of hind limb joints from normal (healthy), arthritic and drug-treated CIA rats (×40 magnification) were analysed by H&E staining. C. Inflammatory infiltration was assessed by scoring the H&E sections. #: $P<0.05$ compared with the CIA group (Adopted from Wang et al., 2016)

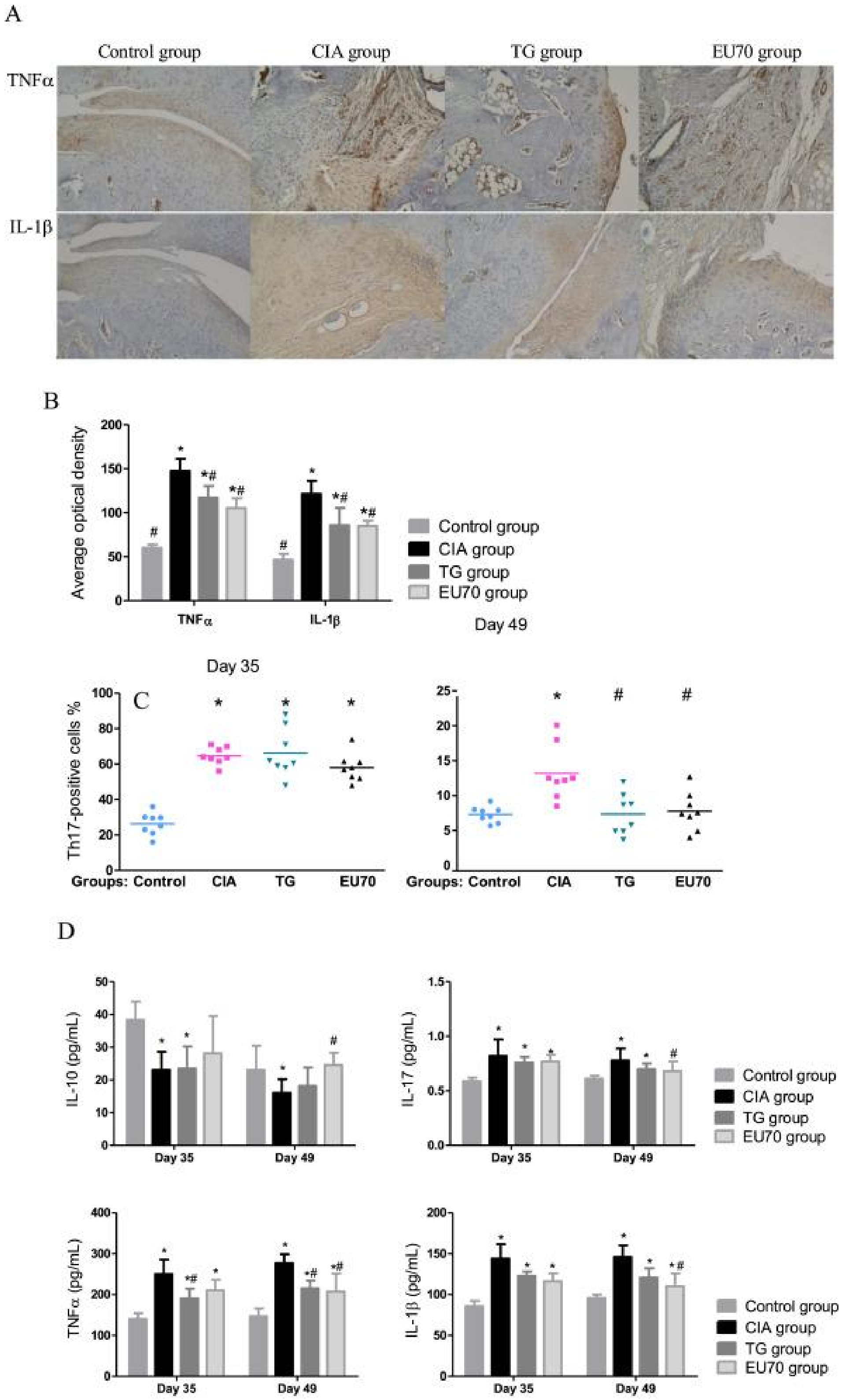

Figure 7 EU70 decreases pro-inflammatory cytokine levels and the number of T cells (Th17-positive cells) and increases anti-inflammatory cytokine levels (IL-10). (A) IHC of TNFα and IL-1β in rat hind limb joints on day 49 (after 4 weeks of drug treatment) (×40). (B). Average optical density of IHC sections from the four groups. (C) Splenocytes were isolated from the rats on day 35 and day 49. Th17-positive cells were stained with a FITC-conjugated Th17 antibody and detected by flow cytometry. (D) Serum IL-10, IL-17, IL-1β and TNFα levels were detected by ELISA. The rats were treated with the different drugs on day 35 and day 49 after model generation. *: P<0.05 compared with the normal group; #: P<0.05 compared with the CIA group (Adopted from Wang et al., 2016)

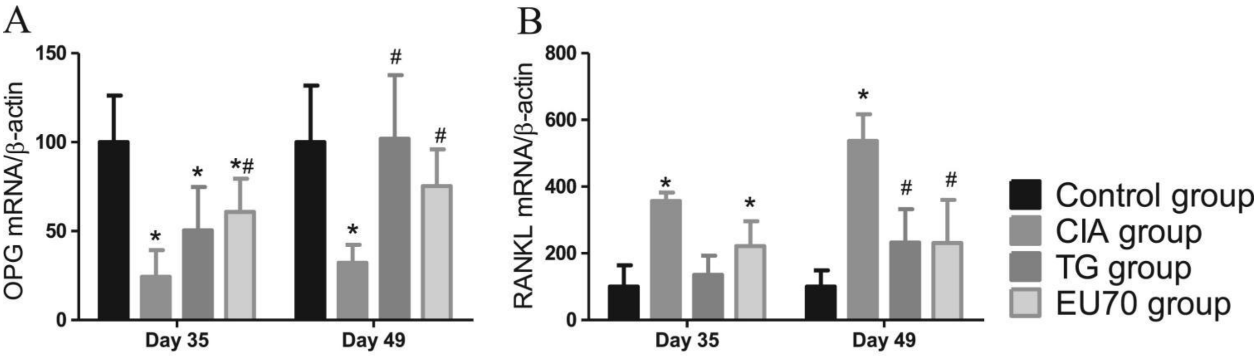

Figure 8 EU70 decreases RANKL mRNA levels and increases OPG mRNA levels in joint tissue. *: $P<0.05$ compared with the control group; #: $P<0.05$ compared with the CIA group (Adopted from Wang et al., 2016)

5.3 Neuroprotective applications

E. ulmoides has also been investigated for its neuroprotective properties. A study focusing on the antidepressant potential of chlorogenic acid-enriched extract from *E. ulmoides* bark found that the extract could promote serotonin release and enhance synapsin I expression, which are crucial for neuron protection and cognitive improvement. The extract demonstrated antidepressant-like effects in animal models, suggesting its potential for treating depression (Figure 9) (Wu et al., 2016). Additionally, *E. ulmoides* has been shown to have broad neuroprotective effects, including benefits for neurodegenerative diseases such as Parkinson's and Alzheimer's. The plant's extracts and active compounds have been found to possess antioxidant, anti-inflammatory, and neuroprotective activities, which contribute to its efficacy in managing these conditions (Huang et al., 2021; Zhao et al., 2022). These findings indicate that *E. ulmoides* could be a valuable natural resource for developing treatments for various neurodegenerative and neuropsychiatric disorders.

