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Geographical Distribution, Chemical Constituents, and Activity Profile of Magnolia

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ABSTRACT

Many Asian countries use the bark of the Magnolia for medicinal purposes. Magnolia has many medical uses, including regulating GI motility, treating cough and asthma, preventing cardiovascular disease, and treating mental illness and brain disorders. To date, 118 magnolia species have been discovered. However, the International Union for Conservation of Nature has designated 231 species as vulnerable and critically endangered. Magnolia leaves yielded 20 isolated chemicals, including 16 lignans with 6 distinct structural types, such as honokiol, veraguensin, sitosterol, and magliflonenone. Magnolia species show pharmacological activities like Neuroprotective, anti-cancer, Anti-microbial, Antiplatelets, Anti-asthmatic, Gastrointestinal, and Hormone regulation. Magnolia bark extracts such as honokiol 2',6-di-(5-propenyl)-1,1'-biphenyl-2,2'-diol, have been demonstrated to benefit health. In recent in vitro and preclinical research, honokiol was found to have anti-inflammatory, anti-angiogenic, anti-oxidative, and anti-cancer activities. Honokiol and magnolol prevented the thromboxane B2 synthesis in response to thrombin, arachidonic acid, and collagen. So, soon, if we cultivate and save the endangered magnolia species through biotechnological means, it will be a boon for mankind.

Keywords: *Magnolia*; Geographical distribution; Pharmacological; Phytochemical; Therapeutic activity.

INTRODUCTION

The *Magnoliaceae* family of flowering plants, which belongs to the Magnoliales order of flowering plants, includes evergreen and deciduous trees and shrubs. The family is crucial to evolution since it possesses several traits considered to be evolutionary primitives. The flower components are arranged in spirals rather than rings, and the distinction between sepals and petals is less evident than in other angiosperms (Poivre & Pierre, 2017). The family's distribution in the Northern Hemisphere is significantly more fragmented than during the late Cretaceous and Tertiary periods. Roughly 66 percent of all known species reside in Asia (Veltjen et al., 2022). The southern and eastern parts of this span from India and Sri Lanka through Indochina and Malaysia, China, Korea, Japan, and even the southernmost regions of New Guinea. The distributions of the remaining species span from southern Brazil through northern Mexico, Central America, the Caribbean, and the eastern United States. The genus Magnolia family *Magnoliaceae* has more than 300 plant species (Wang et al., 2020). This genus can be found in both subtropical and tropical areas of Asia and America (Ramyashree & Hemalatha, 2020). The decorative attributes, lumber, medical raw materials, cosmetic oils, and essential oils of several Magnolia species are highly prized. An assessment by the International Union for Conservation of Nature (IUCN) criteria 147 species of Magnolia were classed as threatened, critically endangered, and vulnerable due to continuous deforestation, habitat destruction, and over-harvesting. This manuscript aims to discuss the geographical distribution, chemical constituents, and activity profile of Magnolia (Song et al., 2019).

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DISTRIBUTION OF MAGNOLIA

The Liriodendron (often known as tulip tree) genus is divided into three subgenus groups within the *Magnolioideae* subfamily, including two Liriodendron species (Kinho et al., 2022). The List of *Magnoliaceae* has 280 listed species of magnolia, 125 of which are designated for exceptional preservation. 42% of magnolias are classified as critical endangers, 45% as endangered, 3% as vulnerable, 4% as near threatened, 5% as least concern, and 1 % having insufficient data availability. Different species of Magnolia were put in Figure 1.

