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Magnolia officinalis: botanical characteristics, pharmacological properties and current evidence from preclinical studies

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Abstract

Magnolia officinalis, commonly known as "Houpo" in traditional Chinese medicine, has a documented history of use spanning over 2,500 years. It remains a widely traded botanical product in both Chinese and Japanese herbal pharmacopeias, where its bark has been traditionally employed in the management of various conditions, including anxiety, depression, gastrointestinal and respiratory disorders, stroke, and musculoskeletal pain. However, while its historical relevance in traditional medicine is well-established, the scientific basis for many of its purported benefits remains incompletely validated. This review critically examines the current scientific literature concerning the phytochemical composition, pharmacological properties, therapeutic applications, and safety profile of *M. officinalis* bark, using databases such as PubMed, ScienceDirect, HerbMed, and Google Scholar. Particular focus is placed on its two principal neolignan constituents, magnolol and honokiol, which have attracted considerable attention due to their reported antioxidant, anti-inflammatory, neuroprotective, anticancer, and anxiolytic effects. Although a growing body of *in vitro* and *in vivo* evidence supports the biological activity of these compounds, notable limitations persist, most notably, a lack of high-quality clinical trials, standardization in extract preparation, and a comprehensive understanding of their pharmacokinetics and drug interaction potential. While preliminary data suggest promising therapeutic avenues, the current body of evidence does not yet support widespread clinical translation. Thus, continued rigorous investigation, including mechanistic studies and well-designed human trials, is essential before *M. officinalis* and its active constituents can be considered viable candidates for modern pharmacotherapeutic development.

Key words: magnolia bark, traditional Chinese medicine, pharmacological properties, limitations.

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Introduction

Traditional Chinese Medicine (TCM) has a documented history extending over more than 2,500 years and is founded on a progressive body of theoretical frameworks and clinical observations developed by successive generations of practitioners and scholars.[1] According to the Chinese Pharmacopoeia (2010 edition),[2] three primary materials of frequent medicinal use are described in relation to *Magnolia officinalis*: the bark of *Magnolia officinalis* Rehder & E. Wilson, commonly referred to as "Houpo" or "Houpu" in Chinese, a name that reflects the thick ("hou") and unprocessed ("pu") nature of the bark. The plant is also known as "Chuan houpu", indicating its historical origin in the Sichuan region of China. In addition, "Tuhoupu", where "tu" is a term particularly used in Guangxi Province, is sometimes employed as a substitute source.[1] Other recognized medicinal materials include the flower bud of *M. officinalis*, known as "Houpohua", as well as the flower buds of *Magnolia biondii* Pamp., *Magnolia denudata* Desr., and *Magnolia sprengeri* Pamp., collectively referred to as "Xinyi" or "Xinyihua". Furthermore, a non-official species, *Magnolia obovata* Thunb., is occasionally cited as an alternative source of *Magnolia* spp. bark.[2] Historically, *Magnolia* spp. bark has been incorporated into numerous traditional Chinese medicinal formulations, including "Banxia Houpo Tang", "Xiao Zhengai Tang", "Ping Wei San", and "Shenmi Tang". In contemporary clinical practice in China, several prescriptions containing Houpo continue to be widely used, such as Hange-Koboku-To and Saiboku-To. [3]

Phytochemical composition

- Major significant bioactive components isolated from the bark of *M. officinalis* appear to be the polyphenolic neolignans, magnolol and honokiol.
- Magnolol was named after its source, genus *Magnolia* plants, and honokiol was named after "Honoki", a Japanese name of *M. obovata* Thunb.
- Magnolol and honokiol are two hydroxylated biphenolic isomers (neolignans, $C_{18}H_{18}O_2$), the *ortho-ortho*-C-C and *ortho-para*-C-C dimers of 4-allyl-phenol, respectively. [1]