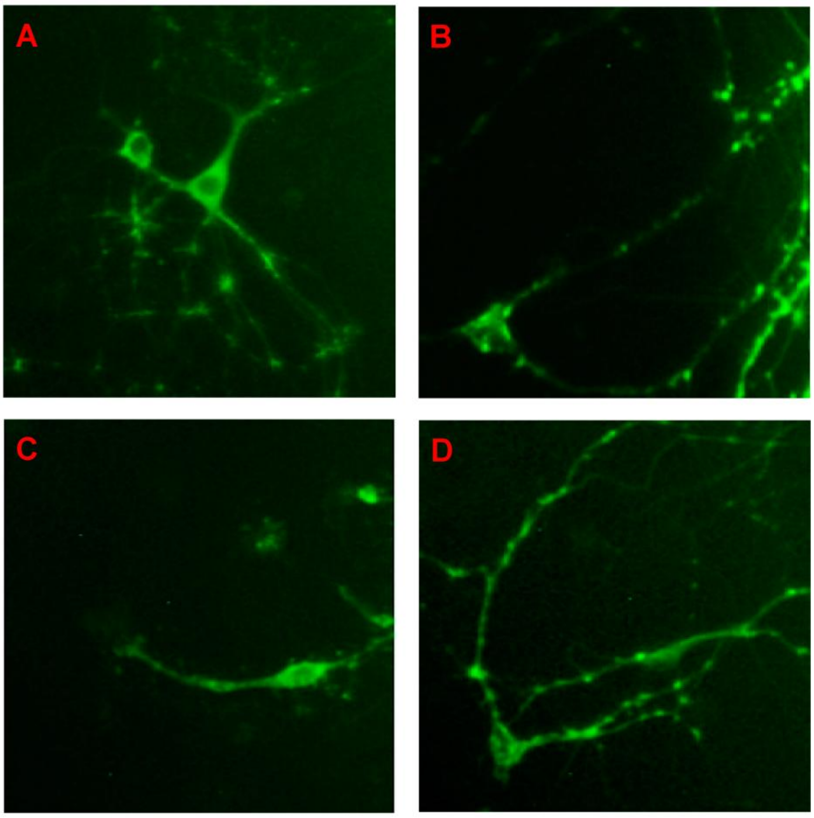

Figure 9 The effects of CGA ± Cort on the expression of synapsin I in the cells of fetal rat raphe neurons. (A) Control; (B) CGA treatment; (C) Cort treatment; and (D) Cort + CGA treatment. Notes: Fluorescence microscopy shows the representative images of neurons stained by FITC. The cells were treated with culture medium with 0.1% DMSO (control), or 1 nM CGA ± 10 µM Cort. The results are representative of at least three independent experiments (Adopted from Wu et al., 2016)

6 Traditional vs. Modern Applications

6.1 Traditional medicinal uses in Chinese medicine

Eucommia ulmoides, known as Dù-zhòng in Chinese, has been a cornerstone of traditional Chinese medicine (TCM) for nearly two thousand years. Historically, various parts of the plant, including the leaf, stem, bark, and staminate flower, have been utilized to treat a wide array of ailments. Traditional applications include the treatment of lumbar and knee pain, osteoporosis, hepatoprotection, paralysis, intestinal hemorrhages, vaginal bleeding, abortion, spermatorrhea, foot fungus, and anti-aging (He et al., 2014). The plant's use is deeply rooted in Chinese medicine theory, emphasizing its role in disease adaptation and overall health maintenance (Wang et al., 2019).

6.2 Modern pharmacological research

Modern research has significantly expanded our understanding of the pharmacological properties of *Eucommia ulmoides*. Studies have isolated and identified numerous active compounds, including lignans, iridoids, flavonoids, phenols, steroids, and terpenes, which exhibit a wide range of biological activities. These compounds have been shown to possess antihypertensive, antihyperglycemic, antihyperlipidemic, antioxidant, anti-inflammatory, neuroprotective, anti-fatigue, anti-aging, anti-cancer, and immunoregulatory properties. For instance, chlorogenic acid-enriched extracts from the bark have demonstrated neuroprotective and antidepressant-like effects by promoting serotonin release and enhancing synapsin I expression (Wu et al., 2016). Additionally, iridoid glycosides from the seed meal have shown significant anti-inflammatory activities (Ma et al., 2022).

6.3 Integration of traditional knowledge with modern science

The integration of traditional knowledge with modern scientific research has opened new avenues for the comprehensive utilization of *Eucommia ulmoides*. Traditional uses have provided a foundation for identifying potential therapeutic applications, which modern pharmacological studies have further validated and expanded upon. For example, the traditional use of *Eucommia ulmoides* for treating hypertension and diabetes has been supported by modern studies demonstrating its efficacy in managing these conditions through various bioactive compounds (Huang et al., 2021). Moreover, the exploration of different parts of the plant, such as leaves and seeds, which were traditionally underutilized, has revealed their potential for pharmaceutical and nutraceutical applications (Xing et al., 2019). This holistic approach not only enhances the medicinal value of *Eucommia ulmoides* but also promotes sustainable use of the plant resources.