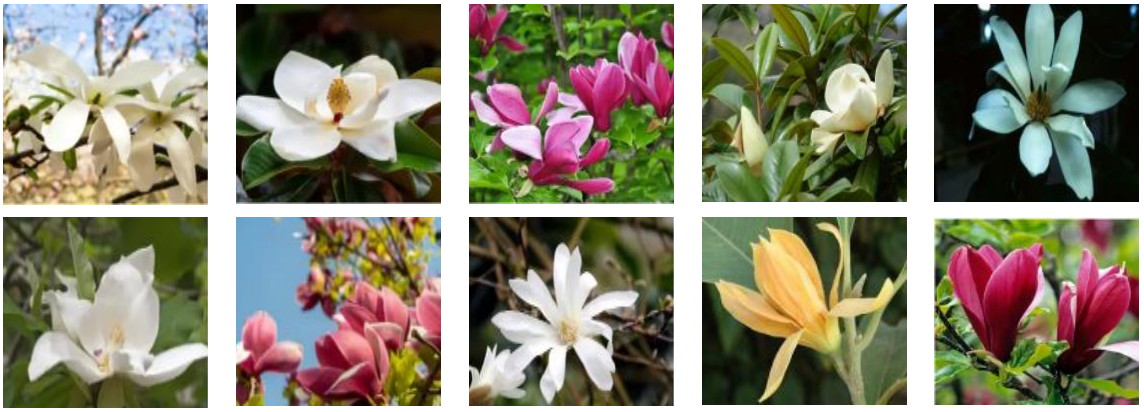

Figure 1. Different Species of Magnolia

Figure 2. Geographical distribution of Magnolia

A total of 118 magnolia species were also being researched as of this year. However, the International Union for Conservation of Nature has designated 231 species as "vulnerable" or "critically endangered." These changes are very certainly caused by new species. The Mexican Cloud Forest Trees Red List has suggested protecting a few magnolia species. More over half of the 280 species that make up the Magnoliaceae family are found in North and South America such as *M. decastroi, M. faustinomirandae, M. Jaliscana, M. lacandonica, M. lopezobradorii,* and *M. mayae* (Arora et al., 2012). Currently, magnolias may be found in both tropical and temperate regions such as India, Sri Lanka, China, Malaysia, Korea, Japan, and Papua New Guinea. From the northernmost United States to the southernmost Brazil, Mexico, Central America, and the Antilles, they encompass a sizable chunk of the American continent. The Magnolia genus exhibits allopatric speciation, in which new species develop when populations are geographically separated and subjected to selective pressure. They are frequently scarce in woody areas (Singh et al., 2015). They can be found at altitudes of 45 to 3,380 meters. 4.9% of people live at or below sea level, followed by 38.4% in the 102–1000 m, 41.0% in the 1003–2000 m, and 18.7% above 2000 m (Ong et al., 2020). At elevations between 38 and 800 meters above sea level, you can find the *M. calimaensis* of Colombia, the *M. Dixon* of Ecuador, the *M. sirindhorniae* of Thailand, and the *M. stellate* of Japan. While *M. sororum* is found between 1,000 and 2,800 meters

above sea level in Columbia, and *M. wilsonii* is located between 1,580 and 2950 meters above sea level in China. (2000 to 3300 m) (Ong et al., 2020) (Figure 2). Among many other types of plants, magnolias can be planted effectively depending on the conditions they require to flourish (Wang et al., 2022).

CHEMICAL CONSTITUENTS OF VARIOUS MAGNOLIA

Dung and his Coworkers have previously documented the chemical compositions of essential oils derived from *M. hypolampra* leaves, trunk, bark, fruit pulp, and fruit kernels cultivated in Vietnam (Wang et al., 2022). The leaf oil of *M. hypolampra* (syn. Talauma gioi) was found to contain eight different chemicals, with elemicin (59.4%), caryophyllene (18.9%), humulene (6.2%), and (E) nerolidol (5.9%) being the most prevalent. The two most pervasive substances in the trunk oil were reported to be camphor (26.8%) and caryophyllene (5.7%), along with the other nine chemicals found. The research could not distinguish many components of the trunk oil (62.4%) and leaf oil (20.4%), principally sesquiterpenes. The essential oils from the leaf or the twig employed in this investigation did not contain any elemicin, (E)-nerolidol, or camphor. Even though the levels of -caryophyllene and -humulene in leaf oil were lower than previously thought (2.9% and 0.4%, respectively), these two substances were present in leaf oil in considerable amounts. Additionally, the percentage of caryophyllene in the twig oil was substantially lower than anticipated (1.4% vs. 5%) (Zhang et al., 2020). Magnolia species include the cucumber tree-like *Magnolia acuminata*, *M. grandiflora, M. virginiana,* and *M. calophylla*. Only 9 of the 70 chemicals discovered in *M. grandiflora* leaves have ever been previously reported. A monoterpene hydrocarbon was the most frequent substance in Magnolia volatiles (84% in *M. calophylla*, 87% in *M. acuminata*, 68% in *M. virginiana*, and 45% in *M. grandiflora*). In the volatile profiles of *M. acuminata* (67%) and *M. grandiflora* (17%), the monoterpene (Z/E) ocimene predominated, while pinene did so in *M. calophylla* (64%) and M. virginiana (37%). A volatile substance known as ocimene has been linked to the floral scent of *M. kobus* and *M. grandiflora*. All Magnolia species reportedly released alpha-pinene, pinene, D-limonene, gamma-terpinene, and terpinolene in *M. kobus* and *M. grandiflora* flowers. Monoterpenoids (38%) and sesquiterpenes (25%), with germacrene A and -bisabolene accounting for up to 39% of the sesquiterpene content, made up the majority of the volatile mixture of *M. grandiflora* (Figure 3) (Hirsch et al., 2017).