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Pharmacological properties

Neuroprotective and Central Nervous System - related effects

Magnolia officinalis has been widely cited in the ethnopharmacological literature for its diverse biological activities, including reported antibacterial, antitumor, anti-inflammatory, antioxidant, and purported anti-aging effects.[3] The main findings from preclinical and clinical studies are summarized in Table 1. Neolignans represent the primary active compounds of *M. officinalis* and these are magnolol and honokiol. These molecules have demonstrated a broad spectrum of pharmacological effects in preclinical studies, including potential neuroprotective activity relevant to Alzheimer's Disease (AD).[3] Specifically, they have been shown to inhibit beta-amyloid (Aβ) aggregation, reduce neuroinflammation, suppress acetylcholinesterase activity, and alleviate mitochondrial dysfunction *in vitro* and in animal models. Additional reported mechanisms include enhancement of microglial phagocytosis, modulation of oxidative stress, and influence on gut microbiota composition. These effects

Table 1. Summary of preclinical and clinical studies on *Magnolia officinalis* and its main bioactive constituents.
CNS, Central Nervous System; GABA; Gamma-Aminobutyric Acid; ROS, Reactive Oxygen Species; COX, Cyclooxygenase Enzyme; LOX, Lipoxygenase Enzyme; GI, Gastrointestinal Tract; MMP, Matrix Metalloproteinase.

Disease / Condition	Experimental Model	Compound / Extract	Dose / Concentration	Main Findings
Alzheimer's disease	*In vitro* assays, mouse models	Honokiol, Magnolol	Variable (mg/kg)	Inhibition of β-amyloid aggregation, reduction of neuroinflammation, improvement of mitochondrial function
Anxiety / CNS disorders	Rodent behavioral models	Honokiol, dihydrohonokiol	0.2–10 mg/kg	Anxiolytic- and diazepam-like effects mediated by GABA-A receptor modulation
Neuroprotection	SH-SY5Y human neuroblastoma cells	*Magnolia officinalis* extract	µg/mL range	Attenuation of glutamate-induced cytotoxicity and intracellular ROS production
Inflammation	Cell-based enzyme and signaling assays	Magnolol, Honokiol	µM range	Inhibition of COX and LOX pathways with reduced prostaglandin and leukotriene synthesis
Gastrointestinal spasm	Guinea pig isolated ileum	Ethanol extract	–	Inhibition of acetylcholine-induced smooth muscle contraction
GI motility	Mouse models	Magnolol, Honokiol	mg/kg	Improved gastric emptying and increased intestinal propulsion
Intestinal barrier injury	Zebrafish model	*Magnolia officinalis* extract	–	Reduction of inflammatory markers and preservation of tight junction integrity
Gut microbiota modulation	Zebrafish and mouse models	*Magnolia officinalis* extract	–	Increased abundance of beneficial bacteria and decreased pathogenic microbial species
Antiviral activity	*In vitro* cell systems and food matrices	*Magnolia officinalis* extract, magnolol, honokiol	1–5 mg/mL	Reduction of murine norovirus and feline calicivirus titers
Respiratory disorders	*In vitro* assays, isolated airway tissue	*Magnolia officinalis* extract	–	Antibacterial activity and bronchodilatory/spasmolytic effects
Pulmonary hypertension	Rat model	Magnolol	mg/kg	Attenuation of pulmonary vascular remodeling and right ventricular hypertrophy
Hypertension	Spontaneously hypertensive rats	Magnolol	100 mg/kg/day	Improvement of insulin-mediated vasodilation and endothelial function
Type 2 diabetes	Mouse models (HFD, db/db, KKAy)	Honokiol, *Magnolia officinalis* extract	17–200 mg/kg	Reduction of hyperglycemia and improvement of insulin sensitivity
Cancer (breast)	*In vitro* cancer cell lines	Magnolol	µM range	Inhibition of proliferation, invasion, and MMP-9–associated pathways

appear to be mediated by several signaling pathways, notably Nuclear Factor kappa-light-chain-enhancer of activated B cells (NF-κB), Extracellular Signal-Regulated Kinase (ERK), AMP-Activated Protein Kinase/ Mechanistic Target of Rapamycin/ Unc-51-Like Autophagy Activating Kinase 1(AMPK/mTOR/ULK1), and Cyclic Adenosine Monophosphate/ Protein Kinase A/ cAMP Response Element-Binding Protein (cAMP/PKA/CREB).[4] Despite these mechanistic insights, it is important to note that most of the evidence supporting these neuroprotective effects originates from animal studies or cellular assays, with a significant gap in clinical validation. Moreover, the complexity and redundancy of the implicated signaling pathways raise questions about specificity and dose-dependency under physiological conditions.