By bridging the gap between traditional practices and modern science, researchers can develop more effective and accessible treatments, ensuring that the rich heritage of traditional Chinese medicine continues to benefit contemporary healthcare.

7 Safety and Toxicology of *Eucommia ulmoides* Compounds

7.1 Toxicity studies and findings

E. ulmoides Oliver, commonly used in traditional Chinese medicine, has been subjected to various toxicity studies to evaluate its safety profile. Acute and sub-chronic toxicity tests, including the Ames test, bone marrow micronucleus assay, and chromosomal aberration assay, have shown that *E. ulmoides* extract (EUE) is non-genotoxic within specific dose ranges. However, long-term administration of high doses has been associated with nephrotoxicity. Specifically, a 13-week study revealed dose-dependent increases in nephrotoxicity-related indices and pathological changes in renal tissues, which were partly reversible after ceasing the low dosage but persisted at higher dosages (Luo et al., 2020). Additionally, while *E. ulmoides* has demonstrated various pharmacological benefits, further toxicity and clinical studies are warranted to establish more detailed safety data on both crude extracts and pure compounds (He et al., 2014).

7.2 Safe dosage and administration

Clinical trials have explored the safe dosage and administration of *E. ulmoides* extracts. For instance, a controlled clinical trial involving healthy adult subjects administered 500 mg of *E. ulmoides* extract three times daily for eight weeks, and another group received 1 g three times daily for two weeks. Both dosages were well-tolerated, with no reported toxicity (Greenway et al., 2011). The maximum tolerated dose in animal studies was found to be significantly higher than the clinical doses used in humans, indicating a wide safety margin. Specifically, the maximum tolerated dose was not less than 168 g/kg, which is 1260 times the clinical doses used in human adults.

7.3 Long-term effects and safety in clinical use

Long-term use of *E. ulmoides*, particularly at high doses, has been associated with nephrotoxicity in animal studies. A 13-week administration led to dose-dependent nephrotoxicity, with some pathological changes in renal tissues being partly reversible after ceasing the low dosage but persisting at higher dosages. In clinical settings, *E. ulmoides* has been used traditionally for various ailments, and modern pharmacological research supports its efficacy in treating conditions such as hypertension, diabetes, and osteoporosis (Wang et al., 2019; Huang et al., 2021). However, the long-term safety in clinical use remains to be fully established, necessitating further studies to ensure its safe application in prolonged treatments.

In conclusion, while *E. ulmoides* exhibits a promising safety profile at recommended dosages, caution is advised for long-term and high-dose use due to potential nephrotoxicity. Further research is essential to fully understand the long-term safety and establish comprehensive guidelines for its clinical use.

8 Industrial Applications and Market Potential

8.1 Commercial extraction and production of *E. ulmoides* compounds

E. ulmoides, a traditional Chinese medicinal plant, has garnered significant attention for its diverse bioactive compounds, including lignans, iridoids, flavonoids, phenolics, steroids, and terpenoids. The commercial extraction and production of these compounds involve various methods tailored to maximize yield and maintain the integrity of the active ingredients. For instance, the extraction of iridoid glycosides from *E. ulmoides* seeds has been optimized using ethanol and other solvents, demonstrating strong antioxidant activities (Niu et al., 2016). Additionally, the stability and conversion phenomena of these compounds under different conditions have been studied to ensure their efficacy in commercial products (Ma et al., 2022).

The bark, leaves, seeds, and male flowers of *E. ulmoides* are utilized in different extraction processes, each part offering unique bioactive profiles suitable for various applications. The male flowers, for example, are rich in asperuloside, which has shown potential in delaying muscle aging by improving mitochondrial function (Chen et al., 2023). The leaves, on the other hand, contain compounds with soluble epoxide hydrolase inhibitory activity, which are beneficial for anti-inflammatory purposes (Bai et al., 2015).