ACTIVITY PROFILE OF MAGNOLIA

Anticancer activity of Magnolia

A substance found in magnolia bark extracts known as honokiol, also known as 2',6-di-(5-propenyl)-1,1'-biphenyl-2,2'-diol, has been demonstrated to benefit health. In recent in vitro and preclinical research, honokiol was found to have anti-inflammatory, anti-angiogenic, anti-oxidative, and anticancer activities (Park et al., 2011). Honokiol disrupts several signaling pathways involved in the growth and spread of cancer. These include NF-B (nuclear factor-kappa B), EGFR (Epidermal Growth Factor Receptor), and mTOR (mammalian target of Rapamycin), all of which have a role in controlling different cellular processes in mammals. (mTOR) (Mohd Nor et al., 2016). Honokiol has demonstrated promise in treating head and neck cancer, whether administered alone or in conjunction with other therapies. In vivo, research has shown the ability to stop tumor growth and improve survival in mice cancer models in several intriguing findings. With various drug administration methods, honokiol'sn pharmacological, pharmacokinetic, and pharmacodynamic properties are being investigated.

Anti-platelets Activity of Magnolia

Honokiol and magnolol prevented the thromboxane B2 synthesis in response to thrombin, arachidonic acid, and collagen. Collagen and arachidonic acid prevented intracellular calcium rise (Shih & Chou, 2012). Collagen increased intracellular calcium when indomethacin was present, but magnolol blocked this action. Obovatol antiplatelet activity may cause its antithrombotic effects (Ni et al., 2020). Obovatol's antiplatelet effects are due to its capacity to inhibit PLC (Phospholipase C) phosphorylation. Obovatol could therefore be used to treat cardiovascular diseases (Xie et al., 2020). The importance of these medications in treating various illnesses is highlighted by the fact that Magnolol (20-60) microMolar dose-dependently increased the activity and intracellular level of PPAR (Peroxisome proliferator-activated receptor)-beta/gamma in platelets. Flavonoids considerably lengthened the activated partial thromboplastin time, prothrombin time and blocked thrombin production (Zhu et al., 2022).