Anti-inflammatory and antioxidant activity

Honokiol and magnolol have been shown to exert their anti-inflammatory effects primarily through the inhibition of eicosanoid biosynthesis. Specifically, suppression of prostaglandins D2 and E2 (PGD2, PGE2), leukotrienes C4 and B4 (LTC4, LTB4), and thromboxane B2 (TXB2) has been observed, possibly via downregulation of phospholipase A2, cyclooxygenase (COX), 5-lipoxygenase, and related enzymes. However, these findings are based predominantly on isolated enzyme or cell models, and their relevance to systemic inflammation in humans remains unverified.[2]

Although magnolol and honokiol have been proposed as potential therapeutic agents for various diseases, including cancer, neurological disorders, and gastrointestinal (GI) conditions, their actual use in clinical practice is minimal and not evidence-based.[4-8] While both compounds can cross the Blood–Brain Barrier (BBB) and have shown neuroprotective properties in animal models, no randomized clinical trials have confirmed their efficacy in treating psychiatric or neurodegenerative diseases in humans.[9-13]

Recent studies suggest that these neolignans may influence the Phosphoinositide 3-Kinase / Protein Kinase B / Mechanistic Target of Rapamycin (PI3K/Akt/mTOR) and ERK pathways,[14,15] potentially contributing to Oligodendrocyte Precursor Cell (OPC) differentiation and remyelination processes.[16,17] However, this remains speculative, as a direct evidence of therapeutic effects on White Matter Ischemia (WMI) or remyelination in chronic cerebral ischemia is lacking.[18] Thus, while the preclinical data are mechanistically promising, the translational gap to human application is considerable and warrants caution in interpreting these findings.

Magnolol and honokiol appear to exhibit comparable pharmacokinetic properties, with both showing dose-independent, first-order kinetics and the capacity to readily cross the BBB. This characteristic has underpinned their investigation in Central Nervous System (CNS) disorders, with preclinical animal models reporting anxiolytic, diazepam-like effects, particularly for honokiol and its metabolite dihydrohonokiol.[19] However, these behavioral outcomes, while promising, lack validation in human studies and remain confined to a limited number of experimental settings. Likewise, the observed antidepressant-like effects of magnolol and honokiol, potentially mediated through modulation of serotonergic turnover in brain regions such as the frontal cortex, striatum, and nucleus accumbens, remain speculative and require further elucidation.[20]

Importantly, the increasing popularity of *Magnolia officinalis* extracts in unregulated health and wellness markets has raised concerns regarding their misuse and self-medication, particularly among vulnerable populations. A recent study identified three distinct user profiles: i) individuals with psychiatric histories using *Magnolia* spp.-derived products as a perceived "natural" alternative to benzodiazepines or as a means of managing withdrawal symptoms; ii) individuals with a history of polydrug use combining *Magnolia* spp. extracts with synthetic cannabinoids (e.g., Spice) or other Gamma-Aminobutyric Acid (GABA)ergic substances such as phenibut or Gamma-Hydroxybutyrate (GHB); and iii) naive users consuming *Magnolia* spp. products under the misconception that they are harmless dietary supplements or effective weight loss agents. These patterns of non-prescribed, unsupervised use underscore the need for rigorous toxicological and pharmacovigilance studies, as interactions with CNS-active agents may pose significant health risks.[20]

Mechanistically, honokiol has been characterized as both a GABA_A receptor modulator and a Cannabinoid Receptor 1 (CB1) agonist, two targets critically involved in mood regulation.[21] While such dual activity may suggest therapeutic potential in disorders such as anxiety, depression, and stress-related conditions, it also implies a non-selective pharmacological profile, which could result in unpredictable or adverse effects, particularly in polypharmacy contexts.[22]

Furthermore, *in vitro* data suggest honokiol may exert neuroprotective effects against glutamate-induced excitotoxicity, a key pathological process in mood and neurodegenerative disorders.[21] In SH-SY5Y human neuroblastoma cells, treatment with *Magnolia Officinalis* Extract (MOE) was shown to attenuate glutamate-induced cytotoxicity, reduce intracellular Reactive Oxygen Species (ROS) production, and preserve neuronal function. While these findings support honokiol's antioxidant and neuroprotective potential, their translational relevance remains uncertain, as such *in vitro* models only partially replicate the complex pathophysiological environment of the human CNS.[23-25] Overall, despite encouraging mechanistic data, the absence of clinical trials and the potential for misuse warrant a cautious and evidence-based approach to the promotion of *Magnolia officinalis*-derived compounds for CNS applications.