8.2 Market demand and economic impact

The market demand for *Eucommia ulmoides* and its derivatives is driven by their extensive pharmacological properties, including antihypertensive, antihyperglycemic, antihyperlipidemic, antioxidative, anti-osteoporosis, antitumor, immunomodulatory, and neuroprotective activities (He et al., 2014; Wang et al., 2019). These properties make *E. ulmoides* a valuable resource in the pharmaceutical, nutraceutical, and functional food industries.

The economic impact of *E. ulmoides* is significant, particularly in regions where traditional Chinese medicine is prevalent. The plant's various parts are used to produce health supplements, herbal formulations, and functional foods, contributing to a growing market for natural and plant-based products (Zhu and Sun, 2018). The development of *E. ulmoides* as a feedstock for bioactive products further enhances its market potential, offering opportunities for commercial exploitation in diverse sectors.

8.3 Future prospects for pharmaceutical applications

The future prospects for pharmaceutical applications of *E. ulmoides* are promising, given the ongoing research and development in this field. The plant's compounds have shown potential in treating a wide range of conditions, from hypertension and diabetes to neurodegenerative diseases and cancer (Zhao et al., 2022). The neuroendocrine-immune regulatory network of *E. ulmoides* suggests its applicability in maintaining homeostasis and treating NEI-related diseases.

Moreover, the antidepressant potential of chlorogenic acid-enriched extracts from *E. ulmoides* bark, which promote serotonin release and neuron protection, highlights the plant's potential in developing natural antidepressant drugs (Wu et al., 2016). The unique properties of *E. ulmoides* rubber (EUR), a natural polymer with applications in environmental, agricultural, and biomedical engineering, also open new avenues for research and industrial use (Wei et al., 2021).

In conclusion, the commercial extraction and production of *E. ulmoides* compounds, coupled with the growing market demand and economic impact, underscore the plant's significant industrial applications. The future prospects for pharmaceutical applications are vast, with ongoing research likely to uncover new therapeutic uses and enhance the commercial viability of this traditional medicinal plant.

9 Concluding Remarks

Eucommia ulmoides, a traditional Chinese medicinal plant, has been extensively studied for its diverse pharmacological properties. The plant contains a wide array of bioactive compounds, including lignans, iridoids, flavonoids, phenols, steroids, and terpenes, which contribute to its medicinal efficacy. These compounds exhibit a range of therapeutic activities such as antihypertensive, antihyperglycemic, antihyperlipidemic, antioxidant, anti-osteoporotic, antitumor, immunomodulatory, and neuroprotective effects. Specific compounds like chlorogenic acid have shown potential in neuroprotection and antidepressant activities by promoting serotonin release and enhancing synapsin I expression. Additionally, iridoid glycosides from the seeds and male flowers of *E. ulmoides* have demonstrated significant antioxidant and anti-aging properties.

The pharmacological potential of *E. ulmoides* suggests several promising avenues for future medicinal applications. The neuroprotective and antidepressant properties of chlorogenic acid-enriched extracts highlight the potential for developing treatments for neurological disorders and depression. The anti-inflammatory and antioxidant activities of iridoid glycosides suggest their use in managing chronic inflammatory conditions and oxidative stress-related diseases. Furthermore, the estrogenic properties of certain compounds in *E. ulmoides* indicate potential applications in hormone replacement therapy and the management of menopausal symptoms. Future research should focus on clinical trials to validate these effects in humans and explore the safety and efficacy of *E. ulmoides*-derived compounds in various therapeutic contexts.

E. ulmoides has a long history of use in traditional Chinese medicine, and modern research has validated many of its traditional uses while uncovering new therapeutic potentials. The plant's diverse bioactive compounds and their wide-ranging pharmacological activities make it a valuable resource for developing new medicinal products. As research progresses, it is crucial to conduct comprehensive clinical studies to establish standardized dosages, safety profiles, and mechanisms of action. The integration of *E. ulmoides* into modern medicine could provide natural and effective treatments for a variety of health conditions, reinforcing its role as a significant medicinal plant.

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Conflict of Interest Disclosure

The authors affirm that this research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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