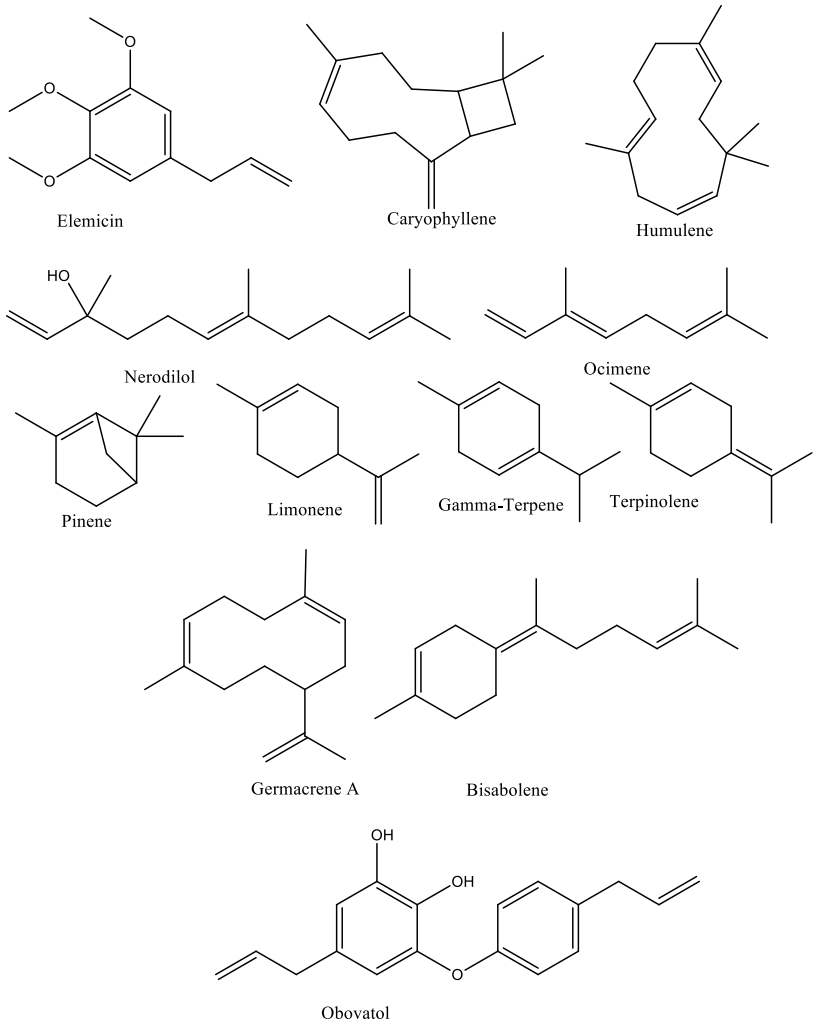

Figure 3. Chemical constituents of Magnolia

Role of Magnolia in Parkinson's Disease

Through Magnolol (MN) preventing neuroinflammatory and amyloid pathology through the inhibition of and promotion of A degrading enzymes and avoiding neuroinflammatory and synaptic dysfunction through the regulation of PI3K/Akt/GSK-3 (Glycogen synthase kinase 3) and NF-B signaling pathways, MN was able to ameliorate cognitive deficiencies (Kim et al., 2017). The ligand-binding domain of the peroxisome proliferator-activated receptor alpha may interact with Magnolia (Figure 4). A measure of anti-inflammatory cytokines, luciferase activity, was decreased by f, whereas normal levels were recovered by GW9662 (Figure 5) (Wang et al., 2021). By increasing the expression of Nrf2-ARE, MN decreased A-induced reactive oxygen species as determined by luciferase activity (Chen et al., 2018).

Role of Magnolia in Gastrointestinal Disorders

The Chinese herbal treatment *M. officinalis*, also known as magnolia officinalis Rehder and EH Wilson, is popular in Asia for problems with gastrointestinal motility. The effects of *M. officinalis* ethanol extract (MOE) were investigated on *in vivo* GI motor functions and in vitro ICC (Interstitial Cells of Cajal) pacemaker potentials (Ho et al., 2021). *Magnolia officinalis* total phenols alleviate the intestinal dysmotility induced by intraperitoneal atropine (5 mg/kg) in rats (TPM: total phenols of *Magnolia officinalis*). TPM-pretreated/atropine-treated, atropine-treated, and control rats were randomly assigned to one of