Safety and toxicity

The safety and toxicological profiles of magnolol and honokiol, either as isolated compounds or as constituents of concentrated *Magnolia officinalis* Bark Extract (MBE), have been partially characterized through preclinical studies. Both *in vitro* and *in vivo* genotoxicity assessments suggest that MBE does not exhibit mutagenic or genotoxic properties under standard testing conditions.[1] Additionally, a subchronic oral toxicity study conducted in accordance with Organisation for Economic Cooperation and Development (OECD) guidelines identified a No-Observed-Adverse-Effect Level (NOAEL) above 240 mg/kg body weight, indicating a relatively wide safety margin at moderate doses.[26]

However, while these data are reassuring, they should be interpreted with caution. Toxicological evaluations in animal models do not always predict human outcomes, especially in the context of long-term or chronic exposure. Moreover, the vast majority of available studies have focused on acute or subchronic exposure; the absence of long-term, high-quality human clinical data constitutes a critical limitation in confidently assessing the safety of MBE and its constituents.

Both magnolol and honokiol undergo extensive phase II metabolism, particularly glucuronidation, and are subject to relatively rapid systemic clearance.[27] Nonetheless, despite their relatively short half-lives, the potential for pharmacokinetic interactions remains a concern, especially given their polyphenolic nature and broad bioactivity.[28] Notably, both preclinical and anecdotal reports have suggested that honokiol and MBE may potentiate the effects of GABAergic medications, such as benzodiazepines, raising concerns about sedative synergy, enhanced CNS depression, or unexpected pharmacodynamic interactions when co-administered with psychoactive agents.[29] Furthermore, given the increasing availability of

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Magnolia officinalis-based supplements on the commercial market, often consumed without medical supervision, a lack of regulatory oversight and standardized dosing protocols poses a potential public health concern. Therefore, while current toxicological evidence does not indicate high inherent risk at moderate doses, systematic human studies are urgently needed to confirm these findings, establish safe therapeutic windows, and better understand drug–herb interactions under real-world conditions.

Gastrointestinal effects

Magnolia officinalis has long been utilized in traditional Chinese medicine for the management of GI disorders. Both magnolol and honokiol have been shown to act as non-competitive muscarinic antagonists and to inhibit smooth muscle contraction in gastric fundus and ileum preparations; in fact the experimental results indicated that magnolol and honokiol significantly inhibited the contractility of isolated gastric fundus strips of rats treated with Ach or 5-HT and isolated ileum of guinea pigs treated with Ach or CaCl2, and both of them behaved as non-competitive muscarinic antagonists.[30] Their effects appear to involve interference with both calcium-dependent and calcium-independent pathways, suggesting a potential calcium-antagonistic mechanism; additionally, *in vivo* murine models demonstrated that these compounds improved gastric emptying and increased intestinal propulsive activity, potentially implicating them in the modulation of gut motility.[30]

However, the translation of these findings to clinical efficacy remains speculative. To date, no robust clinical trials have confirmed the anti-spasmodic or pro-motility effects of *M. officinalis* extracts in human subjects. Moreover, the assumption that magnolol and honokiol are solely responsible for these activities may overlook synergistic or antagonistic effects of other minor constituents within the extract.[30]

In a further investigation, the effects of honokiol on ethanol-induced hepatic steatosis were explored, focusing on its potential mechanism involving the inhibition of Sterol Regulatory Element-binding Protein-1c (SREBP-1c) maturation.[31] The study demonstrated that honokiol could suppress the maturation and DNA binding activity of SREBP-1c to lipogenic gene promoters, resulting in decreased lipid accumulation in H4IIEC3 cells and in rats subjected to a standard Lieber-DeCarli liquid ethanol diet.[31] While these findings suggest a plausible molecular mechanism for honokiol's hepatoprotective effects, it is important to note that these results are limited to preclinical cellular and animal models. The translational relevance to human alcoholic steatosis remains uncertain, as the complexity of human liver pathology and interindividual variability in ethanol metabolism may significantly influence honokiol's efficacy.

In the GI tract, *Magnolia officinalis* and its principal constituents have been reported to modulate GI hormones, substance metabolism, intestinal barrier integrity, and gut microbiota composition. These multifaceted actions are proposed to alleviate not only local GI discomfort but also distal conditions such as depression, asthma, and metabolic disorders.[32] However, while these findings are encouraging, the mechanistic evidence is still preliminary, and definitive proof of causality and clinical relevance is lacking.

A specific study investigated the protective effects of *M. officinalis* against intestinal damage induced by *Polygala tenuifolia* Willd., a traditional Chinese medicinal plant commonly used for Alzheimer's disease but associated with notable GI side effects.[33] Using Hematoxylin-Eosin (H&E) staining, Enzyme-Linked Immunosorbent Assay (ELISA), and Transmission Electron Microscopy (TEM), the study evaluated structural damage, inflammatory markers, oxidative stress, and tight junction integrity in zebrafish intestine.[33] The findings suggested that *M. officinalis* ameliorated intestinal pathology and upregulated barrier gene expression, potentially via downregulation of pro-inflammatory cytokines Interleukin-1 beta (IL-1β), Interleukin-6 (IL-6), Tumor Necrosis Factor-alpha (TNF-α) and inhibition of the Phosphoinositide 3-Kinase/Protein Kinase B/Nuclear Factor kappa-light-chain-enhancer of activated B cells (PI3K/AKT/NF-κB) signaling pathway.[33] Nevertheless, these results are limited by the use of a zebrafish model, which, despite its utility, may not fully recapitulate mammalian or human GI physiology and disease complexity.

The purported ability of *M. officinalis* to beneficially modulate gut microbiota composition is increasingly recognized as a therapeutic avenue for intestinal injury.[34,35] In this context, *M. officinalis* was reported to increase the relative abundance of presumed beneficial microbes (e.g., *Lactobacillus* spp., *Blautia* spp., and *Saccharomyces cerevisiae*) while decreasing pathogenic bacteria (e.g., *Plesiomonas* spp. and *Aeromonas* spp.).[33] While these shifts suggest a favorable microbial modulation, the functional consequences of such changes remain to be rigorously demonstrated, and the long-term impacts on host health have yet to be elucidated.

Antiviral and antimicrobial activity

A study evaluated the antiviral potential of *Magnolia officinalis* extract and its principal constituents, honokiol and magnolol, against human norovirus surrogates, Murine Norovirus (MNV) and Feline Calicivirus (FCV), both *in vitro* and within model food systems.[36] Given that norovirus remains a major global cause of foodborne illnesses and non-bacterial gastroenteritis, the investigation addresses a relevant public health issue. Pretreatment or cotreatment with *M. officinalis* extract at 1 mg/mL led to modest reductions in MNV and FCV titers, ranging from 0.6 to 1.8 log units. Honokiol and magnolol demonstrated significant antiviral activity against these surrogates, although the exact antiviral mechanisms remain incompletely understood. Notably, virus-infected cells treated with the extract exhibited significantly elevated glutathione levels ($p < 0.05$), and the extract alongside honokiol and magnolol showed dose-dependent antioxidant effects, including ferric ion reduction and free radical scavenging of 2,2-Diphenyl-1-Picrylhydrazyl (DPPH) radicals. When tested in various food matrices, including apple, orange, and plum juices, treatment with 5 mg/mL extract reduced viral titers by >1.6 log or rendered them undetectable, while reductions of 0.9 and 1.6 log were observed in milk for MNV and FCV, respectively.[36] These findings suggest a potential role for *M. officinalis* extract as an antiviral agent in food safety applications; however, the clinical relevance and effectiveness against human norovirus remain to be validated, particularly in complex and variable food environments.