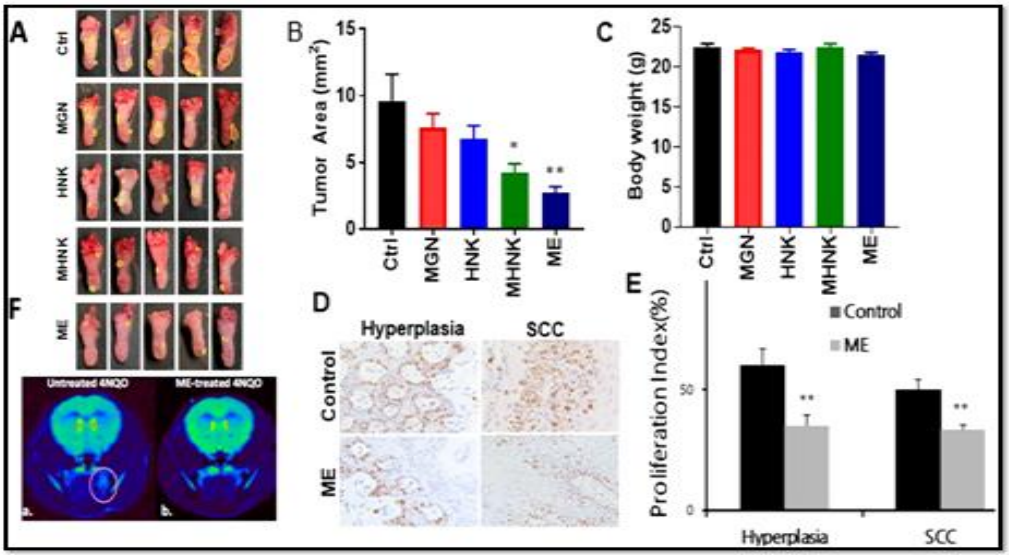

Figure 4. Inhibitory Effect of ME on 4NQO-induced oral cancer. a Representative images of 4NQO induced lesions. b Tumor area per mouse from 4NQO only (control) mice versus those treated with ME or individual agents from ME (*n* = 15). c Body weights of mice following the full duration of treatment with ME or its individual agents. d Representative IHC images for Ki-67. e Quantitation of Ki-67 from IHC analysis of animals. f Representative colorized T2w MRI scans of 4NQO mice (a) without and (b) with ME treatment. The lesion in the untreated mouse is encircled. *$P < 0.05$; **$P < 0.01$ (Hirsch et al., 2017)

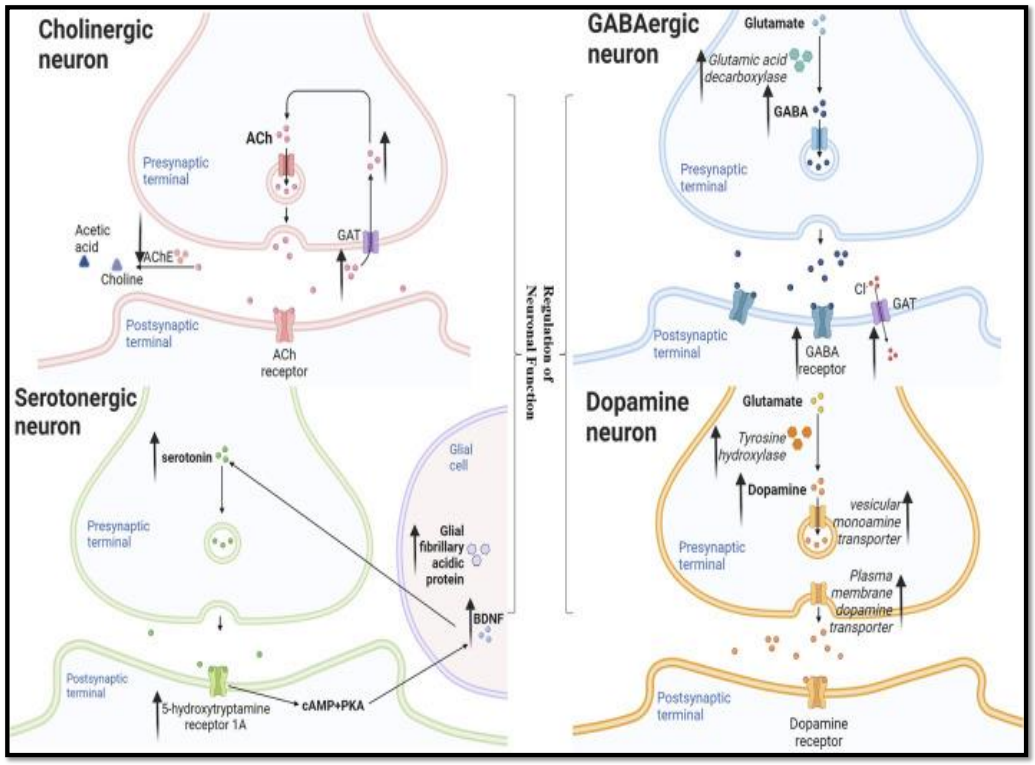

Figure 5. Neolignans' mechanisms for regulating neural activity. (Zhu et al., 2022)

days of TPM treatment were given. Atropine reduces interstitial cells of Cajal numbers in the stomach's sinuses, ventriculi, and the stomach's body, while TPM enhances this effect. This was measured with the concentrations of other gastrointestinal hormones 20 minutes after the injection of atropine, including gastrin (GAS), motilin (MTL), and somatostatin (SS). Western blotting showed that c-kit and SCF expressions were reduced after atropine injection but recovered after pretreatment with TPM. These results suggest that the protective advantages of TPM medication against atropine-induced stomach dysmotility may be attributable to the modulation of the c-kit/SCF signaling pathway (Hu et al., 2011). An ethanol extract of *Magnolia officinalis* contains components that have been preliminary identified chemically. At 30 mg/kg, MOE protects against ethanol-induced acute stomach damage lasting up to 120 mg/kg. As demonstrated, MOE also lowers oxidative stress and blocks the inflammatory NF-B signaling pathway (Bekhit et al., 2021).