MOE has been investigated for its effects on targets relevant to airway pathologies, including antibacterial activity and pulmonary and tracheal relaxation. The extract exhibited inhibitory effects against common respiratory pathogens such as *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Streptococcus pneumoniae*. These antimicrobial actions were accompanied by spasmolytic and antispasmodic effects, hypothesized to stem from MOE's modulation of multiple receptor systems including H1 histaminergic, β2-adrenergic, muscarinic receptors, and type I calcium channels, which collectively contribute to bronchodilation.[37] Although these multifactorial effects underscore the therapeutic promise of MOE in airway disease management, these conclusions are primarily based on preclinical and *in vitro* models; rigorous clinical trials are necessary to confirm safety, efficacy, and appropriate dosing before recommending MOE as a dietary supplement for respiratory conditions.

Cardiovascular effects

Honokiol and magnolol have been reported to exert cardiovascular modulatory effects via multiple molecular mechanisms, reflecting their traditional use in Chinese medicine as agents to promote blood flow and resolve stasis. Their therapeutic potential has been explored in conditions such as atherosclerosis, thrombosis, hypertension, and cardiac hypertrophy, although the clinical evidence remains preliminary.[38]

For instance, a study demonstrated that magnolol attenuated pulmonary arterial hypertension in a rat model by suppressing the expression of endothelin-1 and angiotensin II, key mediators of vasoconstriction and vascular remodeling.[39] Additionally, magnolol mitigated right ventricular hypertrophy and pulmonary vascular remodeling induced by hemodynamic stress, while restoring the expression of proteins involved in mitochondrial function and endothelial integrity, including Sirtuin 3 (Sirt3), β-catenin, and Vascular Endothelial cadherin (VE-cadherin).[39] These findings suggest a multifaceted cardioprotective role; however, the translation of these effects to human pathophysiology remains to be rigorously evaluated.

Metabolic and antidiabetic effects

Further, Liang *et al.*[40] reported that magnolol administration (100 mg/kg/day for 3 weeks) modulated insulin-mediated aortic vasodilation in spontaneously hypertensive rats. The compound appeared to restore insulin-induced activation of protein kinase B (AKT) and endothelial nitric oxide synthase (eNOS), reduce tribbles homolog 3 (a negative regulator of insulin signaling), and increase peroxisome Proliferator-Activated Receptor Gamma (PPARγ) expression.[41] While these mechanistic insights are promising, they are largely confined to animal models, and dose translation to humans as well as long-term safety remain unaddressed. Moreover, potential off-target effects and interactions with existing cardiovascular medications require thorough investigation before clinical application.

Glycemic control remains the cornerstone for preventing diabetic complications,[42] and emerging evidence suggests that the major bioactive constituents of *Magnolia officinalis* bark, particularly honokiol and magnolol, may contribute to this effect.[43,44] *In vitro* studies have demonstrated that honokiol and magnolol enhance glucose uptake in human and murine adipocytes in a concentration-dependent manner, primarily through activation of insulin signaling pathways.[45] These findings corroborate earlier reports by Atanasov *et al.*[43] and Choi *et al.*[44] which showed that magnolol and honokiol respectively increase basal glucose uptake in 3T3-L1 preadipocyte cells.

More compellingly, *in vivo* investigations using diabetic animal models have provided preliminary support for the hypoglycemic potential of *Magnolia* spp. bark constituents. For example, Sun *et al.*[46] reported that oral administration of honokiol at 200 mg/kg daily for 8 weeks significantly reduced blood glucose levels in a type 2 diabetes mouse model induced by High-Fat Diet (HFD) combined with Streptozotocin (STZ). Similarly, another study by Sun *et al.* found that *Magnolia* spp. Extract (ME), administered at 0.5 g/kg once daily for 4 weeks, attenuated hyperglycemia in db/db mice, a well-established Type 2 Diabetes Mellitus (T2DM) model. Lower doses of honokiol (100 mg/kg daily for 5 weeks) also showed efficacy in preventing hyperglycemia in KKAy mice, a genetic model of obesity and diabetes.[47]

Interestingly, a much lower honokiol dose (17 mg/kg daily for 16 weeks) improved insulin resistance in HFD-fed mice, although it did not significantly alter fasting blood glucose or plasma insulin levels.[48] These data indicate that while higher doses of honokiol (100–200 mg/kg) exhibit clear hypoglycemic effects, lower doses may require longer treatment durations and may primarily impact insulin sensitivity rather than glucose levels per se.

The discrepancies in effective dosing observed across studies likely reflect variations in the purification and isolation methods of *Magnolia* spp. extracts, leading to differences in bioavailability of the active compounds following absorption.[42] Consequently, standardization of extract preparation and pharmacokinetic profiling are critical for translating these findings into clinical applications.

Anticancer potential

Matrix Metalloproteinases (MMPs), particularly MMP-2 and MMP-9, play important roles in tumor invasion and metastasis.[49,50] However, whether their activity drives malignancy or reflects aggressive tumor behavior remains unclear, and clinical targeting of MMPs has faced challenges due to lack of specificity and off-target effects.

Preclinical studies suggest that magnolol possesses anticancer activity, acting through inhibition of proliferation, induction of apoptosis and differentiation, suppression of angiogenesis, prevention of metastasis, and reversal of multidrug resistance. Despite these promising findings, robust clinical evidence is still lacking, and it remains to be clarified whether magnolol directly inhibits MMP-9 or modulates upstream pathways. Understanding these mechanisms will be critical for its development as a targeted anticancer agent.[51]

Precautions and limitations of use

The use of *Magnolia officinalis* and its main bioactive constituents, magnolol and honokiol, is generally considered safe for short-term administration; however, clinical evidence remains limited. Use during pregnancy and lactation is not recommended due to the lack of safety data. *Magnolia officinalis* may potentiate the effects of sedatives, anxiolytics, and anticoagulant or antiplatelet drugs, potentially increasing the risk of excessive sedation or bleeding. Reported adverse effects are usually mild and include GI discomfort and CNS symptoms, although causality is not always clearly established. While preclinical toxicological studies suggest a wide safety margin, the long-term safety in humans has not been adequately evaluated, and variability in the phytochemical composition of commercial extracts represents an additional limitation for standardized therapeutic use.[52-54]

Conclusions

This review examined the extensive pharmacological profile attributed to *Magnolia officinalis*, with particular attention to its effects on the digestive, nervous, cardiovascular, and metabolic systems. A growing body of preclinical evidence supports its antibacterial, anticancer, analgesic, anti-inflammatory, antioxidant, and anxiolytic activities, most of which are primarily associated with its two major neolignan constituents, magnolol and honokiol. However, it is important to underscore that the majority of these findings remain confined to *in vitro* experiments or animal models, and their direct translational relevance to human physiology has yet to be conclusively demonstrated. *M. officinalis* appears to modulate a range of molecular pathways implicated in oxidative stress,

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inflammation, mitochondrial dysfunction, and neurotransmitter imbalances, pathophysiological processes central to neurodegenerative and psychiatric disorders. Its ability to cross the BBB adds to its theoretical utility in CNS disorders, although this feature alone does not guarantee the therapeutic efficacy. In the GI tract, *M. officinalis* demonstrates spasmolytic activity, modulation of gut microbiota, and preservation of intestinal barrier integrity. While these findings are promising, they are largely limited to controlled laboratory settings, and the complexity of host-microbiota interactions in humans necessitates cautious interpretation. Similarly, its purported cardiovascular, antihypertensive, anti-atherosclerotic, and antithrombotic benefits, are supported by experimental models but require validation through robust human trials. The extract has also shown potential in glycemic control, particularly in animal models of type 2 diabetes, suggesting possible utility in metabolic syndrome. Regarding safety, current toxicological data suggest a favorable profile at therapeutic doses. Yet, possible interactions with pharmaceuticals, particularly GABAergic agents and drugs with narrow therapeutic indices, must be carefully considered, especially given *M. officinalis'* modulatory effects on central neurotransmission. In conclusion, *Magnolia officinalis* presents as a promising multi-target botanical agent with therapeutic potential across a spectrum of diseases. Nonetheless, the current evidence base is predominantly preclinical, and substantial gaps remain regarding clinical efficacy, long-term safety, pharmacokinetics, and optimal formulation. Rigorous, well-controlled human studies are essential to substantiate its therapeutic value and guide its integration into evidence-based medical practice.

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