Antimicrobial Activity of Magnolia

An investigation by (Chacón-Hernández et al., 2020) Honokiol and magnolol, two of the leading chemical constituents of Magnolia officinalis, were examined for their antibacterial potency. A two-fold serial dilution experiment was used to establish each chemical's minimum inhibitory concentration (MIC) for assessing antibacterial activity in the brain heart infusion medium. The results showed that honokiol and magnolol have a marked antimicrobial effect (MIC = 25 microgram/mL) against *Actinobacillus actinomycetemcomitans*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Micrococcus luteus*, and *Bacillus subtilis*. Still, they did not show antimicrobial activity (MIC > or = 100 microgram/mL) for *Shigella flexneii*, *Staphylococcus epidermidis, Enterobacter aerogenes, Proteus vulgaris, Escherichia coli*, and *Pseudomonas aeruginosa*. Results showed that honokiol and magnolol, albeit to a lower extent than tetracycline, exert powerful antibacterial effects against periodontal disorders. For this reason, we advocate using honokiol and magnolol as a supplement to periodontitis treatment. Maria del Rosario and associates investigated the phytopathogen *Clavibacter michiganensis* subspecies michiganensis and a wide range of human multi-drug-resistant illnesses to see if an ethanol extract of *Magnolia dealbata* seeds and its active components honokiol (HK) and magnolol have antibacterial properties. To ascertain whether *Magnolia dealbata* extract (MDE) and its associates had any impact on the viability of human peripheral blood mononuclear cells, the MTT test was performed. MDE and its active components (inhibition zone > 10 mm) inhibited the development of a wide range of bacteria and yeasts, including *Candida michiganensis, Pseudomonas aeruginosa, Acinetobacter baumannii, Acinetobacter lwoffii, Candida albicans, Candida tropicalis,* and *Trichosporon beigelii*. Only a negligible amount of MOE inhibited *S. typhimurium*. Total volatile base nitrogen levels, thiobarbituric acid reactive material, and Enterobacteriaceae and Pseudomonas growth were all reduced in the treated lamb. The cold mutton treated with 4% MOE had the most enticing appearance, exquisite flavor, and overall appeal studies. The extract inhibited the growth of each of the five different phytopathogenic bacteria types that were examined. There was a growth suppression of 8.22 to 100% (Reyes-Zepeda et al., 2022). The ethanolic extract of *M. tamaulipana* should be further studied as a new control agent due to its antibacterial properties.

Anti-asthamatic Activity of Magnolia

In recent decades, bronchial asthma has become more common and severe, posing serious global public health challenges. Numerous conventional and alternative treatments can be used to treat asthma (Arredondo-Valdés et al., 2021). There are several herbal medications available, each claiming to be a superior asthma cure. The majority of scientists now conquer that plant cells serve as the factories that create all the various compounds (Azlan et al., 2022). MOE reduced the ROS production and reduces mitochondrial respiration in oral cancer cells, inhibiting STAT3 Signal transducer and activator of transcription 3) expression, activating AMPK (5' AMP-activated protein kinase), and promoting Prx (Peroxiredoxin) oxidation. Using low-temperature EPR, we validated the effects of ROS-mediated oxidative stress, increased ROS, and complex I inhibition in orthotopic oral malignancies in mice (Simon et al., 2022) (Figure 6). To effectively prevent and treat asthma, it is necessary to develop polyherbal formulations that include multiple herbs, each of which targets a different aspect of the disease's pathophysiological cascade (Cui et al., 2021).

Role of Magnolia in Hormone Regulation

Women with menopausal symptoms and mild to severe mood and sleep disorders who do not require psychopharmacological treatment may benefit from combining isoflavones with lactobacilli (Mali & Dhake, 2011). It has been

Table I. Pharmacological Activity Profile of Magnolia

SN	Pharmacological Activity	Species/Chemical Constituents of Magnolia
1.	Anticancer Activity	Honokiol
2.	Anti Platelet Activity	Honokiol, Magnolol, Obovatol
3.	Anti Parkinson's Activity	Magnolol
4.	Effective in Gastrointestinal Disorder	*Magnolia officinalis*
5.	Antimicrobial Activities against *Actinobacillus actinmycetemcomitans*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Micrococcus luteus*, and *Bacillus subtilis*	Honokiol, Magnolol, and *Magnolia dealbata*
6.	Anti Asthmatic Activity	Ethanolic extract of *Magnolia officinalis*.
7.	Hormonal Regulation and Anti Sleep Disorder Activity.	Honokiol, and Magnolol.

demonstrated that isoflavones reduce symptoms of normal menopause. Anxiety, irritability, and insomnia were among the psycho-affective symptoms that magnolia bark extract was clinically found to affect (Huang et al., 2019). Lignan can potentially treat various endocrine conditions connected to insulin dysregulation, such as polycystic ovary syndrome.

DISCUSSION

Magnolias are a beautiful family of trees and shrubs offering practical elements like timber, medicines, and scented oils. Thus, botanic gardens often feature a lot of them. Even though there has been a recent trend toward exclusively presenting the most visually stunning cultivars, more and more collections are realizing their potential as endangered species. *Magnolia salicifolia* demonstrated substantial anti-allergic effects per the passive cutaneous anaphylaxis (PCA) test (Szałabska-Rąpała et al., 2021). The significant elements of dried flower buds from *Magnolia salicifolia* were examined for their anti-inflammatory effects in mice using the pouch granuloma method. Neolignans (magnoshinin and magnolia), but not alkaloids, fatty acids, essential oils, or lignans, significantly reduced the development of granuloma tissue (Dũng et al., 1997). When taken orally, magnoshinin exhibited a significant inhibitory effect that was virtually as strong as taking half as much hydrocortisone acetate. To treat various diseases, many researchers investigated the pharmacological effects of bioactive ingredients of *Magnolia macrophylla*, such as magnolol, honokiol, 4-O-methyl honokiol, and obovate (Wei et al., 2023). The most enormous simple leaves and blooms of any tree in the area are seen on bigleaf magnolias, which are endemic to North America. It is a rare native deciduous pyramidal tree with one stem that can grow to 30 to 40 feet before developing a rounded, spreading crown. In the tropics, it might be a semi-evergreen plant. The massive oblong-obovate leaves of Ashe magnolia can grow up to 3 feet long and 1 foot wide. Some believe this tree is a subspecies of the bigleaf magnolia because of its vast, up to two feet long leaves (Han & Long, 2010). Chemical compositions of essential oils derived from *M. hypolampra* leaves, trunk, bark, fruit pulp, and fruit kernels cultivated in Vietnam. The leaf oil of *M. hypolampra* (syn. Talauma gioi) was found to contain eight different chemicals, with elemicin (59.4%), caryophyllene (18.9%), humulene (6.2%), and (E) nerolidol (5.9%) being the most prevalent (Wang et al., 2016). The two most pervasive substances in the trunk oil were reported to be camphor (26.8%) and caryophyllene (5.7%), along with the other nine chemicals found. Magnolia species show pharmacological activities like neuroprotective (Liu et al., 2015), anti-cancer, antimicrobial, anti-platelets, anti-asthmatic, gastrointestinal disorders, and hormonal regulation. Magnolia bark extracts known as honokiol, also known as 2',6-di-(5-propenyl)-1,1'-biphenyl-2,2'-diol, have been demonstrated to benefit health. In recent in vitro and preclinical research, honokiol was found to have anti-inflammatory, anti-angiogenic, anti-oxidative, and anti-cancer activities (Bhatt et al., 2023). Honokiol and magnolol prevented the thromboxane B2 synthesis in response to thrombin, arachidonic acid, and collagen (Table I).

CONCLUSION

Finally, we concluded that various species of Magnolia's are critically endangered but the activity of species showed a greater spectrum such as anticancer, antimicrobial, anti-Parkinson, hormonal regulator, and effective against various gastrointestinal disorders. So, if we cultivate and save the endangered Magnolia species through biotechnological processes such as tissue culture, and callus formation along with the use of modern generation cultivation process then it will be a boon for mankind.

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CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors have no conflicts of interest, financial or otherwise.

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